Witness Name: Charles Hay
Statement No.: WITN3289030
Exhibits: WITN3289031-033
Dated:09/09/20

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF PROFESSOR CHARLES HAY

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 26 May 2020.

I, Charles RM Hay, will say as follows: -

Section 1: Introduction

Professor Charles Richard Morris Hay MBChB MD FRCP FRCPath
Consultant Haematologist Manchester Royal Infirmary ('MRI') since December 1994.
Director Manchester Adults Haemophilia Comprehensive Care Centre since December 1994
Senior Lecturer in Haematology Liverpool University and Director Liverpool Haemophilia Centre, Royal Liverpool Hospital 1987-1994.
Professor of Haemostasis and Thrombosis.

Director UK National Haemophilia Database since 2002.
Member UK Haemophilia Centre Doctors Organisation (UKHCDO) Regional Committee and then Advisory Committee since 2007 (when the name of the committee changed).
Vice Chairman UKHCDO 1997 - 2005.
Chairman UKHCDO 2005-11.
My full Curriculum Vitae has already been provided to the Inquiry

Clinical Review

1 Mrs Ronan had been managed by Manchester Royal Infirmary since 1957. Originally, she would have been under the care of Dr Israels and Dr Irvine Dellamore and then Dr Richard Wensley. In 1991 to 1994 she would have been under the care of Dr Guy Lucas. I was Mrs Ronan's Haematologist between December 1994 until 2003, when Dr Paula Bolton-Maggs joined us as Consultant Haematologist and assumed her care. When Dr Paula Bolton Maggs retired, Mrs Ronan's care was assumed by Dr Bolton-Maggs successor, Dr Jecko Thachil. Dr Thachil was Mrs Ronan's consultant Haematologist at the time of her final illness and death in January 2014.

2 In 1994, when I took up post at MRI, I was single handed, but as we acquired more consultants specialising in Thrombosis and Haemostasis, first in 1999 and then in 2003, the patients were divided up and reallocated amongst at first two and then three consultants. Unit policy, for example around management of liver disease, was reached by consensus amongst the consultants in Thrombosis and Haemostasis and, until about 2010, the Thrombosis and Haemostasis Consultants did all of their ward rounds together. In this way, all of us knew all of our regular patients and were able to pick up their management on call and able to comment on their management. By 2013, the Wednesday ward round was the only ward round attended by all the consultants together, the other ward rounds being conducted by the consultant on-call for that day.

3 I remember Mrs Ronan well. She was a very pleasant and good humoured lady and it was always a pleasure to see her. She suffered recurrent gastrointestinal bleeding for which she often had to be admitted to hospital. She was consequently also joint-managed by a series of consultant Gastroenterologists over the years.

4 I have prepared this response with the assistance of Mrs Ronan's medical records. These run to three volumes and are complete, as far as I can determine, containing records going back to 1957. I produce correspondence from those medical records to which I have referred in the course of preparing this statement as WITN3289031 Exhibit 1 (paginated).

5 Mrs Ronan had, type 3 von Willebrand's disease. This is the severest form of von Willebrand's disease, and is rare. It is inherited as an autosomal recessive condition. That is to say that it is inherited from both parents, both of whom are carriers and who are usually asymptomatic. The bleeding pattern associated with type 3 von Willebrand's disease is very variable from one family to another, some patients bleeding very regularly into their joints leading to arthritis, and others not.

6 Mrs Ronan had arthritic ankles secondary to bleeding into those joints. Most such patients bruise easily, have heavy periods if female, and suffer from nosebleeds. It is common, as with Mrs Ronan, for such patients to develop angiodysplasia (abnormal small blood vessel formation) of the gut in middle-age. These abnormal blood vessels in the bowels may bleed quite seriously from time to time. At one time or another she also bled from gastric erosions. Recurrent and sometimes serious gastrointestinal bleeding were a problem throughout her adult life and for most of that time she was co-managed by gastroenterology, first by Dr Makin and subsequently by Dr Simon Campbell. These recurrent bleeds led to her having an unusually extensive transfusion history of red cells and platelets as well as von Willebrand concentrate, to control each of these episodes of GI haemorrhage.

