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INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DR NICOLA CONNOR

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Section 1: Introduction

1. I am Dr Nicola Connor. My date of birth is GRO-C and my professional address is UKHSA, 61 Colindale Ave, London NW9 5EQ. I received an MBBS from University College and Middlesex School of Medicine, London in 1991; an MSc from London School of Hygiene and Tropical Medicine, London in 1996; and I have been a member of the Faculty of Public Health since 1999 (Fellow since 2008).

2. I am a Consultant Epidemiologist in the HIV & STI Division of the UK Health Security Agency ("UKHSA") and currently interim Head of the HIV section. Previously, I have worked on the national chlamydia screening programme and HIV testing. From 2000 to 2002, I was seconded to the Department of Health ("DH") as a Senior Medical Officer in the Creutzfeldt-Jakob disease ("CJD") policy unit. I then led the CJD section at the Health Protection Agency ("HPA") from 2002 to 2012, during which time I was also medical secretary to the CJD Incidents Panel.

3. The following table outlines my employment history:

Table 1 – Employment History

May 2012-present	Consultant Epidemiologist HIV & STI Division (chlamydia screening programme, HIV testing, HIV section).
March 2002-May 2012	Consultant Epidemiologist. Head of the CJD Team, Medical Secretary to the CJD Incidents Panel. Health Protection Services, Colindale, HPA.
Nov 2000-Feb 2002	Senior Medical Officer: CJD Policy Unit, Department of Health (secondment from the Public Health Laboratory Service ("PHLS")).
1999-2000	Senior Medical Officer: Environmental Transmission of Infection Unit. Secretariat for the CMO's Communicable Disease Strategy, Department of Health (secondment from

	PHLS).
1996-1999	Senior Registrar: PHLS Communicable Disease Surveillance Centre.
1994-1996	Research Registrar: PHLS Communicable Disease Surveillance Centre.
Maternity/other leave	I took the following periods of maternity / childcare related leave: April 2000-Nov 2000 May 2002-Dec 2002 March 2007-Feb 2008 Oct 2004-Jan 2006

4. The HPA, the predecessor to Public Health England ("PHE"), which has since been superseded by the UK Health Security Agency ("UKHSA"), was a non-departmental public body set up by the UK government in 2003, to protect the public from threats to their health from infectious diseases and environmental hazards. I am aware that the HPA worked closely with the National Blood Transfusion Service ("NBTS") and the Blood Products Laboratory ("BPL") to protect public health. There was a joint NHS Blood and Transplant ("NHSBT") / PHE Epidemiology Unit. This co-led the Transfusion Medicine Epidemiology Review ("TMER"), a collaborative project between The National CJD Research & Surveillance Unit ("NCJDRSU") and the UK Blood Services. The main purpose was to investigate whether there is any evidence that CJD or variant Creutzfeldt-Jakob disease ("vCJD") may have been transmitted via the blood supply. I worked with Dr Pat Hewitt on vCJD blood issues. She was employed by the National Blood Service and was a member of the CJD Incidents Panel ("CJDIP"). I understand that Dr Hewitt has given evidence to the Inquiry and she would be best placed to address issues relating to the National Blood Service.

5. During my secondment in the Department of Health (2000-2002), I was a member of the Department of Health/Medical Research Council ("DH/MRC") Research Advisory Group on Transmissible Spongiform Encephalopathy ("TSEs") and an observer on the Advisory Committee on Dangerous Pathogens ("ACDP") Working Group on TSEs.

6. I have not previously given evidence or been involved in any other inquiries, investigations, criminal or civil litigation in relation to human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or vCJD in blood and/or blood products.

7. As head of the CJD section for the HPA, I was responsible for notifying patients that the CJD Incidents Panel had advised that they had increased risks of CJD. This included working with UK Haemophilia Centre Doctors Organisation ("UKHCDO") and other medical groups, doctors, hospitals responsible for patient care, and with patient organisations. I worked closely with the Department of Health, devolved administrations and blood services. My team was responsible for carrying out individual risk assessments, producing information and co-ordinating the notification exercise.

Section 2: Actions and Decisions

8. We worked with professional bodies and patient groups (see further below for details) to disseminate information on the risk of vCJD and blood/blood products. We also worked through the health protection/public health structures to share information – eg. health protection briefings and The Health Protection Report ("HPR"). We liaised with our counterparts in the devolved administrations as we had a UK-wide remit [WITN7091015]. Through our Department of Health contacts, we also worked with the hospitals to disseminate information to hospitals when appropriate.

9. As far as I am aware, I was not involved in, and I do not remember advising on risk reduction measures such as donor selection and exclusion policies; importation of plasma from the USA and elsewhere; leucodepletion and prion filtration; product withdrawal, quarantine and recall; or surveillance

infrastructure. I was aware of these issues, but do not recall that I gave advice regarding or implemented these policies.

10. The National CJD Surveillance Unit, Edinburgh, set up and ran the national surveillance system for CJD. I worked closely with this group over many CJD issues. We were involved in a separate project - the enhanced surveillance of people at risk of CJD.

11. I do not remember having any criticism of the above measures. My general view was that public health policies regarding patient safety and CJD risks were precautionary and aimed at minimising any potential risk.

