Witness Name: Dr Paul Trenchard
Statement No.: WITN3604005
Exhibits No.: WITN3604006
Dated: 27 March 2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR PAUL TRENCHARD

ADDENDUM

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

I, Dr Paul Trenchard, will say as follows: -

1. This further statement is provided as an Addendum because my first statement (WITN3604001) was limited by the concurrent rapid deterioration in my father's health, and his death, within the 2-week period set by the above request (see paragraph 28 of my first statement). Section 1 summarises relevant parts of Mr Lane's Statement (WITN2365001) and of my original response (WITN3604001). The core context is his wife's 30-year remission (in effect, cure) from Acute Myeloblastic Leukaemia (AML) and how that was complicated by progressive debility (morbidity), and eventual death (mortality) in 2015, due to transfusion-transmitted Hepatitis C Virus (HCV) infection. Section 2 generalises Section 1 as a prelude to the rest of the Addendum.

2. Section 3 of the Addendum provides an overview of the way multidisciplinary clinical research and development (R&D) has cumulatively evolved over the past 50-years:
   i. towards long-term remission for acute leukaemia (i.e. towards cure);
   ii. towards the virus-free safety of blood products (in parallel with 2.i);
   iii. towards a balanced framework (as a combination of 2.i & 2.ii) for retrospective patient-specific considerations of HCV infection by platelet transfusion.

   Cited reports and research papers carry open/public access, unless stated otherwise.

   The patient-specific context (30-years) of Mrs Lane's personal clinical history (paragraph-1, above) is reviewed within this expanded historical context (50-years). It is hoped that Mr Lane, and others who have experienced similarly harrowing family experiences, may wish to review their current perceptions about blood services in the light of this Addendum.

   The Addendum has been designed to be read in conjunction with Exhibit WITN3604006 which comprises detailed schematic diagrams that illustrate and summarise topics 2.i, 2.ii and 2.iii, above. It is important to note that the text of the numbered paragraphs in this Addendum provides the explanatory narrative for the correspondingly numbered elements of the diagrams (see WITN3604006).

Section 1: Summary of Original Response (WITN3604001) to Statement WITN2365001

3. The specific questions asked of me by the inquiry related to those parts of Mr Lane's witness statement (WITN2365001) which took issue with the use of the term *'full testing'* of donor blood in Wales for the period 1985/6. Retrospectively, he alleges that I frequently used that term, at that time, and regards such use to have been wrong because the associated testing processes did not include a test for the Hepatitis C Virus.

4. My original statement (WITN3604001) countermanded this view (paragraph 3, above) by:
   i. indicating that Mr Lane's argument was illogical and unsound; particularly because it referred to a time (1985/6) that predated the discovery of the Hepatitis C Virus (Spring 1989) and the implementation of HCV testing of blood donors in the UK (Autumn 1991);
   ii. providing extracts from two published documents (the Penrose Inquiry and a Hepatology Review paper) that were consistent with the professional use of the term *'fully tested'* according to contemporary clinical consensus (Exhibits WITN3604003 and WITN3604004, respectively).

5. My original statement (WITN3604001) also drew attention to:
   i. Mr Lane's lack of awareness and/or confusion about some important aspects of blood service development and procedures (see paragraph-21 of WITN3604001);
   ii. a range of inconsistencies in Mr Lane's statement (see WITN3604002).

6. As an extension of Paragraph-5.i (above), Mr Lane's statement (WITN2365001) refers a number of times to my wide-ranging involvement in discussions during 1985/6, but overlooks the fact that these were largely, if not entirely, in relation to providing contemporary reassurances about the risk of HIV transmission by blood transfusion and, correspondingly, that the *'full-testing'* of donor blood had expanded to include HIV testing (from Autumn 1985) following the discovery of this AIDS-related virus (Spring 1984).

7. As an extension of Paragraphs 5.i and 5.ii (above), Mr Lane comments in Sections 4.2 and 4.3 of his statement (WITN2365001), that:

   'All patients and relatives were concerned about blood transfusions and were concerned at stories in the press about AIDS, Hepatitis C all were told all blood fully tested. As a result, a number of discussions took place as to the risk of catching AIDS from transfusion of platelets on Ward A7 during our time on A7 in 1985/86.'

   This is confused and untrue because it is logically impossible for there to have been any stories about Hepatitis C at that time (see paragraph-4.i, above).

Section 2: Generalisation from Section 1 that Invites a Cumulative R&D Perspective

8. From the previous points, and using Mr Lane's statement (WITN2365001) as a basis for generalisation, it may be reasonable to postulate that:

   When a false argument (see paragraphs 3 & 4, above) forms part of a statement that is both inconsistent in structure and lacks knowledge of some important facets of haematological and blood transfusion history and development (paragraphs 5, 6 & 7, above), then there is an increased risk that the statement might be inappropriately critical of blood transfusion practices and staff. This risk may be increased if personal tragedy is the fundamental catalyst in the compilation of such a statement.

9. The underlying tragedy for Mr Lane's family, and specifically his wife, was that it was not until 1997 that she was notified, as a consequence of cumulative and ongoing multidisciplinary medical R&D, that a donor had tested positive for HCV in the post-1991 testing era. It appears that that donor had donated many years previously, from which one platelet product was retrospectively traced as having been transfused to Mrs Lane in 1986, during her Autologous Bone Marrow Transplant (ABMT) treatment schedule (intended to be curative for acute leukaemia), and had transmitted Hepatitis C.

10. In contrast with the fact that Mrs Lane's ABMT resulted in cure (an impossible outcome without platelet transfusion support), Mr Lane's statement provides a harrowing account of family stresses that followed the delayed and unexpectedly superimposed diagnosis of Hepatitis C (paragraph-9, above): sufficient, from a human perspective, for compassionate allowances to be made in line with Paragraph-8 (above).

11. However, from a clinical perspective, Mrs Lane's ABMT in Wales was the first in the UK (WITN2365001, Section 2.3) and the apparent cure was an early success (1986). Alternatively, if the process had failed to prevent relapse, she might not have lived long enough for her progressive HCV infection to become clinically evident and be monitored.

12. It follows that, despite the personal desperation wrought by the course of Mrs Lane's HCV infection, the associated clinical monitoring extends the scientific perspective, by adding important data into the cumulatively evolving clinical database for this disease, which could only begin definitively once HCV had been discovered and could be measured. This Addendum encourages a balanced overview, based upon an historical understanding of cumulative multidisciplinary R&D.

Section 3: Balanced Overview within a 50-year Framework of Multidisciplinary R&D

13. The cumulative evolution and interplay of cause-and-effect events in the disease histories of individuals infected by transfusion-transmitted HCV is very complex because it spans approximately 50-years of cumulative multidisciplinary R&D.

14. In relation to this, the main relevant clinical considerations are:
    i. Clinical Haematology & Transfusion Medicine and Science;
    ii. Hepatitis Virology & Reciprocating Transfusion Science;
    iii. Patient-Specific Overview & Retrospective Statistics.

i- Clinical Haematology & Transfusion Medicine and Science

15. Taking Clinical Haematology & Transfusion Medicine and Science first, the interplay of R&D between the clinical treatment of life-threatening haematological diseases and the supportive advancements in transfusion medicine has been reviewed for acute leukaemia in an article by Cannas & Thomas in 2015: *'Supportive care in patients with acute leukaemia: historical perspectives'* (Blood Transfusion, 13:205-20). It identifies a sequence of important issues: some are introduced (underlined) below, together with the associated quotations (*'italics'*): .....