7 One of my first actions on becoming MRI Centre Director in 1994 was to change all my patients with severe von Willebrand;'s disease from 8Y factor VIII concentrate to Haemate P factor VIII concentrate. I made this change because Haemate P has much better preservation of high molecular weight von Willibrand multimers than 8Y. That is to say, that the von Willebrand molecules are far more completely preserved in Haemate P than 8Y and therefore it corrects von Willebrand's disease far better and more reliably than 8Y. Although we did not know this at the time, this change also reduced the risk of exposure to variant Jacob Kreutzfeld disease ('vCJD'), since 8Y was a concentrate manufactured from UK plasma and Haemate P was manufactured from American and European plasma, which is thought to be free from the vCJD prion risk.

8 Mrs Ronan was reviewed regularly in outpatients. She almost invariably attended alone. Her liver function tests were monitored regularly from the 1980s and she was aware that these tests were abnormal during that time. Prior to the advent of HCV-testing in 1982, persistent abnormalities of liver function in such a patient, in the absence of markers for chronic hepatitis A or B would have been taken as probable evidence on Non-A, Non-B hepatitis, now known to be caused by hepatitis C. I assume that this would have been discussed with her by my predecessors because she was aware of it when tested for HCV.

9 She was first tested for hepatitis C on 29/7/1993 by my predecessor, Dr G Lucas - WITN3289031 page 1. I doubt that she was specifically consented for this test since it was not the practice then or now for specific consent for such a test to be sought either by haematologists or hepatologists. There would have been a presumption that this test

would have been positive, given her treatment history and history of chronic elevated transaminases. It would be regarded as just part of the investigation of chronic liver disease that was already under surveillance.

10 The result of this test appears to have been initially overlooked and was not mentioned in the letter following her December 1993 review, but is mentioned in the clinic letter of 25/5/1994, WITN3289031 page 2, in which Dr Lucas wrote:

"I told her that there was serological evidence of past infection by hepatitis C. (This is as a result of previous exposure to the virus as a result of treatment before 1985 with "non-heat treated" factor VIII). She knows that her liver function tests are borderline abnormal, suggesting chronic infection, although she has no symptoms attributable to this. She was understandably concerned to hear this, but appreciates no treatment is currently indicated and that we propose to monitor her liver function tests every 6 months."

11 Dr Monica Bolton, the Haemophilia Centre Clinical Assistant, also wrote to the GP informing him of this on 8/6/1994.WITN3289031 pages 3-4.

12 I assumed care of Mrs Ronan in December 1994 upon taking up post as Consultant Haematologist at Manchester Royal Infirmary.

13 We continued to monitor her liver disease. There was thankfully never any evidence of progressive liver disease and so never any suspicion of cirrhosis. I discussed this with her at length in January 1996, when I wrote:

"She has chronic hepatitis C with consistently mildly abnormal transaminases. This has been causing her a great deal of worry in recent months, partly because of this issue in the media. I feel sure that she is a candidate for interferon treatment which we have discussed at length today and she is keen to try this. I will review her in three months with a view to starting it. In the meantime, we will ask her health authority for permission to pay since we do not have a separate budget for interferon." WITN3289031 page 5.