12. In my view the Department of Health generally accepted CJD Incident Panel advice. The Inquiry has referred me to and provided a copy of a letter dated 16 February 2011 in which I advised the GP of a patient who had been notified of his increased risk of vCJD that the MRC Prion Unit had developed a blood-based assay for the detection of prion activity in vCJD [PHEN0002385]. I was referring to a prototype test for vCJD, which was being developed by the National Prion Clinic and is still mentioned on its website. This test was discussed in a paper published in the Lancet in 2011 "Detection of prion infection in variant Creutzfeldt-Jakob disease: a blood-based assay – The Lancet" [WITN7091002]. I do not know whether it is usual for a prototype test to be advertised on the NHS website.

Section 3: Surveillance

13. Surveillance of vCJD was based on clinical diagnosis and investigative tests. This would be effective at picking up unusual cases of young people with dementia/ataxia. However, we were concerned that this could miss cases where vCJD was not suspected eg. in elderly with higher rates of dementia. As

relatively few post-mortems are carried out in this group, there was always a concern that cases might have been missed.

14. In addition, we were concerned that infected people may have been missed because they never had/or had not yet developed symptoms. This is why my colleague, Professor Noel Gill, set up a national archive of tonsillar and appendix tissues, so that they could be tested anonymously for prion disease, thus revealing the underlying prevalence in the country.

15. I do not think that vCJD not being a notifiable disease was a particular problem in terms of surveillance. The problem was not having a non-invasive test for picking up pre-clinical and subclinical diseases.

Section 4: Notification exercises

16. In relation to the CJD 1997, 1999 and 2000 notification exercises, I was not working on these notification exercises. I started work in the CJD policy unit of the Department of Health in November 2000.

2004 Notification Exercise

17. In 2004 the HPA and the UKHCDO notified patients who had received plasma products manufactured using plasma from donors who had subsequently developed vCJD. As head of the CJD section, I was initially responsible for preparing for and then leading this notification, including the assessment, management and communication of public health risk, and liaising with key stakeholders. The notification started in September 2004, and Dr Kate Soldan took over my role when I took a 15-month career break (for childcare) in October.

18. The CJDIP considered ethical aspects of the impact of its work from the very beginning. Much of the public consultation around the Framework document [WITN7091003] focused on ethics and risks/benefits to patients.

19. The Framework document referenced above sets out the principles of the Panel's advice, which include the ethical issues surrounding notification: 'Incidents should be managed according to the following principles:

- To protect patients from the risk of acquiring TSEs in healthcare settings.
- To provide consistently high-quality advice and information to people who may have been put at risk.
- To respect where possible the wishes of those who do not want to be informed.
- To be open about the risk of acquiring TSEs in healthcare settings and the scientific uncertainties surrounding this risk.
- To increase knowledge about the risk of spreading TSEs through medical procedures.
- To protect the confidentiality of infected patients and those at risk of acquiring TSEs.
- To ensure that, wherever possible, actions taken to protect the public health do not prejudice individual patient care.'

20. There were many CJDIP discussions about the impact of this difficult information for patients and their families; issues with openness and transparency; and the difficulties surrounding the very uncertain nature of the risks involved. The Panel debated the ethical impact of its decisions many times over the years. The Panel included lay members, a psychologist, a lawyer, two ethicists (Dr Bobbie Farsides and Dr John Saunders) as well as doctors and scientists.

21. Another example of the Panel's detailed ethical considerations can be seen in a letter regarding giving information to an at-risk patient [DHSC5167217].

22. In addition, the HPA organised a seminar on the ethical aspects of a potential blood test for CJD in 2005 [DHSC5415552].

23. The criteria used to identify those who should be notified is in the vCJD and plasma products report 2005; I have outlined this criteria below [WITN7091004]:

24. 'In September 2004 the Health Protection Agency (HPA) together with the Scottish Health Protection Centre for Infection and Environmental Health (SCIEH), co-ordinated a major patient assessment and notification of possible exposure to vCJD through plasma products in the UK. This was a part of the public health response to reduce the possibility of onward transmission of vCJD.'

25. 'The aim of the patient notification exercise was to implement certain public health precautions in order to reduce the risk of further transmission of vCJD. This required the identification and the notification of plasma product recipients who had received sufficient implicated product to be considered 'at-risk' of vCJD infection.'

26. 'The level chosen at which patients were considered 'at-risk' through plasma products was exposure to a potential infectivity of $0.02ID_{50}$ (ie. 1%) or greater, to be consistent with decisions made for patients exposed through surgical instruments. This decision followed the recommendation from a Panel sub-committee in April 2003.' [HCDO0000254_119]

27. 'Estimates of potential infectivity in whole blood, blood components and plasma fractions from a donor with vCJD were estimated by a specially commissioned risk assessment [...]'

28. A plasma products risk assessment based on precautionary assumptions had been carried out by DNV (Des Norske Veritas, an accreditation body) on behalf of the Department of Health. [NHBT0008380 and MHRA0007248] This risk assessment provided estimates of infectivity within the different plasma fractions in blood. The Department of Health had constructed a risk calculator which used this risk assessment to estimate the infectivity in units and vials of plasma products used to treat patients.

29. The HPA further developed the risk calculator and applied it to batches of plasma products that had been sourced from donors who later developed vCJD. This was discussed by the CJD Incidents Panel in February 2004, [DHSC0006557] and at technical sub group meetings of the CJD Incidents Panel in March 2004 and April 2004. [DHSC0004206_071 and WITN7091010]. This calculated the potential infectivity per unit of plasma product. These plasma products were grouped according to infectivity. The CJD Incidents Panel used a 1% additional risk cut off level to decide whether exposed patients should be considered at risk of vCJD for public health purposes.