16. ..... the interactive R&D timescale for platelet support in acute leukaemia: *'Unlike red blood cells, the history of platelet transfusions has only developed over the past 40 years.'* ;

17. ..... the inevitability of rapid death in the absence of treatment: *'Without any treatment, patients with acute leukaemia died within a few weeks.'* (cf. WITN2365001, Section 2.1);

18. ..... that: *'Before the 1970s, thrombocytopenic bleeding was the major cause of serious morbidity and mortality in patients undergoing intensive chemotherapy.'* ;

19. ..... the necessity of platelet support: *'Platelet transfusions are indispensable for supportive care of patients with haematological diseases.'* (cf. WITN2365001, Section 4.1);

20. ..... a significant discovery in transfusion science was made in 1971: *'In the 1970s platelet transfusion became routine practice when Scott Murphy and Frank H. Gardner provided evidence that platelet function was best preserved when platelets were stored at room temperature with agitation, ...'* (as published in the Journal of Clinical Investigation, 50:370-7);

21. ..... that this discovery was pivotal in *'revolutionising platelet therapy'*, by facilitating two areas of therapeutic advancement:
    i. **minimisation of haemorrhagic mortality**: ..... *'This* [discovery] *resulted in the introduction of prophylactic platelet transfusions for patients with leukaemia, and dramatically changed the causes of death among patients with this malignancy, such that haemorrhage as a major cause of death was virtually eliminated.'* ;
    ii. **facilitation of therapeutic intensification**: ..... *'Furthermore, the practice of prophylactic platelet transfusions enabled therapy intensification.'* ;

22. ..... that: *'New methods for platelet transfusion were introduced in the 1980s using cytapheresis techniques, which led to an increase in platelet transfusion therapy to support myeloproliferative therapies including intensive chemotherapy and stem cell transplantation currently used in the treatment of leukaemia.'* (cf. WITN2365001, Section 2.16);

23. ..... that: *'This was refined in the 1990s with methods of collecting leucocyte-reduced platelet products.'*

24. In the specific case of Mrs Lane, her treatment in 1985/6 coincided with the time period when progress in therapeutic intensification had increased enormously, and with that came unwanted side-effects.

25. Section 2.6 of WITN2365001 describes the specific early complication for Mrs Lane, of shingles and the consequent long-term morbidity of blindness in one eye, constant pain and issues with memory and balance; and, in Section 2.7, transient ischaemic attacks.

26. In addition, Section 2.8 of WITN2365001 indicates that the therapeutic intensification by full body radiation, prior to ABMT, was particularly responsible for skin radiation burns to both legs: it may also have predisposed significantly to the morbidity already described above.

27. Ultimately, and sadly, Sections 5.1-5.19 and 6.1-6.6 of WITN2365001 comprise the harrowing account of family stresses that followed the delayed and unexpectedly superimposed diagnosis of Hepatitis C. Sections 3.1, 5.8 & 5.9, 5.13 & 5.14 emphasise the associated clinical progression of: general deterioration and vertigo from 2008; and cellulitis, hospital and death in 2015 (certified as hospital acquired pneumonia & cirrhosis due to Hepatitis C).

28. In brief summary of Paragraphs 16-27, above, the following sequentially interlinked chain of cause-and-effect advancements can be listed (also see diagrams in WITN3604006):
    i. time-dependent advancements in platelet provision and transfusion;
    ii. enabling prophylactic prevention of haemorrhagic death from platelet deficiency;
    iii. enabling progressive intensification of acute leukaemia treatment towards cure;
    iv. creating significant risk of post-intensification side-effects (morbidity & mortality).

ii- Hepatitis Virology & Reciprocating Transfusion Science

29. Running alongside the progress in Clinical Haematology and Transfusion Medicine and Science has been the interplay of R&D between Hepatitis Virology and Transfusion Science, in working towards the virus-free safety of blood transfusion.

30. The pivot point for this was 1964, when Baruch Blumberg discovered the Australia antigen.

31. One researcher (H. J. Alter) comments: *'The chronological events surrounding the Australia antigen stand out as a monument to non-directed medical research and as a tribute to investigative perseverance. This tale of serendipity began in the mid-1960s .....'* (Seminars in Liver Disease, 1981; 1:2-6 [not available through open access]).

32. Another researcher, Robert H. Purcell, has referred to the subsequent time period as *'the Golden Age'* of hepatitis research (Gastroenterology, 1993; 104:955-963 [includes quotation cited in paragraph-31, above]).

33. In contrast, the complex and not-so-golden catch-up problems for Transfusion Science, in its efforts towards the virus-free transfusion of blood, has been carefully explored in The Penrose Inquiry (2015, Final Report, Volume 4, Section 25). A few extracts from this, based on Scottish data and contemporary thinking in transfusion science in the 1980s, have already been presented in Exhibit WITN3604003; and some parts are introduced (<u>underlined</u>) and quoted (*'italics'*) below in support of the following time-related sequence of virology-associated advancements, with particular emphasis on the protracted enigma of Non-A Non-B (NANB) hepatitis and its elusive causality: .....

34. ..... <u>pre-1964 >> a lack of regional standardised policies and practices towards protection against the transmission of infection by blood</u>: *'Before the discovery of the 'Australia' (or 'hepatitis-associated') antigen, later renamed the Hepatitis B surface antigen (HBsAg), there were few, if any, settled Scottish National Blood Transfusion Service (SNBTS) protocols to guide practice at donation sessions. Individual Regional Transfusion Directors (RTDs) were free to develop and apply their own policies and practices for the protection of recipients of blood, blood components and blood products from transmission of infection.'* ;

35. ..... <u>1971/72 >> the commencement of total donor screening and a commitment to improved and standardised testing for transfusion-transmissible viruses</u>: *'Professor Cash discussed a range of clinical practices that might reduce the risk of virus transmission and commented on the tests available for the Australia antigen. He said that the recent introduction of total donor screening in Scotland was a major step forward but left much still to be done. More sensitive tests were required and there was a need for improved facilities and for a national reference laboratory for the supply of standardised reagents.'* ;

36. ..... 1971/72 >> suspicions anticipating that advances towards improved HBV testing may not account for all cases of post-transfusion hepatitis: *'He concluded: [W]e must not assume that the elimination of all antigen-positive units will solve the post-transfusion hepatitis dilemma. Current evidence strongly suggests that the present limitations, which have been calculated to represent a detection rate as low as 25 per cent, cannot be entirely explained on insufficient sensitivity of existing methods, and that other agents are responsible for a significant proportion of the problem.'* (Cash, Principles of Effective and Safe Transfusion, Proceedings of the Royal Society of Edinburgh (B), 71 (Supplement); 5:1971/72);

37. ..... early 1970s >> general fact-limited confidence in improved HBV testing: *'In the early 1970s, the risk of transmission of viral hepatitis, so far as it was understood,* ***was thought to be*** *mitigated by what were regarded as increasingly sophisticated screening tests for the Hepatitis B virus (HBV) antigen and antibody and these became the main means of protecting the blood supply.'*;

38. ..... The final *'Conclusions'* part of Section 25 of the Penrose Inquiry (WITN3604003) opens with the phrase: *'In about 1983, on the eve of the AIDS epidemic as it was to develop in the UK, ...'* ; and all the subsequent statements of concluding fact and thought and belief, including eight bullet-points, are quoted in full in the following table, but have been rearranged slightly in order to create the four sub-titled compartments shown:

