Witness Name: Professor Geoffrey Dusheiko
Statement No.: WITN3754005
Exhibits: WITN3752006-019
Dated:23 January 2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF GEOFFREY DUSHEIKO

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 26 November 2019.

I, Geoffrey Dusheiko, will say as follows: -

Section 1: Introduction

1. My name, address, date of birth and professional qualifications are as follows: Geoffrey Mark Dusheiko, Liver Unit, Kings College Hospital London UK. GRO-C 1948 MB BCh (Wits) FCP(SA) FRCP FRCP (Edin).

2. The positions I have held as a doctor, the organisations in which I have held these positions and my role and responsibilities in these positions are as follows:

- Intern, Medicine Baragwanath Hospital, Johannesburg, 2 January 1973 to June 1973
- Intern, Surgery Baragwanath Hospital, Johannesburg, July 1973 to December 1973
- Locum Tenens positions January 1974 to July 1974: Paediatric Ward Northwick Park Hospital, Middlesex, U.K; Dr H.B. Valman, General Practice, Johannesburg; A.E.C.I, Modderfontein
- Sen. Intern Paediatrics, Johannesburg Childrens Hospital, July to December, 1974
- Sen. Intern Cardiology , Johannesburg Hospital, January to June, 1975

- Registrar Medicine (Respiratory, Endocrine, Neurology, Coronary intensive care units, Haematology, General medicine), Johannesburg Hospital, July 1975 to July 1978
- Research Fellow, Liver Unit, Johannesburg Hospital, July 1978 to July 1979
- Visiting research associate, Liver Unit (South African Medical Research Council Fellow), Liver Diseases Section, National Institutes of Health Washington DC USA, August 1979 to July 1981
- Senior Physician (Consultant), Hillbrow and Johannesburg Hospital, August 1981 to December 1983
- Unit Head (Consultant and Ward Head), Hillbrow and Johannesburg Hospital, January 1984 to December 1987
- Guest Researcher (Vice Chancellor's Research Award), Dept of Microbiology, University of Minnesota USA, September 1986 to March 1987
- Senior Lecturer, Academic Dept Medicine, Royal Free Hospital School of Medicine, January 1988
- Reader in Medicine, Royal Free Hospital School of Medicine, 1989
- Professor of Medicine, Royal Free Hospital and University College School of Medicine 1996
- Emeritus Professor of Medicine, University College London Medical School, January 2014
- Consultant Hepatologist, Royal Free Hospital London, 2014-2016
- Consultant Hepatologist, Liver Unit, Kings College Hospital London UK, 2016-to date
- Interim Deputy Director, Blood safety, Hepatitis HIV and STI National Infection Service, Public Health England, March 2019 to December 2019

3. I have served on NICE panels, National Institutes of Health USA hepatitis consensus panels, EASL guidelines committees, World Health Organisation advisory boards, the Skipton Fund, NHS EIBSS and have advised Thalassemia and Haemophilia Societies in the past.

Section 2: Responses to criticism of W0017

4. Thank you for the opportunity to respond to W0017. I note the date of the witness statement, 20 December 2018. I have reviewed the clinical notes.

At paragraphs 10, 12 and 28 of her statement, witness W0017 states that in November 1995 she began treatment with the drug Interferon as part of a trial. She recalls that

she was informed that an American company had been funding the trial but had withdrawn the funding because the results were not conclusive.

5. W0017 kindly consented to participate in a trial of pegylated interferon (PEG Roferon Study NV14704) WITN3754010. First generation formulations of pegylated interferon were being developed and being evaluated at this time: Polyethylene glycol (PEG) added to interferon increased the half-life of interferon in the body and thus could reduce the frequency of injections. These research endeavours attempted to achieve more stable and efficacious antiviral activity. W0017 had expressed a written interest in being treated with interferon and consented to participate in a trial of a first generation pegylated interferon WITN3754008. She was randomized to begin therapy with Roferon A in November 1994 WITN3754011. The notes indicate that the study was explained and discussed in detail WITN3754007, WITN3754010.