30. Again, quoting from the vCJD and plasma products report 2005 [WITN7091004], 'Patients with bleeding disorders and congenital antithrombin III deficiency, and those with primary immunodeficiencies, were in regular receipt of plasma products. In addition, some patients with other conditions, including secondary immunodeficiencies, certain chronic neurological conditions, allogeneic bone marrow transplant recipients, some autoimmune illnesses, plasma exchange recipients, patients with severe burns, patients with acquired antithrombin III deficiency and those requiring rapid warfarin reversal may also have received sufficient implicated product to be considered 'at-risk', i.e. exposed to a potential 1% risk ($0.02ID_{50}$) or more.'

31. Continuing quoting from the vCJD and plasma products report 2005: 'The CJD Incidents Panel recommended the following action in relation to each batch of

implicated product, according to the likelihood of recipients surpassing the 'at-risk' threshold [...]:

HIGH: These batches should be traced and the individual recipients considered 'at-risk' of vCJD for public health purposes.

MEDIUM: Efforts should be made to trace these batches and to assess the potential additional risk to individual recipients to determine if special precautions should be taken for public health purposes.

LOW: These batches do NOT need to be traced and the recipients do not need to be informed. The potential additional risk from particular implicated batches of albumin 20%, intramuscular human normal immunoglobulin, anti-D, and from factor VIII products manufactured using implicated albumin as an excipient, is considered negligible.'

32. 'Patient group management strategies were developed through negotiation with professional and patient group representatives, with the aid of expert opinion of condition-specific professional representatives, the UK national blood services, and NHS Trust medical directors and pharmacists contacted through the HPA/CJD Incidents Panel network'.

33. 'Arrangements were made for each patient group on the basis of:

- their likelihood of surpassing the 'at-risk' threshold;
- estimated numbers of patients possibly affected (obtained from professional representatives using patient registers and assessing the proportion of patients receiving UK sourced plasma products for treatment during the timeframe of exposure);

- the feasibility of identifying which batches had been received, and at what doses, for individual patients using structures and systems for tracing that existed during the timeframe of exposure; and
- the possible impact of the public health measures to be implemented.'

34. 'Three main patient groups were identified, and notification strategies were developed for each group as described below [...]:'

PATIENTS WITH BLEEDING DISORDERS

35. 'These were patients cared for by specialist haemophilia centres and doctors that are members of the UKHCDO. It was considered unlikely that there were significant numbers of patients cared for by units or individuals not associated with the organisation.'

36. 'Information on batch exposure had been kept rigorously on paper and electronic format. It was considered possible to trace the individuals exposed to implicated batches and calculate their exposure to potential vCJD infectivity, although some logistic difficulties were anticipated.'

37. 'The UKHCDO and Haemophilia Society argued that since a single dose of implicated plasma concentrate would be sufficient to place a recipient 'at-risk' and because future batches were likely to be implicated as more vCJD cases arise, all patients with bleeding disorders treated with UK-sourced pooled factor concentrates or antithrombin between 1980 and 2001 should be considered 'at-risk' and asked to take public health precautions, rather than just those who had received the known implicated batches (i.e a 'population' approach, with individuals' 'at-risk' status not dependent on assessment of their potential batch-specific exposures, was taken with this patient group). [...]'

PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

38. 'The professional association for health professionals caring for individuals with these conditions is the UK Primary Immunodeficiency Network (PIN). It was considered unlikely that there were significant numbers of patients cared for by units or individuals not associated with the organisation.'

39. 'This group of patients had experience of previous notifications of batches contaminated with hepatitis C. Information on batch exposure had been kept rigorously on paper and electronic format. It was considered possible to trace the individuals exposed to implicated batches and calculate their exposure to potential vCJD infectivity, although some logistic difficulties were anticipated.'

40. 'It was considered possible that a very few patients may have received sufficient implicated product to be affected. UK PIN preferred an 'individual' approach with only those patients assessed to have received sufficient of an implicated batch being asked to take public health precautions. The patient organisation, the Primary Immunodeficiency Association (PIA), expressed a preference not to notify because of the uncertainty involved, but agreed these patients could not be excluded from the public health notification [...]'.

PATIENTS WITH OTHER CONDITIONS

41. 'The remaining patients were cared for by different specialities and without a condition-specific professional organisation, where treatment with plasma products may have been 'off-licence' and batch information may not have been as rigorously recorded as for the groups above.'

42. 'An estimate of the expected numbers who may be considered 'at-risk' was not possible. The only way for these individuals to be traced and their potential exposure assessed was through NHS hospital trusts. Informal feasibility studies by representatives of the UK national blood services and Scottish Centre for Infection and Environmental Health (SCIEH), and discussions with medical directors and pharmacists suggested that there would be great variability in the ability of Trusts to trace implicated batches to individual patients and assess potential exposure.'

43. 'Despite the potential difficulties, it was considered important that such efforts be made, although only where batches were traceable and recipients could be easily identified as having received implicated batches would the trace-back effort be considered proportionate to any possible public health benefit. Clinicians would be asked to forward individual batch exposure details to the HPA for assessment of whether the patient should be considered 'at-risk'.' [ABMU0000056]

44. This report was presented to the CJDIP in May 2004 - Minutes CJDIP May 2004 [PHEN0000502]. The panel agreed that:

(1) Products would be stratified by estimated infectivity.

