Witness Name: Simon Mead

Statement No.: WITN7066001

Exhibit: RLIT0000725

Dated: 23rd April 2022

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF SIMON MEAD

I provide this statement in response to a request under Rule 9 Request of the Inquiry Rules 2006 dated 22nd October 2021

I, Simon Mead, will say as follows: -

Section 1: Introduction

1. ***Please set out your name, address, date of birth and professional qualifications.***

   Professor Simon Mead, Institute of Prion Diseases, University College London (UCL), 33 Cleveland St, W1W 7FF. Date of birth GRO-C 1969.

2. ***Please set out your employment history including the various roles and responsibilities that you have held throughout your career, as well as the dates.***

   Professional History

2004-2007 MRC Investigator Scientist and Specialist Registrar National Hospital for Neurology and Neurosurgery (NHNN), London

2007 Ongoing. Consultant Neurologist NHNN and Lead Clinician NHS National Prion Clinic, UCL Hospitals NHS Foundation Trust

2007-2012 MRC Program Leader Track

2007-2010 Honorary Senior Lecturer UCL Institute of Neurology

2010-2014 Honorary Reader UCL

2012-2018 MRC Prion Unit Programme Leader

2014 Ongoing. Professor of Neurology UCL

2018 Ongoing. Deputy Director MRC Prion Unit at UCL

2018 Ongoing. National Institute of Health Research Senior Investigator

3. ***Please set out your membership, past or present, of any committees, associations, parties, societies or groups relevant to the Inquiry's Terms of Reference, including the dates of your membership and the nature of your involvement.***

2008-2019 CJD Resource Centre Oversight Committee member, Public Health England (I am unclear if this committee still meets, but not since 2019)

2008 Ongoing. Creutzfeldt-Jakob Disease Support Network Committee member

2009-13 Creutzfeldt-Jakob Disease Incidents Panel, Public Health England, committee member

2011-2019 Advisory Committee for Dangerous Pathogens Transmissible Spongiform Encephalopathy subgroup (previously the Spongiform Encephalopathy Advisory Committee), Public Health England, committee member

2018 Member NICE Guidance update (Surgical Instrument Decontamination)

2020 Ongoing. Chair Advisory Committee Dangerous Pathogens (DHSC) TSE Subgroup

4. ***The Inquiry is aware that you provided oral evidence to the House of Commons Science and Technology Committee: Blood, Tissue and Organs Screening in March 2014 (TSTC0000049). Please review the statements and views you expressed to the Inquiry and set out whether your views have changed in any way. If your views have changed since making the statement please explain how they have changed and why.***

   My views have not significantly changed. The passing of time and the absence of any more cases of vCJD transmitted by blood means that there is now a less compelling case to justify work towards a screening blood test for vCJD than there was in 2014.

5. ***Please confirm whether you have provided evidence or have been involved in any other inquiries, investigations, criminal or civil litigation in relation to the human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products. Please provide details of your involvement.***

   I provided evidence as a medical expert in a civil litigation case in 2018. This case concerned my views about the risks of vCJD related to plasma transfusion in the UK.

Section 2: Assays and Testing

6. ***During the Parliamentary Inquiry into blood, tissue and organ screening (TSTC0000049), you mentioned that there is "a consensus that the key thing to move forward is a prevalence study to try and develop a blood***

test from there". Has there been any action in relation to such a prevalence study being conducted? Please give details.

In the report I am quoted as saying, "It strikes me now that there is scientific consensus that the key thing to move forward with is a prevalence study to try to develop a blood test."

There has been a further prevalence study, referred to as Appendix III which studied the prevalence of abnormal PrP deposition in appendices removed prior to 1980, and from people born after 1996 as a control group for Appendix II, reported in Acta Neuropathol 2020 Jun;139(6):965-976. **[RLIT0000725]**

As far as I am aware there has been no action in relation to a prevalence study using blood as the analyte.