Table of Penrose Inquiry Conclusions:

INITIAL BASELINE KNOWLEDGE	
Hepatitis B was ***known*** *to be a disease with potentially serious outcomes for patients.*	
It was ***known*** *that HAV was almost never transmitted by blood, while .....*	
[It was **known**] *..... HBV was not the only hepatitis virus that presented risk of transfusion-transmitted hepatic disease. However:*	
• ***Knowledge*** *of the prevalence of NANB Hepatitis in the UK, including Scotland, was at a very early stage of development*	
UNKNOWN & UNMEASURABLE	**TESTING DEFICIENCIES**
• *Samples testing negative for Hepatitis B (and, where tested for Hepatitis A, also negative for that infection) necessarily still included an* ***unknown*** *proportion that were infected with Hepatitis B .....*	• *Screening tests for Hepatitis B* ***remained imperfect*** *.....*
..... and an ***unknown*** *proportion that were infected with NANB Hepatitis or both.*	*..... and were* ***still believed to fail*** *to identify a significant minority of Hepatitis B infected donations.*
• *The exact proportion of donations infected with NANB Hepatitis* ***could not be determined*** *by exclusion using existing screening tests for Hepatitis A and Hepatitis B*	• ***There was no serological or other screening test*** *for the NANB Hepatitis agent of transmission.*
PREMATURELY EVOLVING THOUGHTS - NOT FACTS - about NANB	
• *Because of the emphasis on clinical symptoms and overt jaundice as indications of viral hepatitis, NANB Hepatitis was* ***thought to be rare*** *in Scotland.*	
• *NANB Hepatitis was generally* ***thought to have a benign prognosis****.*	
• ***The risks for the patient*** *that might be associated with the transmission of NANB Hepatitis* ***were thought to be low*** *relative to the risks associated with the conditions for which they required blood transfusion in surgery or in medical treatment of their primary conditions.*	

39. ..... this NANB view persisted until the late 1980s: *'By the autumn of 1983 a view had emerged that NANB Hepatitis was not a major problem in Scotland and was generally not a serious disease. That view persisted into the late 1980s. Screening for HBV continued, with increasing sophistication, but also with increasing awareness that the results were of little relevance to NANB Hepatitis.';*

40. ..... by the autumn of 1983: *'..... attention was moving from non-A, non-B Hepatitis (NANB Hepatitis) to AIDS and .....* [with] *growing awareness of the need for protocols on donor selection in that context and implementation of the first structured guidance on donor selection in Scotland'.*

41. From this position of altered focus, and in marked contrast with the ongoing elusiveness of the definitive causality of NANB, it is easy to interpose the relatively short 4-year time-span from AIDS-suspicions in the USA, to routine HIV testing of blood donors in the UK, as summarised in the next three paragraphs.

42. In mid-1981, suspicions were developing about the emergence of Acquired Immuno-Deficiency Syndrome (AIDS) in the New York gay community.

43. In the Spring of 1984, Robert Gallo discovered the Human Immunodeficiency Virus (HIV) as being the causal agent of AIDS.

44. In the Autumn of 1985, routine HIV testing of blood donors was implemented in the UK and existing donors were directed to exclude themselves from further donation if they were in a high-risk group for HIV.

45. From Paragraphs 13-44 (above), it is reasonable to deduce and generalise that R&D is:
    i. partly *retrospective* (look back) to acquire a relevant meaningful knowledge base within a given scientific discipline;
    ii. partly *prospective* (look/move forward) in building upon look back data in the advancement of that discipline;
    iii. partly *delayed* (catch up) when it is necessary to wait for an advance in one discipline to be achieved (as an R&D effect/outcome), before it (as a reciprocal new causality) can enable advancement in another.

46. This expanding evolutionary sequence of a *caused effect* becoming a *subsequent cause* of a *new effect/outcome*, and the ways such chains may also overlap, through *cross-links & loops* between the R&D strategies of different disciplines, including catch up delays, has already been illustrated for the time-dependent interplay of Clinical Haematology & Transfusion Medicine and Science (paragraphs 15-28, above).

47. Such reciprocation between disciplines can become very pronounced when blood transfusion practice has to catch up with advances in virology that lead to the discovery of a new agent for transfusion-transmitted viral disease and the associated development of a suitable screening test. This is illustrated above for HIV/AIDS and below, for HCV.

48. Eventually, after more than 20-years, the longstanding suspicions about NANB hepatitis were confirmed through the unrelenting efforts of virology R&D and the consequent discovery of the causal agent, the Hepatitis C Virus (HCV), in the Spring of 1989.

49. Subsequently, a test for HCV became available (hepatitis C virus antibody: abbreviated as anti-HCV or HCV positive [+ve]) and was adopted and implemented by UK blood services in 1991.

50. At last, **blood services** could **catch up** with the virology of Hepatitis C.

51. This enabled **blood services** to simultaneously **look forward** to the routine testing of all subsequent donors/donations. The UK-wide screening of blood donors for HCV began in September 1991 and added a further dimension to the definition of *'full testing'*.

52. This also provided scope for collaborative R&D in blood services to evaluate: *'The contribution of transfusion to HCV infection in England'* (K. Soldan et al., Epidemiol. Infect. [2002], 129, 587-591). In this study, eight blood centres in England collated anti-HCV testing data throughout the first 4-months of routine testing of blood donors from the outset of implementation in September 1991 and established a long-awaited statistic: namely, a prevalence of anti-HCV of 0.066% (1 in ≈1,500 donors).

53. In general, **blood services look back** within their own records whenever a blood donor is confirmed positive for HCV, and according to the following sequence of steps:
    i. to note all previous donations and all subsequently manufactured products from all donors confirmed HCV positive;
    ii. to track the subsequent supply and transfusion of each of all products — to which hospital, to which ward, and to which recipient patients — on the basis that each patient so identified might have been infected with HCV by transfusion;
    iii. to note the contact details of each potentially infected patient.

    The study in England specifically attempted careful look back, for the period January 1980 to September 1991, for the initial 4-months of HCV testing data.

54. Such data are used by **blood services** (or sometimes through medical practitioners in *clinical services*) to **catch up** with each potentially infected patient by attempting to make contact in order to:
    i. inform each patient and arrange for counselling and consent for HCV testing;
    ii. arrange for HCV testing if the patient agrees;
    iii. arrange follow-up as appropriate for any patient confirmed positive for HCV.

55. Transfusion services, in collaboration with blood service users, are always seeking to optimise the traceability of all relevant links between regional blood services, blood donors, associated donations, subsequently manufactured blood products, their transfusion to patients, and consequent post-transfusion outcomes. However, Soldan et al. (paragraph-52, above), emphasised the inevitable incompleteness of some of these links:

    'The aim of this lookback was to diagnose patients with transfusion-transmitted HCV who might benefit from care and treatment. For various reasons including loss of records, movement of patients, death of patients and attention to patients' best interests and wishes, not all recipients of blood from known anti-HCV-positive donors received testing. Also, as not all HCV-infected donors gave blood after anti-HCV testing was introduced, many infected donations collected between 1 January 1980 and September 1991 will not have been subsequently identified and will not have entered the lookback programme.'

56. The study also indicated that *'10% of the identified infections had been diagnosed prior to the lookback programme'*. Of course, running concurrently with, but separately from, blood services, *clinical services* were able to *catch up* independently with virology, through regional testing laboratories.