(1) For patients with clotting disorders (haemophilia A and B, von Willebrand disease and congenital antithrombin III deficiency):

1. A single dose of factor VIII (intermediate implicated), factor IX or antithrombin would be sufficient to cross the 1% risk threshold.
2. Public health measures to reduce the risk of infection would be applied to all patients receiving plasma derived, UK sourced products since 1980: the 'umbrella approach'.

3. Patients would be offered the choice to discover whether they had received an implicated product and individual risk assessments would be recorded on the UKHCDO haemophilia database for the long-term follow up of potentially exposed patients.

(2) For patients with primary immunodeficiency syndrome (PID):

1. Multiple doses of implicated intravenous immunoglobulins would be required to cross the 1% risk threshold.
2. The HPA would carry out, record and feedback an individual risk assessment for each recipient of an implicated plasma product. Clinicians would then inform the patients who had received sufficient product to cross the 1% risk threshold and patients would be asked to take public health precautions.

(3) For other groups of patients:

1. High volumes of implicated intravenous immunoglobulin and albumin products would be required to cross the 1% risk threshold.
2. Patients in less well defined groups who may have received sufficient implicated product to pass the threshold might be difficult to trace. A feasibility study would be undertaken in relation to this group. However, the notification of the first two groups of patients would not be delayed by this work.
3. Where possible, an individual risk assessment would be carried out and patients who had received sufficient product would be asked to take public health precautions.

(4) Patients who had received minimal risk products (human normal immunoglobulin, anti-D and factor VIII where the excipient is implicated) would not need to be contacted since it is highly unlikely that any patient would have received the very large doses necessary to cross the threshold.

However, factor VIII recipients would be contacted as part of the 'umbrella approach' for patients with clotting disorders.

(5) The HPA would work with the devolved administrations to ensure the notification took account of the different health organisation structures. CMO would be kept informed about the progress of the notification, including any problems with contacting recipients other than those with clotting disorders or PID. The notification process for these patient groups is summarised in a diagram [HCDO0000656].

45. The rationale for deciding what information was to be given to patients and how it was to be provided was from the vCJD and plasma products report 2005; I have outlined the criteria below [WITN7091004]:

46. 'The proposed management strategies for each patient group and the underpinning information were presented in written and verbal formats to several meetings of the CJD Incidents Panel and Department of Health, and were also presented at workshops for extended groups of professional and patient representatives. Strategies were repeatedly discussed with all stakeholders until consensus was achieved. The proposed approaches were finally endorsed by the CJD Incidents Panel and Department of Health.'

47. 'A toolkit comprising 40 main documents was developed (in consultation with the many stakeholders) to support the identification and notification of 'at-risk' individuals. This included detailed instructions for clinicians regarding the notification of 'at-risk' patients, draft patient letters and clinical notes to assist in patient consultation, patient information sheets, and draft letters for communicating with other clinicians. The toolkit was tailored for the various professional groups involved in the tracing and notification of patients, for other groups who would be involved in supporting the process, and to address general public information requirements. The documents were developed so that they would be relevant for all four countries of the UK.'

48. Professional or patient organisations, support groups and other stakeholders were involved in the notification, as follows:

(a) UK Haemophilia Centre Doctors

(b) UK Primary Immunodeficiency Network of clinicians

(c) UK Medical Directors of Trusts

(d) Clinical Trials Coordinators

(e) Plasma Fractionators' UK Consignees

(f) National Blood Services

(g) General Practitioners

(h) NHS Direct & Regional Colleagues

(i) HPA Local and Regional Services

(j) Other professional and patient support organisations:

a) CJD Support Network, Haemophilia Nurses Organisation, Haemophilia Society, Human BSE Foundation, PIA,

b) ACDP TSE Working Group, CJD Incidents Panel, NCJDSU (Edinburgh), National Prion Clinic, SEAC,

c) British Society for Haematology, World Federation of Haemophilia

(k) Ministries of Health Overseas

(l) Plasma Fractionators' Overseas Consignees

(m) World Health Organisation and European Commission

49. The vCJD and plasma products report [WITN7091004] includes the patient information leaflet. The key advice for notified individuals was:

'If you have been informed that you are 'at-risk' for public health purposes, you are being asked to take the following actions in order to reduce the chance of passing on vCJD to other people: -

- Do not donate blood.
- Do not donate organs or tissues.
- Tell whoever is treating you before you undergo medical, surgical or dental treatment, so they can then arrange any special procedures for the instruments used in your care.
- It would be best if you tell your family about this in case you might need emergency surgery in the future.'

50. The patient information leaflets from the 2004 notification also contained a lot of detailed background information on CJD, risks through blood, the work of the CJDIP and contact details for help/information [CVHB0000011_003].

51. The vCJD and plasma products report 2005 [WITN7091004] also contains as Appendix D, the clinical information document which was sent to clinicians as part of the notification process. This set out the rationale and methodology for the patient risk assessment, notification and public health management. This supplemented the main letter to clinicians which contained instructions for the notification exercise [HCDO0000659 and DHSC5230781].

52. The vCJD and plasma products report 2005 explains how the notification exercise was implemented: 'By the end of December 2004, a total of 9 UK plasma donors were known to have developed vCJD. Collectively they had made 23 blood donations where the plasma had been used to make plasma products.'

53. 'The donated plasma had been used to manufacture a total of 187 batches of plasma products, comprising factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin, anti-D, and 13 batches of plasma fraction intermediate.'