6. The common and less common side effects would have been listed WITN3754007, WITN3754010, WITN3754019. Unfortunately, W0017 developed a transient thyroiditis and subsequent hypothyroidism in April 1995 secondary to interferon alpha WITN3754013, WITN3754014, WITN3754015. She was found to have anti-thyroid microsomal antibodies in March 1995, which increases the risk of thyroid disease in patients WITN3754013. Thyroid hormone replacement rapidly corrected her hypothyroidism and she continued Roferon 3 mu three times weekly for four months WITN3754014, WITN3754016. She subsequently stopped Roferon, to ascertain recovery. After stopping treatment, she relapsed. Her serum alanine aminotransferase rose from 28 IU/ml to 289 IU/ml WITN3754015.

7. I wrote that we could consider interferon and ribavirin WITN3754015. However she subsequently restarted treatment with viraferon 3 mu three times weekly in November 1995 WITN3754016, WITN37540018. Again, her tolerance of interferon treatment was poor and the viraferon was changed to Roferon in January 1996 in the hope that the latter would cause less side effects WITN37540017. However, because of side effects and intolerance, interferon treatment was stopped in June 1996.

8. Fortunately, she cleared hepatitis C in 1996; her HCV RNA became undetectable, and her serum aminotransferases normalised. These have remained normal since the cure of her hepatitis C 24 years ago. The patient has remained free of HCV to this day.

9. The trial was stopped by the Sponsor, Hoffman La Roche. The patient received a personal letter from us dated 10 March 1995 WITN3754012.

10. We wrote *"the drug company conducting the pegylated interferon study, Roche have now had chance to perform some interim analysis on the data collated from the trial. They have now collected data from all of the centres involved. The analyses show that patients who received pegylated interferon either once or twice a week did not gain as much benefit from interferon therapy as those who received the standard therapy of Roferon A at a dose of 3 mU 3 times a week. As far as we know, patients who received the pegylated interferon 3 times a week have received equivalent benefit to those on the standard therapy. In view of the fact that no clear benefit has*

been found in taking the pegylated interferon, the drug company do not think that it is commercially viable and have asked us to discontinue the trial. The last date on which they say that patients can have pegylated interferon is the end of March.

11. *Clearly we wish to provide all our patients with optimal therapy and we are trying to make arrangements for patients who have received pegylated interferon once or twice weekly to undergo a trial of interferon therapy which would be the standard formulation given 3 times a week. The course would be given outside of the drug trial as a standard NHS patient..... Clearly each patient must be managed individually, and we can discuss the matter when we next see you all please do not hesitate to contact me at the hospital... So that we can discuss further management."*

12. We thanked the patient for her participation in the trial; indeed, it is only through the efforts and contributions of patients that we have reached the remarkable advances in hepatitis C treatments that exist to date.

13. The trial was thus stopped for insufficient efficacy, which is not infrequently a logical stepwise process in the development of new drugs. Numerous chemical improvements were subsequently engineered to improve the chemical bonding and number of polyethylene glycol moieties bound to recombinant interferon. These formulations improved the efficacy of pegylated alpha 2a or 2b interferon.

At paragraphs 13 and 27 of her statement, witness W0017 states that in March 1995 she was informed that she had developed an underactive thyroid as a result of Interferon treatment. Witness W0017 goes on to comment that she was not given sufficient information about the possible side effects of Interferon or Ribavirin and that in particular she was not told how the drugs might affect her thyroid. She notes that the information available about the potential effect of these drugs on the thyroid changed over the course of her treatment.

14. Unfortunately, as noted above W0017 developed hypothyroidism in April 1995 secondary to interferon alpha during treatment; we were aware that hypothyroidism is a known side effect of interferon and her thyroid biochemistry was thus regularly checked. Her thyroid antibodies were checked to evaluate the risk. She was found to have anti-thyroid microsomal antibodies WITN3754013, WITN3754014, WITN3754015.

15. I regret that W0017 developed permanent hypothyroidism, which by 1995 was a well-documented if relatively uncommon side effect of interferon alpha treatment. Fortunately, the biochemical hypothyroidism can be corrected, and was.