57. However, considerable diligence and resourcefulness is required to comprehensively manage all avenues of traceability for a positive HCV result that begins with a patient rather than a blood donor. The various reciprocating steps, which eventually feed into the general blood service protocols of Paragraphs 53 and 54 (above), are as follows:
    i. *[clinical services] look forward* to HCV testing of patients who display relevant clinical symptoms and/or signs suspicious of evolving hepatitis, and who may have a medical history of previous blood product transfusion(s);
    ii. *[clinical services] look back* into the clinical records of any patient who tests positive for HCV, and note whether any blood products have been previously transfused and, if so, the corresponding product identification numbers (IDs): the particular complexity of this stage is that ID data may be fragmentary and scattered in separate notes due to different products having been transfused at various times, by different clinical teams, in different hospitals, in different regions (cf. paragraph-55, above);
    iii. *[clinical services] look forward* by notifying blood services of the IDs of all products suspected of transmitting HCV to the index patient, until proven otherwise;
    iv. **[blood services] look back** for each of all suspect product IDs to identify all corresponding donors, each of whom must be regarded as potentially HCV positive, until verified negative;
    v. **[blood services] catch up** with all donors implicated, by: contacting; counselling; obtaining consent for testing; making arrangements for testing; notification of results;
    vi. for any donor confirmed HCV positive, **blood services** will reciprocate the findings into the **look back** protocol already described in Paragraph-53 (above), and then into the **catch up** protocol of Paragraph-54 (above), in order to determine the full extent of transfusion-transmitted HCV infections to patients, attributable to that donor, and to implement appropriate clinical follow up.

58. The foregoing detail about reciprocating R&D within transfusion science is presented as an informative framework that may be sufficient to answer the question raised by Mr Lane in Section 2.14 of his statement (WITN2365001):
    'After a discussion, I can remember commenting how on earth did they manage to track the infected donation from a male donor back over that period of time (i.e. 1997 back to 1986).'

59. It is also relevant to note that ongoing R&D has now revealed that the risk of sexual transmission of HCV is real, but low, at about 5%. In the current knowledge that Mrs Lane was infected by a platelet transfusion in 1986, we now know, statistically, that Mr Lane was consequently exposed to a real risk of becoming infected through his wife. Had such an outcome materialised prior to the Autumn of 1991, he would have tested positive for HCV in the post-1991 testing era, when attending monthly (from mid-1985) to donate platelets by apheresis (WITN2365001, Sections 2.15-2.17), i.e., approximately half-way towards the total of approximately 144 donations that he so splendidly reached by 1997 (WITN2365001, Section 2.17).

60. The implications of such a finding are that:
    i. Mrs Lane's infection with HCV would have been confirmed 6-years earlier, since it would have been traced directly from the hypothetical situation, rather than the route eventually taken (WITN2365001, Sections 2.9-2.14);
    ii. the family would have had to cope with the progression of HCV in two family members, not just one;
    iii. all of Mr Lane's previous donations, estimated as ≈72 for the period 1985-1991 (i.e. half of the 144), would have needed to be traced to all recipients according to the **look back** & **catch up** protocols described earlier.

61. Furthermore, this example and the extended detail on the virology of hepatitis provided above indicate the complexity of some aspects of the natural history of Hepatitis C, and the ongoing evolution of that understanding through multidisciplinary R&D. It is hoped that such detail may be sufficient for affected families to rethink their views on blood services. It may be relevant, retrospectively, to Mr Lane's comment in Section 9.2 of his statement (WITN2365001), that:

    'The Inquiry should understand that up until July 1997 as far as we were concerned, we had beaten AML. When we were told she had HepC, our views of the BTS changed when we were told "no known cure of Hep C".'

62. Paragraphs 29-61 (above) demonstrate the reality of R&D when new measurements become possible, when they generate meaningful statistical data and when, in turn, they are used to probe the uncertainties of the past. The same paragraphs are also a salutary reminder that the concept of *'beating'* a disease is much easier to entertain when associated interactions and eventualities are dormant/obscured or not known: when hope is not compromised by statistical reality. Although these paragraphs are difficult to summarise briefly in words, they are suitable for schematic representation (see second diagram in WITN3604006). Perhaps the words of a prominent climber may suffice as a metaphorical summary (if I recall them adequately): *'You never really conquer a mountain: but, sometimes, mountains let you climb them'*.

iii- Patient-Specific Overview & Retrospective Statistics

a- Prospective Perspectives on Evolving Statistics

63. The discovery of HCV in 1989 and the ability to test for it in 1991, was the turning point towards the progressive unravelling and ongoing understanding of the natural history of Hepatitis C. Some relevant papers are: Seeff, L.B. *'Natural History of Hepatitis C'* (Hepatology, 1997, 26:21S-28S); Alter, H.J. *'HCV natural history: The retrospective and prospective in perspective'* (Journal of Hepatology, 2005, 43:550-552); Westbrook & Dusheiko, *'Natural history of hepatitis C'* (Journal of Hepatology, 2014, 61:558-568).

64. As a direct consequence, since 1991, actual numbers, and associated statistical data, began to replace phrases such as *'... [it] was generally thought to have/be ... [etc.] ...'* which had been the usual limitation on the understanding of NANB hepatitis in the 1980s (see paragraphs 38 [with table] & 39, above).

65. It follows that the clinical history and data for each individual case of HCV, are potential contributors to the expansion of that knowledge (see paragraph-12, above). It may help affected patients and their families to know when such information has been incorporated into clinical studies and has contributed to disease statistics.

66. Similarly, the presentation of statistical findings to affected patients and their relatives may add substantially to their understanding of HCV and, in turn, may reduce the risk of being inappropriately and disproportionately critical of blood services (see postulated general mechanism in paragraph-8, above).

b- <u>Retrospective Perspectives on Consent Limited by Statistical Insufficiency</u>

67. Mr and Mrs Lane changed their view of blood services in 1997 (see paragraph-61, above), and Sections 4.1, 4.4, 4.5 & 8.2 of his statement (WITN2365001) seem to me, subjectively, to carry an implied criticism that: as a senior member of blood transfusion service staff, I had acted in 1985/6 as a rogue medic who had engaged in a personal crusade of misleading patients, relatives, the general public, other doctors, and a research committee, by my alleged use of the phrase *"all Welsh blood is fully tested"*.

68. Mr Lane argued that this phrase was false because the testing did not include HCV testing (WITN2365001, Section 4.5). How could it (paragraph-63, above)? It was an invalid retrospective argument (see counterargument in paragraphs 3-8, above) bordering, perhaps, on defamation by implication. However, it is reasonable to overlook the latter on compassionate grounds (paragraphs 9 & 10, above) and in relation to the generalised mechanism proposed earlier (paragraph-8, above).

69. Mr Lane also states (WITN2365001, Section 4.1), under the sub-heading of *'Consent'*:

    'In terms of consent, I would confirm of course Tricia needed to receive blood platelets as a result of the treatment she was undertaking. I confirm that I can recall a number of discussions with Paul Trenchard ..... when he stated that "all Welsh blood is fully tested".'

    This gives an impression that Mrs Lane may have consented *'to receive blood platelets'* due to my alleged assurances about *'full testing'*. However, the *informed consent* process at diagnosis, in mid-1985, would have been conducted by the clinician in charge at that time (WITN2365001, Section 2.1; see also WITN3604002, Sections 5 & 5.1-5.4), and any discussions with me would almost certainly have been in the context of HIV testing and, therefore, only likely from late-1985 onwards (see paragraphs 6 & 44, above).