54. 'These products were supplied throughout the UK and to 12 countries overseas. At the time of the notification these included 4 countries where there was considered a possibility that some patients could have been exposed to sufficient potential infectivity, according to the UK assessment, to be considered 'at-risk'[...]'

PATIENTS WITH BLEEDING DISORDERS

55. 'Within the UK, an estimated 4000 patients with haemophilia A and B and Von Willebrand's Disease in the UK would have received UK sourced plasma derived Factor VIII and Factor IX during the period 1980-2001, and therefore be considered 'at-risk'. It was considered that few patients with congenital antithrombin deficiency would have required treatment with plasma derived antithrombin.'

56. The vCJD and plasma products report stated that 'It is understood that all these patients were notified (via their haemophilia doctor) of their 'at-risk' status. Individual exposure assessments are being collected and managed by UKHCDO in collaboration with the HPA' [WITN7091004].

PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

57. 'According to the UKPIN, of the approximately 2,500 patients with primary immunodeficiencies in the UK, it is likely that 250 were treated with Vigam, of which 50 may have received implicated batches. All patients treated with Vigam between December 1996 and February 2000 were assessed and notified of their 'at-risk' status via the consultant immunologist managing their care. Clinicians were asked to send individual exposure assessment reports for 'at-risk' patients to HPA CJD Section.'

58. 'Based on information received by the HPA CJD Section in 2004, and a recent post-notification survey of the UKPIN (November 2004) it is understood that none of these patients have had sufficient exposure to vCJD implicated plasma products to be considered 'at-risk' for public health purposes.'

PATIENTS WITH OTHER CONDITIONS

59. 'By the end of December 2004, a total of 73 traceability questionnaires had been received from NHS Trusts, of which 53 reported having received implicated plasma products. Of these 16 reported being unable to trace the recipients of these products. '

60. 'By the end of December 2004, the HPA CJD Section had undertaken a total of 1826 individual exposure assessments for patients suffering from other conditions, of which 0.7% (n=12) had had sufficient potential exposure to vCJD implicated plasma products for patients to be considered 'at-risk' for public health purposes' [WITN7091004].

61. In relation to psychological support, in 2004 the HPA created a 'cadre of experts' (CJD specialist doctors and counsellors) who were available to support local teams involved in patient notifications.

62. The CJDIP included the following comments in the information leaflets, which are included as an annex to the vCJD and plasma products report 2005 "Decisions will need to be made locally regarding how patients will be informed about their potential additional risk of developing vCJD. Many patients are likely to require more than one session to discuss the implications of the news if they are to come to terms with the impact of what they have been told. Advice on managing this process may be sought from a trained counsellor" [WITN7091004].

63. The HPA conducted a small qualitative study to understand the impact of notification on patients. This was published in 2011 and found 'little evidence of sustained psychological distress' [DHSC6630790]

64. I have taken the following information from the CJDIP 7th Annual report 2007 [WITN7091005]: 'In 2006, the HPA Centre for Infections were informed that four batches of plasma products thought to be untraceable at the time of the 2004 notification had now been traced.'

2005Notification Exercise

65. My involvement in the 2006 notification exercise was that I was the consultant responsible for the HPA role in this work. I had a similar role to that in the 2004 notification exercise.

66. There were fewer ethical considerations for this notification as there was no change to the 'at increased risk of vCJD' status of the haemophilia patients who had already been informed.

67. All Haemophilia Centres were also notified through the UKHCDO of the exercise [ABMU0000053]. Patients who had received plasma products for bleeding disorders had previously been informed that they were at risk of vCJD for public health purposes in 2004. Doctors were asked to record their exposure to the newly implicated batches and this information was to be notified to the UKHCDO database. Individual exposure assessments were not routinely carried out for this group of patients. Haemophilia doctors were asked to contact their patients who are 'at risk' of vCJD for public health purposes to tell them about the newly implicated batches of Factor VIII and IX. They were asked to give patients the opportunity of finding out whether they were treated with those

clotting factors [ABMU0000053]. A patient information leaflet, similar to that used in 2004, was also to be shared with patients.

68. In September and November 2006, the National Blood Service and the Welsh Blood Service, in liaison with the HPA, wrote to a total of 131 hospitals asking them to trace individual recipients of the implicated batches [PHEN0002376_002] and [PHEN0002376_003]. At the same time, the UKHCDO notified all haemophilia centres which were asked to record any exposure to the newly implicated batches. By the end of 2006, five hospitals had been able to trace records of the doses given to patients, but none of them had crossed the threshold for increased vCJD infection risk. In May 2007 the Panel received the final report of the notification. This notification did not identify any additional patients 'at risk of vCJD for public health purposes' [WITN7091005].

69. The same arrangements regarding psychological support as for the 2004 Notification applied here (see explanation above).

70. I am aware of another blood notification exercise that took place in 2006, and I quote from the 6th Annual report of the CJDIP regarding 'Other recipients of blood donated by people who have given blood to vCJD cases (CJDIP 6th Annual report 2006) [WITN7091006].