14 I reviewed her in April 1996 and again warned her of treatment side-effects and started her on Interferon 3 mega-units three times a week. WITN3289031 page 6. The commonest side effects, which I would have described to her included general malaise, flu-like symptoms, general tetchiness, fatigue, loss of appetite, potential weight loss and clinical depression which could be severe. The rationale for treatment was that we knew

that patients responded better when they did not have cirrhosis and since there was a risk that, if left untreated, her liver disease could eventually progress to cirrhosis and even hepatocellular carcinoma and liver failure, it was preferable to eliminate the virus as early as possible. This was a standard therapeutic approach to chronic hepatitis C

15 She tolerated this treatment reasonably well and her LFTS improved but she remained HCV antigen positive. The dose was doubled after six months but this did not work either and so treatment was discontinued after 9 months,

16 On the 3rd of February 1999 we reviewed the situation again and discussed the possibility of treatment with Interferon and Ribivarin. I again discussed the side effects with her. These are similar to her previous regime except that they were more severe and also included anaemia and cytopaenias (reduced white cell and platelet counts). She was quite receptive to this and we agreed she should give it further consideration, since it was not clinically urgent. WITN3289031 pages 9-10.

17 In November 1999 she was reviewed by Dr M Bolton, who suggested she moderate her alcohol intake and who noted that Mrs Ronan was not keen to have further treatment for HCV at that time. WITN3289031 page 11. This was discussed further when she was in hospital having her ankle arthrodesed (fixed by cleaning up the joint and screwing it together). By that stage Pegylated interferon was available, with a much better response rate than previous formulations of interferon. We also had HCV genotyping available which showed that she had HCV genotype 1b, a genotype relatively resistant to treatment with a remission rate following treatment with Peginterferon and Ribivarin of only 40%.

18 On the 25th of April 2001 treatment with Peginterferon and Ribivarin commenced. WITN3289031 page 13. This combination is recognised to have wider ranging and more severe side-effects than interferon alone and, indeed, she suffered neutropaenia (low white cell count) necessitating dose-reductions and was unable to tolerate the treatment side-effects, asking to stop treatment in early October 2001. She had failed to respond to the treatment in any case. She had a severe GI bleed during treatment, which she attributed to the HCV treatment, but which was probably unrelated.

19 Dr Paula Bolton-Maggs assumed her care in mid-2003 on taking up her post as Consultant Haematologist specialising in Thrombosis and Haemostasis.

20 On 18/9/2004, Dr Paula Bolton-Maggs and I wrote to Mrs Ronan about vCJD WITN3289031 pages 17-19. This was a standard letter sent to all patients with bleeding disorders at the behest of the Department of Health, as is made clear in the second paragraph. The text, which the medical community regarded as confusing and not at all "patient friendly" was dictated by the DoH and the letter had to be sent out in a hurry in advance of a Parliamentary Question, so that the patients would be informed by us before they read about the matter in the media. If we as a team were able to draft and send letters to the patient, we would have worded them and ensured that this really difficult information was conveyed in a sensitive and patient friendly manner.

21 At her next haematology consultation with Dr Bolton-Maggs on 9 of May 2005, Mrs Ronan's husband also attended. HCV transmission was discussed and her husband was tested for this. Variant CJD was also discussed and her previous use of UK-sourced clotting factor concentrates. She was offered the relative reassurance that after 20 years no bleeding disorder patients had developed vCJD. WITN3289031 page 27. Furthermore, a lookback exercise had been conducted and this showed that, as far as could be determined, she had not been treated with an "implicated batch". An implicated batch is a batch of concentrate which included a donation from a donor who, after donating blood, went on to develop variant Jacob Kreutzfeld disease. This was also discussed with her. WITN3289032.

22 In February 2009, we again wrote to Mrs Ronan about a patient who had died from an unrelated cause but who had been found to have prion protein consistent with vCJD in their spleen at autopsy- WITN3289031 page 28.

23 Dr Jecko Thachil, Consultant Haematologist, assumed care of Mrs Ronan's in March 2012 when Dr Bolton-Maggs retired and he replaced her as Consultant Haematologist.

24 I understand from Mr Ronan's statement that some time in 2013 Mrs Ronan fainted in the car park after attending the hospital. I have no knowledge or memory of this incident. She was Dr Thachil's patient at this time.