70. Nevertheless, this linkage of consent to assurances about blood testing prompts some hypothetical inverse speculation. *'What if, as part of the **informed consent** process in 1985, Mrs Lane had been told that all Welsh blood was NOT 'fully tested': would she have refused treatment with platelets to avoid the risk of infection by a transfusion-transmissible agent that was, as yet, undiscovered and without measure?'*

71. The refinement of this question is critically important because, deep down, whether for Mrs Lane, or other patients with similar clinical histories, the process of *informed consent* for intensive treatment intended to cure, is based upon:
    i. balancing the likelihood of success, ...
    ii. against the likelihood and magnitude of treatment complications: .....
    iii. both relative to the fact of rapid death in the absence of treatment.

72. On this basis, the question could be improved, as follows: *'What combination of therapeutic complications, ...*
    i. *not only physical (onset-time and magnitude of intensity, progression and duration), ...*
    ii. *but also psychological (onset-time and magnitude of intensity, progression and duration),*

    ..... would be sufficiently informative, and statistically compelling enough, to cause a given patient to opt out of the chance of long-term survival and choose prompt mortality?'

c- <u>Retrospective Perspectives on Consent Informed by Statistical Sufficiency</u>

73. In preparing to answer this question, for 1985, some relevant statistics are required, based on multidisciplinary R&D, and are interpolated as follows:
    i. Reports are available from Cancer Research UK, for survival figures for AML in women, for the periods 1980/1 & 1990/1: interpolation for 1985/6 provides 5-year and 10-year survival figures of 28.6% and 20.15% (i.e. ≈27% & ≈20%) respectively.
    ii. Some clinical trials data, for the period 1985-1994, have been published by Blumberg and others, in a paper titled *'Platelet transfusion and survival in adults with acute leukemia'* (Leukemia [2008] 22, 632-635). The variation in platelet requirements fell into three groups, with the mean number of platelets transfused being: 50±26, 128±20, 302±102.
    iii. The likelihood of HCV being transmitted to a patient with AML, if transfused with the largest mean-number of platelets that may be required (73.ii), and using the 1991 HCV prevalence rate in donors provided by the multicentre study in England (paragraph-52, above), is 0.066% x 302 = 19.932% (i.e. ≈20%).

74. These data — cumulatively emerging and combined from ongoing multidisciplinary R&D in haematology, transfusion science and virology — can be extrapolated back, within the evolutionary timeline, to 1985, as a basis for estimating the difference they might have made to the decisional outcomes of patient-specific *informed consent*, at that time. These sorts of data will be referred to, hereafter, as "*retrospective reality*".

75. The *retrospective reality*, at the time of Mrs Lane's AML diagnosis and *informed consent* for intensive chemotherapy, in mid-1985, is that:
    i. the *'full-testing'* of Welsh blood donors included screening for HBV (Hepatitis B Virus) but not HIV or HCV (HIV was added in late-1985: see paragraph-44, above);
    ii. the likelihood of achieving 10-year long-term survival for AML was ≈20% (retrospective statistical projection of paragraph-73.i, above);
    iii. assuming high platelet support for 7-courses of remission chemotherapy and ABMT (WITN2365001, Sections 2.1 & 2.3), the likelihood of becoming infected with HCV was ≈20% (retrospective statistical projection from paragraphs 73.ii & 73.iii).

76. These data provide Mr Lane, and others with similarly harrowing AML and HCV experiences, with a current opportunity to review the decisions that may have been made within the process of *informed consent* prior to 1991. In Mrs Lane's case, diagnosed in mid-1985, the *retrospective reality* data indicate that her chance of achieving long-term 10-year survival through intensive curative AML treatment (≈20%) was the same as the likelihood that she would become infected with HCV as a transfusion side-effect of that treatment (≈20%). *'What if Mrs Lane could have known this, at that time: would she have chosen to die in weeks without platelets, or risk the probability of getting hepatitis and perhaps being cured?'*

77. It is also reasonable to speculate as to whether such decision-making might have been influenced further, if the post-1991 expansion of scientific and clinical knowledge about the natural history of Hepatitis C (see citations above, in paragraph-63, for papers published in 1997, 2005 & 2014) had been available for the process of *informed consent*, rather than the fact-limited clinical consensus of the 1980s, about NANB Hepatitis (paragraphs 38 [with table] & 39, above), which may not have been mentioned at all during the process.

78. It is difficult to imagine that the *retrospective statistical reality* would have been even remotely sufficient to militate against the intuitive or common-sense choice of accepting treatment for the hope of life. Surely, Mrs Lane would have chosen the chance of cure and probable hepatitis; rather than no treatment and rapid death.

d- <u>Retrospective Projection from Ultimate Cumulative Experiential Reality</u>

79. In view of this, the scientific inquisitiveness of Paragraph-72 (above) can be extended to speculate about whether there may be some form of *ultimate reality*, that transcends *statistical reality*, capable of compelling a newly diagnosed AML patient, in the pre-1991 era, to choose the no-treatment option over the hope of cure.

80. From this, and as an extension of Paragraph-72 (above), simple logic would suggest that the most powerful information possible would be the precise knowledge of absolutely everything that such a patient will experience in the way of therapeutic side-effects and complications, from the outset of treatment (if chosen) to their eventual death.

81. This leads to the following patient-specific question: *'What if Mrs Lane could have been informed, with 100% certainty at the time of diagnosis (1985), of all that she and her family would experience clinically, physically and emotionally over the next 30 years, until her death (2015); would she have chosen NOT to be treated?'*

82. Of course, the prospective knowledge gained by being told in detail about such an enormous range of branching eventualities falls far short of the retrospective knowledge gained by actually experiencing the associated realities of pain, excitement, joy, anticipation, anxiety, fear, disability, debility, despair etc. Consent information that cannot convey the scope and scale of *experiential reality* will, correspondingly, be unlikely to raise the patient's fear of what the long-term side-effects will be, to a level that will convince them to refuse treatment. Consequently, the limited perspective of Paragraph-78 (above), remains unchanged.

83. However, in contrast, the *experiential reality* of the last 30-years of Mrs Lane's life was directly and intimately witnessed, and to a large extent co-experienced, by Mr Lane, and partial insights are provided in various sections of his statement (WITN2365001), as follows:
    i. AML remission in 1985 (Section 2.1) and curative ABMT success in 1986, with *'Tears of joy all round ....* [and] *.... in remission for the rest of her life.'* (Section 2.3);
    ii. Despite post-ABMT shingles in 1987 and the long-lasting effects of blindness, post-radiation burns etc. (Sections 2.6-2.8) *'.....* [she] *was determined to try to enjoy a reasonable quality of life, and remained quite active.'* (Section 2.8);
    iii. Following the notification of the possibility of having received blood from an HCV infected donor (Section 2.9), and following subsequent confirmatory testing (Section 5.1), she declined a liver biopsy (Section 5.1);

iv. *'.... [she] took an attitude of whatever will be will be.'* (Section 2.10) and her *'.... view was simply, if she had anything, she simply wanted to die at home.'* (Section 2.12);
v. *'As a result of* [her] *infection with Hepatitis C, she was extremely down and commented "why me", and effectively indicated she simply wanted to be left alone to die at home. Fortunately, after that we discussed and decided that we needed to try and battle on and make the most of it and we were able to enjoy some holidays.'* (Section 5.7) *'..... in places like Antigua and Barbados in 2008 and 2010 respectively .....'* (Section 5.8);
vi. *'.....* [her] *attitude was good but also* [there] *remained one question "why her".'* (Section 5.11);
vii. *'I felt that at the UHW "there had been hope" but in the Royal Glamorgan Hospital (RGH) "there was none". The last two days of my wife's life were pure hell at RGH because she had given up hope. ..... My wife's last words to me were "leave me me in peace, I'm okay". I held her hand to the end and watched her pulse go. I then said "go to your God".'* (Section 5.14).