Further 2006 Notification Exercise

71. 'Following the first two reported cases of probable vCJD transmission via blood transfusion [...] [The European School of Radiology] ESOR carried out a 'reverse risk assessment' to investigate the likelihood that a patient's vCJD infection could be the result of a blood transfusion [...]. As described in the previous annual report, the Panel had recommended that people who have

donated blood to patients who later developed vCJD, should be considered at risk of vCJD for public health purposes, unless their estimated risk is clearly below 1%. The UK CMOs requested, and then accepted, advice on managing other individuals who had received blood from these donors. The next step was for the Panel to consider additional analyses of the 'reverse' risk assessment to estimate the risks to other recipients of blood donated by people who had also given blood to vCJD cases. The UK CMOs accepted the following Panel recommendations concerning this group of blood recipients:

72. For cases where blood recipients have received blood from only a low number of donors, and therefore the implied risk for each other recipient is well above 1%, the Panel in general would advise that other recipients should be traced, informed of their potential exposure to vCJD and considered as at risk of vCJD for public health purposes.

73. For cases where blood recipients have received blood from a high number of donors (say, more than ~90), and therefore the implied risk for each other recipient falls close to or below 1%, the Panel would examine each case individually.

74. 'The UK Blood Services, Health Protection Scotland and the HPA implemented these recommendations following the public announcement in November 2005. Patients were traced and notified in 2006. In Scotland, 156 units of implicated blood components were traced to 90 recipients of whom 22 were living. Of the 20 other recipients traced in England, only three were living and definitely confirmed to have received blood components from the 'at risk' donors. These 25 individuals were notified and asked to take public health precautions. (Since April 1994, all blood transfusion recipients have been deferred from donating blood.) Of this group, 23 are known to be still living (as at 8th August 2007). According to the documents which I have reviewed (HPA Briefing Note February 2009) [WITN7091007] and the HPR article 11 June 2009

[WITN7091011], the CJDIP managed an incident concerning a person with haemophilia who had been found to have evidence of the prion that causes vCJD in his spleen at post mortem (this is discussed below).

2009 Notification Exercises

75. I have not been able to identify any other plasma product notifications in 2009. I have however identified the following event which is relevant to this period.

76. An incident was investigated in 2009, with patients being notified in 2010. In this incident a vCJD case was identified who had received blood from two UK blood donors. The incident was investigated and in 2010 eleven individuals were identified and notified that they were at increased risk of vCJD. [WITN7091016]. They were two individuals who donated blood to the individual who went on to develop vCJD, and nine individuals who had received blood from these two donors.

77. Regarding the person with haemophilia, who had been found to have evidence of the prion that causes vCJD in his spleen at post mortem, the post mortem was carried out as part of a study jointly co-ordinated by the UKHCDO and the National CJD Surveillance Unit. This was the first time that a patient with haemophilia, or any patient treated with plasma products, had been found to be infected with vCJD.

78. I was the lead consultant for the HPA for this notification, working with the CJD Incidents Panel, DH, UKHCDO, NCJDSU, and other colleagues to assess and manage risk, and communicate to affected patients and their doctors.

Notification and criteria

79. This haemophilia patient had been treated in the 1990s with several batches of UK sourced clotting factors, including one batch of factor VIII that was manufactured using plasma from a donor who went on to develop vCJD. The plasma donor developed symptoms of vCJD 6 months after donating the plasma in 1996. The haemophilia patient was in his 70s when he died of a condition unrelated to vCJD, 11 years and one month after receiving the batch of implicated Factor VIII. He had no signs or symptoms of vCJD or other neurological disease when alive [DHSC5559704].

80. Towards the end of 2008, an autopsy specimen from the spleen of the haemophilia patient gave a positive test result for PrPres (a prion particle). The NCJDSU considered this result to be a true positive, indicating that the patient was infected with vCJD.

81. As indicated above, the patient had been treated with a batch of Factor VIII that had been prepared from plasma donated by a donor who later developed vCJD.

82. The donor of the implicated batch of Factor VIII had donated blood on three different occasions. Three recipients of blood components from this donor were traced. Two had died of non-neurological causes. One, who received the implicated blood donation in 1993, was alive and under follow-up by the National Prion Clinic.

83. Four batches of clotting factors were prepared from this plasma, and a total of 257 patients have been reported to the UKHCDO as having received these batches. These figures are likely to be an underestimate due to both under reporting and under-ascertainment.

84. Plasma from the same donor was also used to manufacture 2 batches of medium risk plasma product (albumin 4.5%) and 14 batches of low-risk plasma product (albumin 20%, normal human immunoglobulin).

85. In 2004 the HPA carried out risk assessments for 82 patients who had received albumin 4.5% sourced from this donor. Forty of these patients were reported as having died at the time of these risk assessments. One patient had received sufficient quantities of plasma product to be considered 'at risk' of vCJD for public health purposes. This patient died shortly after being treated with albumin 4.5%, and was therefore not notified.

86. The infected haemophilia patient had also received blood transfusions from several donors.

87. In relation to whom the HPA consulted/obtained advice from in respect of this exercise and what ethical issues were considered, in January 2009, the HPA, UKHCDO, NBS, DH and CJDIP worked together to investigate this incident and to draft letters to haemophilia centre directors and patients.

88. The Panel reviewed the reasons behind the original decision to include patients with bleeding disorders in an 'umbrella' at risk group. This decision was taken because:

(1) It was thought that most patients with bleeding disorders had received large amounts of high-risk plasma products as part of their treatment prior to 1999.

(2) It was thought likely that there could be many future vCJD cases, some of whom would be found to have donated plasma used to make plasma products.