25 On 31/12/13, Mrs Ronan attended the Haemophilia Centre, complaining of tiredness. She was seen by the Haemophilia Registrar, Dr Said. I was on duty on that day according to my diary and Dr Said may have phoned me, but there is no record of that

happening and I do not remember being phoned. Her blood count was checked and she was found to be anaemic with an Hb of about 80g/l. She was sent home by the registrar and not by me.

26 On 6/1/14, Mrs Ronan presented to the Haemophilia Centre at MRI at 12.00. (I was in the Antenatal clinic at that time and not on-call). I produce the clinical notes for Mrs Ronan's admission as WITN3289033 (paginated). I think her usual Consultant, Dr Jecko Thachil was on leave that week. She was initially seen by the Haemophilia Centre Registrar (Dr Said) who consulted with the Haemostasis Consultant on call (Dr Mike Nash). She and her husband gave a history of decreased mobility requiring the help of two people to get about. She had been fully independent until 2 weeks before. She also gave a 6-week history of ear infection and unsteadiness on her feet. Neurological examination showed slow hand-eye coordination and possible double vision. It was not clear to Drs Said and Nash what was wrong and intracranial bleeding was suspected. A CT scan of the brain was arranged and von Willebrand concentrate administered. Later in the day she developed visual hallucinations and was fidgety. Her husband thought she had deteriorated.

27 The CT scan was normal.

28 I saw her for the first time during that admission on the morning of Wednesday 8/1/14 when I did a consultant Ward round with Dr Mike Nash, Consultant Haematologist. On a Wednesday, all the Haemophilia Consultants go around together and we thus see each other's patients. Mrs Ronan's husband was present. When I saw her, she recognised me and said words to the effect "Oh Dr Hay, I think I am losing my mind!" That will live in my memory for ever. She was clearly and very understandably frightened and distressed since she had considerable insight into what was going on. Mr Ronan told me that she had been increasingly confused since before Christmas. Although I had never seen Jacob Kreutzfeld Disease before, it quickly struck me that given the rapid onset of confusion, motor problems and hallucinations, that this was the likely diagnosis. I therefore phoned Dr McKee, Consultant Neurologist immediately, before finishing the ward round, shared my suspicions with him and he immediately agreed to come and see her the same day. We also faxed a formal request across to Neurology for a consultation.

29 Dr McKee attended at 14.30 on 8/1/14. I was not present during that consultation, since I would have been conducting an outpatient clinic at the time. Dr McKee noted myoclonic jerks of the arms, progressive upper limb ataxia [poor coordination of movements of the

arms], left homonymous hemianopia (partial blindness affecting half the visual field, otherwise known as "field loss", -patient often say they can't see their nose), mild upper motor lesion facial palsy (facial weakness), mild rigidity of the left arm and various other neurological signs. His initial impression was that Jacob Kreutzfeld disease was the most likely diagnosis. He suggested some further tests and arranged transfer to the Acute Neurological Unit (ANU) at Hope Hospital, Salford. This is the other side of Manchester to MRI. Almost all Neurology and all Neurosurgery in the Manchester region are based in Hope Hospital, hence the need for transfer.

30 After transfer, we kept in touch by telephone with the ANU every couple of days. At that point we had nothing further to contribute to her management and we knew that her prognosis very poor indeed. This is a condition that progresses with frightening rapidity and for which there is no treatment. We were, nevertheless shocked by the rapidity of her deterioration. She lost the ability to talk within days and lapsed into a coma within a week and sadly died. It must have been a harrowing experience for her family.