84. It appears that Mrs Lane only gave up hope for two brief periods (paragraphs 83.v & 83.vii) during her 3-level experience of long-term survival which, in turn, can be summarised as:
    i. 30-years of life in complete remission (cured) of AML (WITN2365001, Section 2.3);
    ii. 29-years of enduring significant non-transfusion-related side-effects of the curative treatment (see paragraphs 25 & 26, above [WITN2365001, Sections 2.6-2.8]);
    iii. 18-years of coping with the 11-year-delayed discovery and surprise notification, and the gradually emerging progressive side-effects, of Hepatitis C acquired as a transfusion-transmitted complication of the curative treatment (see paragraph-27, above [WITN2365001, Sections 3.1, 5.8 & 5.9, 5.13 & 5.14]).

85. It follows that Mr Lane's cumulative memories and testimony must comprise the best approximation to the *experiential reality* requirements of Paragraph-80 (above). Consequently, he ought to have a confident YES/NO understanding of what Mrs Lane's answer to the question in Paragraph-81 (above) would have been: also, whether his own purely personal choice would be the same; and whether he can answer with certainty and without hesitation on both counts.

86. Without knowing what Mr Lane's answers might be, it is reasonable to generalise from Paragraphs 79-85 (above), on the basis of intuition and common-sense (as applied in paragraph-78, above), that most, if not all, patients, through some combination of their love of life, their love of loved ones and, for some, their love of God (perhaps paragraph-83.vii, above) and, for some, their fear of death, will almost certainly compel them to choose the chance of life and cure now, with hardly a second thought for future side-effects that arise from the treatment required.

87. The simplistic, but realistic psychology of this is that when faced with imminent death without treatment, an AML patient's only chance of living is to be treated. It is an all-or-none decision which, in most cases:
    i. eclipses the statistical likelihood of cure with an intense 100% hope that, if the probability is only 1 in 5, they *'will be THE fortunate one'* of the five;
    ii. eclipses the statistical likelihood of future side-effects with an intense 100% hope — inverted, relative to 87.i — that, if the probability is also 1 in 5, they *'will NOT be the UNfortunate one'* of the five;

iii. supports the inverse hope, with the *experiential unreality* of the distant future, whereby a side-effect poorly understood at the time of consent and which might only emerge and become very serious much later, will only become *experientially real and detrimental* to the quality of life (QOL), if long-term survival is established.

88. On balance, it seems that the hope of cure, in the face of imminent death from AML, dominates the choice of intensive treatment — in preference to none — even if side-effects compromise the Quality Of Life: physically and/or emotionally; in the short-term and/or long-term; whether predictably and/or unexpectedly and/or delayed.

e- <u>Retrospective Reality Check for Therapeutic Disasters</u>

89. In summary, thus far: given the commencement in 1991 of a cumulative statistical understanding of the natural history of NANB Hepatitis, afforded by the discovery of HCV and a suitable test (paragraphs 63-66, above), the retrospective evaluation of the role of such data in the context of any AML patient in the pre-1991 era trying to decide whether to accept curative treatment that may incur significant delayed side-effects — including the possibility that at the time of informed consent there may be some unknown causality capable, eventually, of becoming independently lethal — has been argued from the perspectives of:
    i. insufficient statistical data during the 1980s (paragraphs 67-72, above);
    ii. post-1991 statistical data projected retrospectively (paragraphs 73-78, above);
    iii. retrospectively projected experiential data for Mrs Lane (paragraphs 79-88, above).

    At all three levels, the choice of treatment towards cure, over rapid death, is dominant: irrespective of any likelihood of delayed and/or serious side effects of curative treatment.

90. This 3-part evaluation has been presented in detail (paragraphs 67-89, above), in the hope that it will help anyone aware of similar AML situations in the pre-1991 era, to fully understand the natural likelihood of most patients' choice for cure.

91. On this basis, it would be illogical, retrospectively, to criticise leukaemia specialists or blood services in the 1980s for contributing to and/or accepting the clinical consensus at that time, as documented in the Penrose Inquiry, that: *'NANB Hepatitis was thought to be rare'* and, because of the paucity of clinical symptoms and signs, *'was generally thought to have a benign prognosis'* and, correspondingly, that the *'risks for the patient'* through transmission by transfusion *'were thought to be low relative to the risks associated with the conditions for which they required blood transfusion.'* (paragraph-38 with table, above).

92. For anyone left in any doubt about this, there is a simple test: namely, to calculate what the outcome would have been in the 1980s, had clinical suspicions about NANB hepatitis (paragraphs 38 & 39, above) led to the withdrawal of platelet support for AML treatment and, thereby, the prevention of any curative outcome.

93. In 1985 the UK population was ≈56.5-million and the annual incidence of AML was ≈4 per 100,000 (retrospective approximation from Cancer Research UK data for the period 1993-2016). Therefore, the UK incidence of AML for 1985 was ≈2,260; i.e. ≈22,600 cases for the whole decade, all of whom would have died very quickly without curative treatment and platelet transfusion support. This would have been a shockingly large number of patients dying within a few weeks of diagnosis if treatment had been withheld through over-cautious clinical consensus.

94. It is reasonable to infer that such a policy would have resulted in public outrage, press coverage along the lines of *'The worst treatment disaster/scandal in the history of the NHS'* and, perhaps/probably, judicial review under the common law offence of *'manslaughter by gross negligence'* (i.e. prior to the Corporate Manslaughter and Homicide Act of 2007).

95. Such a hypothetical cull of AML patients, through non-treatment would have ensured that none would have been infected with HCV and, consequently, that there would have been zero natural history of transfusion-transmitted-HCV in AML in the 1980s.

96. By way of a partial comparison (cf. paragraph-78, above), it may be helpful to be aware of the quality of life experienced by severe haemophiliacs who do not receive factor-VIII replacement therapy, as retrospectively documented in a paper by Ikkala and others, titled, *'Changes in the life expectancy of patients with severe haemophilia A in Finland in 1930-79'* (Br J Haematol. 1982, 52:7-12). The authors indicate a median survival of 7.8 years. Such patients are unlikely to reach their teenage years, and their entire childhood will be punctuated by intermittent spontaneous bleeding into joints and soft tissues, by severe pain, and by progressive disfigurement and disability, and premature death. Correspondingly, the parents must endure the emotional pain and grief of watching and supporting their children through their short lives of progressive painful debilitation.

97. In reality, for AML, and perhaps uniquely, it is likely that most patients treated curatively in the 1980s would have had a probability of collateral HCV infection, similar to their probability of cure, i.e. ≈20% (see paragraphs 73-78, above): and only those cured would live long enough to show signs and symptoms of hepatitis in the later period of their longevity, and/or be testable for HCV from 1991.

98. The uniqueness of these circumstances — that the probabilities for AML cure, and for co-infection with HCV, were so similar — also includes:
    i. the lack of any alternative treatment, apart from no treatment;
    ii. the lack of any alternative support product, apart from the essential platelet transfusion requirements provided exclusively by NHS blood services.