(3) The clotting factors used to treat haemophilia patients were high risk plasma products. Haemophilia patients generally receive repeated treatments over a number of years. At the time of the 2004 notification, it was anticipated that, as new vCJD cases were reported, some new plasma donors would be identified. For these reasons, the CJD Incidents Panel, the UKHCDO, the Haemophilia Society and the Department of Health decided to manage all patients with bleeding disorders who had received UK sourced pooled factor concentrates or antithrombin between 1980 and 2001, as at risk of vCJD for public health purposes. This was irrespective of whether they had received clotting factors from a donor known to have developed vCJD. This was the so-called 'umbrella' approach. Patients were offered the option of finding out whether or not they had received clotting factors from a donor who later developed clinical vCJD, but this information did not affect their at-risk status [WITN3775004].

(4) It was thought undesirable to have to give repeated notification messages to the haemophilia community as new vCJD donors came to light. The disruption and distress to the haemophilia community would be minimised if a single, comprehensive notification could be carried out.

89. The exercise was implemented, whereby all haemophilia centre doctors were informed on Monday 16th February 2009. They were asked to send a letter to all their patients with bleeding disorders as soon as possible [WITN7091008].

90. These communications noted that all patients with bleeding disorders who had been treated with UK-sourced pooled factor concentrates or antithrombin between 1980 and 2001 were classified as at risk of vCJD for public health purposes. Special infection control precautions and other safety measures applied to these patients. This new finding did not change this advice. This case did not change the public health vCJD 'at risk' status or management of any patients with bleeding disorders [DHSC5559704].

91. The following is a timeline of the communications that formed the Plasma Product Notification of February 2009 [See WITN7091008 for precise timings of actions]:

Monday 16th February

(1) Toolkit to UKHCDO for haemophilia centre doctors

(2) International communications to affected countries, other countries, EWRS and WHO (qv chronology of international communications for detail)

(3) HPA briefing note to LARS

(4) Clinician Groups letter to UK Primary Immunodeficiency Network, Haemophilia Nurses Association, National CJD Surveillance Unit, BPL, National Prion Clinic, ACDP TSE Working Group, SEAC, SaBTO, CJD Incidents Panel, British Society of Haematology, Royal College of Pathologists.

(5) Patient Groups letter to Haemophilia Society, Primary Immunodeficiency Association, CJD Support Network, Human BSE Foundation, CJD Alliance, World Federation of Haemophilia

92. Tuesday 17th February

(1) press release issued by HPA, supported by internal Q&A

(2) revised web page on HPA website with new text and link to 4 new information documents http://www.hpa.org.uk/vcjdplasmaproducts

93. Friday 20th February

(1) Article published in Health Protection Report

	Haemophilia doctors	Haemophilia patients	Clinician groups	Patient groups	HPA website
Actions for healthcare staff	✓				✓
Background info for healthcare staff	✓				✓
Information for patients-generic	✓	✓			✓
Information for patients-specific	✓	✓			✓
Haemophilia doctors letter	✓				
Letter for patients	✓	✓			
Clinician groups letter			✓		
Patient groups letter				✓	

Summary of Information / Advice provided to those notified as being at risk as well as to partners or family members

94. A letter was sent to haemophiliacs by their clinicians in February 2009: [ABMU0000039]:

"Variant Creutzfeldt-Jakob Disease (vCJD) and patients with bleeding disorders who have been treated with UK plasma products.

We are writing to all our patients with bleeding disorders to tell them about a person with haemophilia who has been found to have evidence of the infection that causes variant Creutzfeldt-Jakob Disease (vCJD) in his spleen at post mortem. All Haemophilia Centres are contacting their patients throughout the UK to give them this information.

Tests carried out on a haemophilia patient who died last year have shown that he was infected with the abnormal prion protein that causes variant Creutzfeldt-Jakob Disease (vCJD). The patient did not die of vCJD, and never had any symptoms of this disease when he was alive. The patient was in his 70s when he died of a completely unrelated cause. The tests were carried out as part of a research study jointly coordinated by the UK Haemophilia Centre Doctors Organisation and the National CJD Surveillance Unit.

This patient had been treated in the 1990s with several batches of UK sourced clotting factors, including one batch of factor VIII that was manufactured using plasma from a donor who went on to develop vCJD.

A final view as to how this haemophilia patient became infected with the vCJD abnormal prion protein has yet to be reached and investigations are therefore continuing to establish this.

This is the first time that the vCJD abnormal prion protein has been found in a patient with haemophilia, or any patient treated with plasma products. This patient did not die of vCJD, and the only reason we know he was infected with the vCJD abnormal prion protein is because of the research tests carried out after he had died.

We are telling you about this case so that you have the latest information about vCJD and clotting factors made in the past from UK plasma.

This new information does not change the way you will be treated.

If you have a bleeding disorder or congenital antithrombin III deficiency[1] and you received clotting factors or antithrombin made from UK-sourced plasma[2] between

[1] Congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.
[2] Factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes, as well as antithrombin.

1980 and 2001, then you should have been told that you have an increased risk of vCJD, and you should follow public health advice (see box).

Advice on how to reduce the risk of spreading CJD to other people

If you have been identified as being at increased risk of CJD, you can reduce the risk of spreading CJD to other people by following this advice.

- Don't donate blood. No-one who is at increased risk of CJD or who has received blood donated in the United Kingdom since 1980 should donate blood
- Don't donate organs or tissues, including bone marrow, sperm, eggs or breast milk
- If you are going to have any medical or surgical procedures, you should tell whoever is treating you beforehand about your at risk of vCJD so that they can make special arrangements for the instruments used to treat you
- You are advised to tell your family about your increased risk. Your family can tell the people who are treating you about your risk of CJD if you need medical or surgical procedures in the future and are unable to tell them yourself.