31 I cannot comment on the manner in which Dr McKee spoke to the couple, but note in the follow-up entry that he wrote that he had *not* informed the family of his suspicions on 8/1/14

32 Neurology and the post-mortem examination confirmed the diagnosis of *sporadic* Jacob Kreutzfeld disease. This is quite distinct from *variant* Jacob Kreutzfeld disease. Variant Jacob Kreutzfeld disease is derived from bovine spongiform encephalopathy (or "mad cow disease") and can be transmitted by cellular blood products (red cells and platelet transfusions). However despite over 30 years of surveillance, it has not been shown to be transmitted by clotting factor concentrates. The current consensus of scientific opinion is that sporadic Jacob Kreutzfeld disease is not transmitted by blood and blood products but the question remains open. It is known that this condition can be transmitted by "brain products" such as dura mater patches and human growth hormone, but despite various lookback exercises over many years, no convincing evidence of transmission of sporadic Jacob Kreutzfeld disease by blood and blood-products has ever been published.

33 The question remains open, however, hence the interest in Mrs Ronan and another patient with a bleeding disorder who developed this condition in the past couple of decades. Whilst rare, this devastating condition is bound to arise from time to time by chance and the investigation examined the statistics around two cases amongst many thousands with bleeding disorders.

34 We also examined Mrs Ronan's extensive transfusion record. Considerable effort was invested by our department and Dr Thachil, her consultant, assisted by Dr Patricia Hewitt at Collindale and Dr Rob Will at the Edinburgh CJD Surveillance unit, to document and donor-trace. In the end, none of the donors were found to have developed CJD themselves.

35 The confidence intervals (a statistical term indicating the degree of uncertainty that there is an association between say treatment and a particular outcome rather than an event occurring just by chance) around a case-series of two patients are so enormous that I did not feel that this could be shown to be greater than a chance occurrence.

36 Sadly, although Mrs Ronan's family have been informed of these conclusions, which were arrived at independently of the Haemophilia Centre, they have difficulty accepting that her devastating CJD was not caused by her treatment. I understand how awful it must have been for them to watch the relentless and rapid progression of this terrible and untreatable condition.

Response to Specific Criticisms:-

1.) Mr Ronan's comments on the nature of the conversation in which Mrs Ronan was informed of her HCV do not relate to me and I cannot comment on them since I was not present. It is well documented that she was tested for hepatitis C in 1993 and informed of the result and the result discussed with Dr Lucas in May 1994, six months before I took up post. Dr Lucas recorded that she was upset at the time.

2.) On 31/12/13, Mrs Ronan attended the Haemophilia Centre, complaining of tiredness where she was seen by the Haemophilia Registrar, Dr Said. I was on duty on that day and Dr Said may have phoned me, but there is no record of this taking place and I do not remember it. Her blood count was checked and she was found to be anaemic with a Hb. of about 80. She was sent home by the registrar and not by me.

3.) I was unaware that Mrs Ronan was ill with CJD until I saw her on the ward round of 8/1/14. Dr Nash, my consultant colleague presumably knew that she was ill from 6/1/14, when the registrar phoned him. I do not believe that any of us had any earlier knowledge of her devastating and sadly untreatable illness than that. One of the characteristic features of CJD is its very rapid onset, without warning, and the frighteningly rapid progression. In some ways it is like dementia but with a very much accelerated course. Sadly, there is still no blood test for sporadic CJD or vCJD, and no treatment.

4.) At the time of her death Mrs Ronan was on the Acute Neurology Unit at Hope Hospital, Salford and I was probably at Manchester Royal Infirmary. Had Mrs Ronan continued to be managed at MRI, our team would have looked in on her regularly but since I do not work at Hope Hospital Salford and had not been her Consultant Haematologist for 11 years, it would not have been appropriate for me to attend her on the Acute Neurology Unit at Hope.

Statement of Truth

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

Signed _____ GRO-C

Dated _____9/9/2020_____

Table of Exhibits

Date	Notes/ Description	Exhibit number
5.08.93 – 6.05.14	Correspondence from Patricia Ronan's hospital records	WITN3289031
22.06.05	vCJD Exposure assessment	WITN3289032
27.12.13 – 9.01.14	Hospital records	WITN3289033