    Consequently, there can be no retrograde criticism of blood services in the context of foreign and/or commercial and/or paid-donor sources of platelets.

99. Long-term survival for AML patients in the 1980s did not prompt public outrage, nor was it heralded as the worst therapeutic disaster for AML patients in the history of the NHS; nor should it now. It was a period of major advances in AML therapy (paragraph-21.ii, above), supported by prior advances in platelet provision and transfusion practice (paragraph-21.i, above), but complicated by the inadvertent transmission of occult and undetectable NANB infection.

100. Furthermore, the long-term follow-up for the longest survivors would yield, following the implementation of HCV testing in 1991, patient-by-patient contributions of clinical and scientific data to the cumulative understanding of the natural history of HCV in AML (cf. paragraph-95, above).

101. All patients are unique. Mrs Lane was particularly unique in being the first AML patient in Wales whose remission induction therapy was supplemented with ABMT, and who remained in complete remission for the remaining 30-years of her life, compromised by infection with HCV for the last 29-years. This means that her clinical history and data, including much of the content of Mr Lane's statement (WITN2365001), should make their own unique contributions to the ongoing cumulative R&D in these areas.

102. The ≈20% likelihood of HCV infection by platelet transfusions, within the curative treatment of AML, in the 1980s, uncomplicated by any possibility of invoking alternative therapies or infective agents, provides important reference data on the natural history of HCV (paragraphs 97-101, above). Accordingly, this should quash any public clamour that it was preventable: it was not (paragraphs 92-95, above). It may be worth considering that such data could act as a blame-neutral comparator, relative to any wider inquiries into other clinical areas compromised by transfusion-transmitted HCV.

f- <u>Retrospective Reality Check for Health Related Quality of Life</u> (HRQOL)

103. Mr Lane's statement (WITN2365001), and the harrowing content of much of it (paragraphs 10 & 83, above), emphasises that Mrs Lane *'was determined to try to enjoy a reasonable quality of life',* (paragraph-83.ii, above), but also that, at a fundamentally crucial point in time: *'As a result of* [her] *infection with Hepatitis C, she was extremely down ..... and indicated she simply wanted to be left alone to die at home .....'* (paragraph-83.v, above).

104. It follows that quality considerations over time, throughout the 30-years of AML remission, are important to note. In a relevant paper by M. J. Cheng and others, titled, *'Adult Acute Myeloid Leukemia Long-term Survivors'* (J Leuk [Los Angel]; 2014, 2(2): doi:10.4172/2329-6917.1000135) the following definitions are given:

> *'A person's quality of life encompasses political, societal/environmental, familial, and health system factors, while health related quality of life (HRQOL) focuses on the effects of health care, illness and treatment on quality of life.'*

105. Mr Lane's account is informative, and — without extensive cross-referencing to specific paragraphs — the following progression can be noted, in accordance with the basic principles introduced previously (paragraph-72, above), in relation to the combination of therapeutic complications, both physical and psychological, and in relation to onset-timing and the magnitude of intensity, progression and duration (paragraph-72, above):
    i. ***hope of cure***, in choice of intense therapy, irrespective of future side-effects;
    ii. ***hope of cure***, in sustaining physical and psychological endurance required for successful remission-induction therapy, and later supplementation with ABMT;
    iii. joyfully ***enhanced hope of cure*** following successful ABMT;
    iv. growing ***confidence in the likelihood of cure*** as year-by-year checks progress;
    v. increasing ***realisation of residual physical limitations of early side-effects*** of curative treatment (shingles, blindness and radiation burns) with worsening of some;
    vi. potential for a ***progressive psychological burden of ongoing limitations*** posed by undiminished, or even worsening, early side-effects (e.g. 105.v);
    vii. ***profound shock at the unexpected notification and confirmation of infection with HCV***, coinciding with the cumulative reality of 12-years of AML remission (105.iv), but also conflicting with it to cause a progressive erosion of hopefulness;

viii. ***consequent depression***, at a time when symptoms and signs of Hepatitis C may not yet have become evident;

ix. 18-more-years, in which the year-by-year progressive assurance of AML-cure (105.iv), would be emotionally and psychologically undermined, and eventually overwhelmed, by the ***unwelcome knowledge of the physically unfelt, seemingly dormant and unreal, presence of HCV;***

x. ***the eventual, and eventually hopeless, emergent reality of progressive physical and psychological debilitation, always displacing and belittling the assurance of AML-cure, through the relentless year-by-year destructive advancement of Hepatitis C, until eventual death***.

106. From various paragraphs, the foregoing list reveals the importance of HRQOL data for long-term AML survivors treated curatively in the 1980s. These data extend the earlier questions (paragraphs 70, 72, 76 & 81), and the answers proffered (paragraphs 86-88), by asking: *'Would Mrs Lane have preferred the diagnosis of HCV, as the surprise of 1997, or at the time of infection, in 1986, and have to live with the lurking uncertainties for 11-years longer than she did?'*

SUMMARY towards A BALANCED OVERVIEW

107. Mr Lane's statement (WITN2365001) presents the extraordinary uniqueness of his wife's 30-year remission from Acute Myeloid Leukaemia (AML), sadly superseded by infection with the Hepatitis C Virus (HCV) acquired from a platelet transfusion during her Autologous Bone Marrow Transplant (ABMT), in 1986: the first of its kind in Wales/UK, implemented as radical consolidation, after 7-courses of intensive curative remission-induction chemotherapy in 1985. Consequent non-transfusion-related side-effects included: shingles and residual unilateral blindness, post-radiation burns etc.

108. Mr Lane's statement (WITN2365001) emphasises that his, and Mrs Lane's, view of blood services changed after the surprise notification in 1997, and subsequent testing, that confirmed transfusion-transmitted HCV-infection 11-years previously, in 1986. It was a profound shock, and his statement includes harrowing details of the eventual emergence of clinical signs and symptoms and subsequent progressive physical debility, including deep psycho-emotional fluctuations, culminating in death in 2015.

109. Mr Lane's statement (WITN2365001) alleges that in 1985/6 I stated — during many discussions with him, and in comments to other people, patients, doctors and a research committee — that *'All Welsh blood was/is fully tested'*: he regarded this to be clearly wrong/misleading because it did not include HCV testing. My original response (WITN3604001; also paragraphs 3-7, above) emphasised that although this was hearsay, the term would have been consistent with professional consensus at that time and, in particular, was logically valid given that HCV was not discovered until 1989 and did not form part of *'full testing'* in the UK until 1991. I also indicated that Mr Lane's statement contained a range of inconsistencies and revealed a lack of awareness and/or confusion about some aspects of blood service development and procedures.

110. This Addendum (WITN3604005), as a further statement to my original response (WITN3604001) to Mr Lane's statement (WITN2365001), presents a 50-year framework of multidisciplinary Research & Development (R&D), encompassing Clinical Haematology & Transfusion Medicine and Science & Hepatitis Virology. The overall intention is that the detail provided, and the accompanying logical arguments, may help Mr Lane and his family – and others who may know of AML patients treated curatively in the 1980s – to a deeper, relevant and balanced understanding of the cross-disciplinary complexities involved in the medical advances in such cases, at that time (paragraphs 8-12, above). Also, how some knowledge of the cumulative evolution of these endeavours, over multiple decades, may afford a fresh perspective on the integral role of blood services, that may not necessarily be critical.