16. W0017 had frequent pre-treatment and on treatment visits and was seen by me, an experienced hepatitis research nurse, and the hepatitis research fellows at which interferon treatment would have been extensively explained and discussed.

17. As we gained more experience with interferon, I made a point of cautioning patients that some side effects of interferon, including autoimmune thyroid disease, might be irreversible and would require long term treatment.

18. W0017's visits are documented in the notes. Her letter of 7 October 1994 indicated *"I have thought long and hard about all this for the last few days and depending upon the results of the last lot of blood tests I had on 29 September 1994 if I am still eligible I would like to be included and try the interferon injections".* The letter also indicates *"I would just be interested to see the results of my latest lot of blood tests as you were repeating some sort of thyroid gland test etc if I were to have the interferon injections."* WITN5754008

19. A handwritten letter from W0017 documents the understanding of the travails of interferon treatment but also states: *"I say exactly the same to you Dr Dusheiko I can't thank you enough all you (for) and your colleagues have done. I have had excellent treatment. I have not been pushed into doing anything, I had everything explained to me thoroughly before I've made my decisions. I can't fault the treatment I've had. I'm so grateful…".* WITN5754006

20. Our research nurse wrote to W0017 on 11 October 1994 *"I am sorry for the delay in writing. I gather that Dr Dusheiko has discussed the possibility of participating in one of our interferon studies and I wondered whether it would be possible for us to have a chat regarding the treatment. Perhaps I could see you on Tuesday 25th October at 11 am when we could discuss any worries that you may have regarding treatment".* WITN5754009

21. I wrote to W0017's general practitioner on 6 October 1994: *"I saw < > again on 29 September 1994. On 28 July 1994 the ALT was abnormal at 61 ….. She may be a candidate for the pegylated interferon study. I have tested markers again and spend some time talking to her about the trial. She naturally has some concerns about how the side-effects might affect her day to day life".* WITN5754007

At paragraph 14 of her statement, witness W0017 states that she was not informed that from September 1996 she would be treated with Ribavirin in addition to Interferon, and only later became aware from reading her prescription.

22. The patient was treated with Roferon A in a study WITN3754010, WITN3754011. Her notes state that was followed with Roferon, Viraferon and a switch back to Roferon. Although according to the correspondence ribavirin was considered WITN3754015, which would have been a reasonable course of action after a lack of response to interferon, I do not see any prescription for ribavirin in her notes.

At paragraph 19 of her statement, witness W0017 states that after being informed by the Royal Free Hospital that she was clear of HCV, she was later told that she could not donate blood due to the ongoing risk of infection. Witness W0017 comments that she felt misled about being cured. Please comment on this.

23. W0017, and her referring physicians, were advised based on successive laboratory reports that she had successfully cleared the virus on interferon, had undetectable HCV RNA by polymerase chain reaction, and therefore had a sustained virological

response. I believe that the fact that she was told she could not donate blood is a question that W0017 should direct to the Blood Transfusion Service.

Section 3: Other Issues

W0017 wrote numerous letters to me and others which are filed in the notes. Good levels of communication were maintained.

Statement of Truth

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

Signed: GRO-C

Dated: 23 January 2020

Table of exhibits:

Date	Notes/ Description	Exhibit number
4 March 1996	Letter from W0017 to Professor Dusheiko	006
6 October 1994	Letter from Professor Dusheiko to W0017's general practitioner	007
7 October 1994	Letter from W0017 to Professor Dusheiko	008
11 October 1994	Letter from research nurse to W0017	009
22 November 1994	Consent form for pegylated interferon study	010
22 November 1994	Prescription sheet for Roferon	011
10 March 1995	Letter re cessation of PEG Rofereon study	012
28 March 1995	Thyroid endocrinology report	013
March-July 1995	Clinical notes for W0017	014
11 May 1995	Letter from Professor Dusheiko to W0017's general practitioner	015

11 December 1995	Letter from Professor Dusheiko to W0017's general practitioner	016
29 January 1996	Letter from Professor Dusheiko re W0017	017
19 February 1996	Prescription sheet for Viraferon	018
1997	Side effects of alpha interferon in chronic hepatitis C	019