If you are unsure about this, and would like more information, please contact the haemophilia centre and make an appointment to come and see one of the clinical team.

Other patients (those who have not been treated with UK plasma factor concentrates) who do not have an increased risk of vCJD, do not need to take any action. Again, please contact the haemophilia centre if you are unsure about your past treatment and your vCJD at risk status.

The information from this case does not change the public health 'at risk' status of any patients with bleeding disorders.

Two patient information leaflets are enclosed: [WITN7091017] and [WITN7091018]:

'Information for people who have an increased risk of CJD', and

'Who has an increased risk of CJD?'

These are also available on the Health Protection Agency website http://www/hpa.org.uk/CJD.

We realise that you may find this new information worrying. Do contact the Haemophilia Centre if you wish to talk about this.'

95. A second letter was distributed to patients by their haemophilia clinicians in June 2009 with an update on the completed incident investigation, but with no change to public health advice.

96. The same arrangements regarding psychological support to notified patients as for previous notifications applied (see explanation above).

97. The umbrella approach to notification was informed by professionals considering their patients' best interests, and public health, based on the scientific evidence available at the time.

98. In 2012, HPA proposed that a revised plasma products risk assessment should be carried out, following a revised blood component risk assessment conducted by the DH in 2011 [Iron-Pres-01670969]. This was done in response to the lack of clinical cases in blood transfusion recipients, which suggested the assumptions in the DNV risk assessment may have been too precautionary. This led to a change in the umbrella approach in 2013. People with bleeding disorders who had only received UK plasma products between 1980 and 1989 were then denotified in 2013, and taken out of the 'at risk' group [WITN3775004].

99. One could also ask whether the 'precautionary principle' approach taken by the DH and the CJD Incidents Panel was the correct approach. In my view, this approach led the CJD Incidents Panel always to take the most pessimistic scenario in any risk assessment, to minimise any potential and very uncertain risk of transmitting CJD between people. However, the downsides of this advice were clear, expensive and real eg. distress to patients, delays in surgery, costs of disposing of surgical equipment.

100. I have reviewed the documents to which the Inquiry has referred to me - [ABHB0000054] and [ABMU0000039]. I believe this was CJDIP advice regarding the highly transfused patients and pre-surgical assessment. Letters would have been sent from the HPA CJDIP secretariat.

101. In 2009 the guidance for pre-surgical CJD assessment was revised to identify and notify highly transfused patients with ≥80 donor exposures if they present for high-risk surgery. This was agreed by the CJD Incidents Panel [DHSC5612126].

102. This guidance had been difficult to create and had been the subject of many discussions between the CJDIP and the DH about how to manage patients who had received blood or from high and very high numbers of donors. There were concerns about the potential impact on surgical instruments with uncertain numbers of patients involved.

103. Three years later, the HPA carried out an evaluation of this pre-surgical assessment initiative [DHSC6710275] and [DHSC5623932]. Between July 2009 and the end of 2012, eleven highly transfused patients had been identified in this way. Of these only four had been correctly identified prior to high-risk surgery; others were identified preceding medium risk procedures. The total number identified falls short of the estimated numbers expected (50-60 per year in England). [PHEN0000135]

104. The risk assessment underpinning this work was later revised, and pre-surgical screening changed [WITN7091009] so that it only affected patients who had >300 donor exposures. This happened in 2013, after I had left the CJD team.

105. With regards to the pre-surgical screening and patient notification of the highly transfused group of patients and in at-risk patient notifications in general, the CJD Incidents Panel was very aware of the potential impact of its advice on patients and hospitals.

106. A specific concern was the impact of advice to quarantine surgical instruments that had been used on patients who were at increased risk of vCJD. The Panel tried to reduce the impact, while still following scientific guidance from the Advisory Committee on Dangerous Pathogens ("ACDP") TSE Working Group [DHSC5348411] and [DHSC5328492].

107. The ACDP Joint working group was chaired by Don Jeffries, who was also interim chair/deputy chair of the CJD Incidents Panel. The ACDP joint working group issued guidance on the management of surgical instruments and attempted to deal with some of the problems encountered by at-risk patients and their doctors. eg. managing endoscopes, rectal biopsies [DHSC5004570].

108. I am not aware that the HPA (as opposed to the CJDIP) took measures to address any consequential disadvantage to patients from such measures, but there may have been discussion with local teams concerning specific incidents/concerns. In my opinion, the CJDIP were diligent in reviewing their guidance to minimise delays e.g. through recommending modifications to endoscopes – sheaths etc that would reduce the impact on hospitals. The CJDIP worked with the DH to recommend and fund endoscope refurbishment, to avoid adverse impact on at-risk individuals requiring surgery [DHSC5623932].

Section 5: Other Issues

109. I believe that Professor Noel Gill (former head of my department) was involved in trying to set up a post-mortem tissue archive to determine the prevalence of abnormal prion protein. He had previously successfully set up tonsil and appendix tissue archives. I have found a relevant document concerning the post mortem project, but I do not remember any additional details nor do I remember any details regarding the problems he encountered, other than that I do not believe the coroners wanted to participate [DHSC5590317 and WITN7091012].

Statement of Truth

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

Signed..... GRO-C .....

Dated.....29/04/2022.....