111. The relevant interlinked cause-and-effect advancements in Clinical Haematology & Transfusion Medicine and Science (paragraphs 15-28, above; 1st-diagram in WITN3604006), are that:
    i. the intentionality of R&D in Clinical Haematology in the 1980s was towards intense, potentially curative, treatment for AML, including supplementary ABMT, which carried known significant risks of intensity-related side-effects (morbidity);
    ii. this (111.i) was made possible by prior R&D in Transfusion Medicine and Science, in the 1970s, that led to massive improvements in the storage and supply of platelets by blood services, and became the indispensible support requirement for curative AML therapy, in the 1980s.

112. Subsequent reciprocating cross-links between R&D in Hepatitis Virology & Transfusion Science (paragraphs 29-62, above; 2nd-diagram in WITN3604006), are:
    i. Transfusion-transmitted NANB Hepatitis was under consideration in the 1980s, as being, in the absence of a known agent/test, of minor concern relative to transfusion benefits for patients, and particularly in the specific context of AML, where avoidance of transfusion was not an option;
    ii. Once HCV as the causal agent of NANB Hepatitis had been discovered (1989), and routine testing had been implemented in the UK (1991), a very complex and intricate tapestry of disease transmission *loops & links* began to emerge through tracing studies, based on two routes, in which the ***2nd***, loops back into the ***1st***:
        - either, ***1st, from within blood services*** (paragraphs 53-56), from an HCV-positive donor → previous donation records → all manufactured products → all transfusion recipients;
        - or, ***2nd, from within clinical services*** (paragraph-57), from an HCV-positive patient → records of patient's transfusion history, in all locations → referral of each transfusion record (potentially more than one; potentially each from a different donor) → blood services → identification, contact, and HCV testing of all implicated donors → each HCV-positive donor then followed-up as in the first bullet-point.

113. The last part of this Addendum uses the preceding multidisciplinary R&D framework as a basis for developing a patient-specific overview of intensified curative treatment for AML, in the 1980s (paragraphs 63-106, above; 3rd diagram in Exhibit WITN3604006 plus 2 expanded graphs). Post-1991 R&D data/reports are retrospectively projected back to 1985 (paragraphs 73-76, above) in order to understand better how Mrs Lane's clinical history contributes uniquely to the uniqueness of curative AML therapy, at that time.

114. Mr Lane's concerns that he had been misled by the term *'full testing'*, in 1985/6, because it did not include HCV, were stated under the heading of *'Consent'* and that *'of course* [his wife] *needed to receive blood platelets as a result of the treatment'* (WITN2365001, Sections 4.1-4.5): but this left an impression that the consent was linked to the assurance of *'full testing'*; and also left doubt about whether this would have been so, if Mrs Lane had known the real risks of HCV transmission at that time.

115. These real risks drawn from post-1991 data/reports, can be estimated as follows:
    i. incidence of HCV positive donors at outset of routine HCV testing =0.066%;
    ii. maximum mean-number of donor platelets for curative AML therapy =302;
    iii. risk of HCV from 302 platelet support transfusions (i.e. [115.i] x [115.ii]) ≈20%;
    iv. AML 10-y. survival in women (Cancer Res. UK), interpolated for 1985/6 ≈20%;

    THEREFORE likelihood of AML cure ≈ (20%) ≈ risk of platelet-transmitted HCV.

116. The uniqueness of this for the natural history of transfusion-transmitted HCV during curative treatment of AML, in the 1980s, is that:
    i. many patients would have been infected through platelet transfusion support (likelihood proportional to total dose, relative to 1 in 5 [≈20%] for maximum dose);
    ii. no alternative support — only platelets supplied exclusively by UK blood services;
    iii. only those cured would live long enough to develop symptoms of HCV (116.i);
    iv. to have withheld support in the UK, 1980-89, the non-treatment consequence would have been ≈22,600 deaths, each within a few weeks of AML diagnosis.

117. These unique factors should preclude any criticism of *'therapeutic disaster'* for the clinical management of AML in the 1980s. Such a view could only be true if treatment were to be withheld, allowing all patients to die quickly, with no chance of cure — no 30-year survivors — and no opportunity for retrospective R&D. Mrs Lane's unique clinical history forms part of the unique statistical data pertaining to the natural history of NANB/HCV Hepatitis in AML in the 1980s.

118. In general, patient-specific retrospective statistical and experiential projections seem to indicate strongly that most, if not all, AML patients in the 1980s would have chosen curative therapy, rather than none, irrespective of long-term or hidden side effects.

119. However, considerations of long-term side-effects in Mrs Lane's case, in relation to health-related quality of life (HRQOL), lead to the question of whether she would have preferred to know in 1986 that she had hepatitis, and live with the knowledge, uncertainty and anxiety of that for 11-years: rather than waiting until 1997 for a surprise introduction to the same knowledge and consequent emotional burden?

120. Transfusion-transmitted NANB/(HCV) in the 1970s and 1980s, in general, may be a *natural disaster*, but not as we have come to understand the term — by the suddenness of its enormity — but, rather, by the enormity of its period of immeasurable and unpreventable invasiveness (20+ years, pre-1991). It became a *natural therapeutic disaster* once it became measurable, researchable and manageable. Relief and resolution of natural disasters is usually managed by different organisations working cooperatively together towards a common goal, as fast as possible. For the case above, the narrative focuses on the R&D *links & loops* between Clinical Haematology, Transfusion Medicine and Science & Hepatitis Virology, stretching back over 5-decades.

121. Correspondingly, the National Institute of Diabetes & Digestive & Kidney Diseases (in the USA) published a research update on June 9, 2016, titled: *'Story of Discovery: Hepatitis C: from non-A, non-B hepatitis to a cure.'* and commented that: *'although the narrative is not quite finished, the battle against hepatitis C is evolving into one of the biggest modern success stories in scientific research.'*

122. In addition, an apt piece of ancient advice, from a re-calibrated militant with a change in awareness and focus, is: *'whatever is true, whatever is honourable, whatever is right/just, ... whatever is of good report, if there is any excellence and anything praiseworthy, take account of these things.'* (Bible, Phil 4:8-9).

123. **In Conclusion**, I hope that this Addendum will achieve some, if not all, of its informative intentions, aimed towards any readers with a retrospective interest in the history of AML in the 1970s and 1980s, and that the uniqueness of platelet-transmitted NANB/HCV, as an unavoidable risk/complication of the intensive curative treatment of AML in the UK in the 1980s, will encourage the following further considerations:
    i. that it should be regarded as a *blame-less* part of the still-evolving natural history of transfusion-transmitted HCV;
    ii. that it could be regarded as a relevant reference comparator, for evaluative cross-correlation with other clinical areas of inquiry into transfusion-transmitted HCV;
    iii. that quality of life data, for long-term survivors, could be used in retrospective R&D studies, including whether patients/relatives surprised by an HCV diagnosis — through look-back long after infection — might have preferred that delay, rather than to live sooner (as infected) in the knowledge of the lurking presence of HCV.

Statement of Truth

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

Signed GRO-C

Dated 27 MARCH 2020

Table of exhibits:

Date	Notes/ Description	Exhibit number
27 March 2020	A 7-page sequence that presents three detailed diagrams and two expanded graphs, designed to summarise different aspects of 50-years of Cumulative Multidisciplinary R&D: the included numbers correspond with the numbered paragraphs of the Addendum which provide the explanatory narrative for the schematics of this exhibit.	WITN3604006