7. ***The Inquiry understands that an aspect of your role at the National Prion Clinic is geared towards the development of tests to detect prions in blood. Additionally, an assay has been developed for the diagnosis of vCJD in symptomatic individuals. Could you please outline the test and process currently used to diagnose vCJD both for those with symptoms and for those who are not exhibiting symptoms? You may wish to refer to NHBT0033626.***

Patients presenting with symptoms that raise the possibility of vCJD are referred to the National Prion Clinic and National CJD Research and Surveillance Unit. Both teams work with local clinicians to establish a diagnosis. We send a team comprising a neurologist and a nurse to visit the patient. This doctor will take a clinical history and examine the patient, review investigations acquired locally, including those that might be used to exclude other conditions, MRI brain scan, EEG brain wave test, cerebrospinal fluid testing, and genetic testing. At this initial assessment and shortly thereafter a provisional diagnosis is made, with reference to established diagnostic criteria and experience, which is usually strongly influenced by the pattern of symptoms and examination features, and characteristic features on MRI brain scan, and by cerebrospinal fluid tests. Follow up assessments might include

the option to transfer the patient to the NHNN for further investigations, which might include tonsillar biopsy, and blood assay for vCJD termed the Direct Detection Assay (DDA). The DDA can only be done at the Institute of Prion Diseases. A definitive diagnosis of vCJD is made only after post-mortem examination of the brain.

At present there is no test process to diagnose vCJD infection in people who do not have symptoms.

8. ***In the article you co-authored 'Detection of prion infection in variant Creutzfeldt-Jakob disease a blood based assay' [NHBT0033626], the findings demonstrate the ability to detect prion infection in blood. The article goes on to state that the assay will be further investigated. Has there been further investigation? Please give details.***

   Little progress has been made since this article. The research Programme that funded work on the blood test was closed down by the MRC at their quinquennial review of the MRC Prion Unit in 2016. I was not a part of this Programme nor have knowledge of MRC's deliberations.

Section 3: Knowledge of Risk of vCJD transmission via blood transfusions and blood products

9. ***A summary of the steps taken by the organisations you were a part of to ensure that the Government, Blood Services, NHS bodies, medical profession and patients were informed and educated about the risks of vCJD transmission via blood and blood products.***

   Staff from the Department of Health attended all the ACDP TSE Subgroup meetings and so became directly aware of the deliberations on vCJD transmission by blood and blood products. These meetings where relevant also included invited experts e.g. Professor Marc Turner from SABTO and Dr Patricia Hewitt from NHS Blood and Transplant who had direct responsibilities for blood services and safety.

The National Prion Clinic has an extensive and ongoing package of information, education and feedback, including:

- Small group seminars prompted by individual patient diagnoses at hospitals and nursing homes around the country
- Annual open day events where we invite patients, relatives, representatives from Government and other stakeholders to hear about progress in research. These days include small group workshops where attendees may feel more confident to raise questions for experts
- Participation in the CJD Support Networks programme of education and information including attendance and presentation at the annual Family Support Meeting
- A website www.nationalprionclinic.org with detailed pages accessible to lay people about prion diseases, including risk factors and exposures
- A telephone and email helpline to respond to urgent individual requests for information
- Book chapters and medical journal papers that describe the current situation in prion diseases
- Responses to meet with experts from other disciplines and policymakers for detailed discussion

10. ***An account of your understanding of the relative risks of vCJD infection from the use of domestically sourced blood and/or blood products and the use of commercially supplied blood products. You may wish to refer to PHEN0000601.***

The issues raised in **PHEN0000601** have become more pertinent, particularly the discordance between model predictions of the risk of vCJD based on the Appendix studies and the number of observed cases. If 1 in 2000 (a prevalence figure derived from Appendix II) people are infected with vCJD and infectious in blood then we should have seen many more cases of blood transmitted vCJD by now. There are some possible explanations for why cases have not manifested themselves, including a failure to be diagnosed

correctly by UK services, and that precautions put in place, like universal leukodepletion of blood in 1998 were particularly efficacious. A further possibility is that the assumption that 1 in 2000 are infected and infectious via blood is not correct.

My view is therefore that the situation remains uncertain in terms of the risk of the domestic supply vs commercial supply. In the best-case scenario, the risk is zero, or trivially close to zero, because there is not a prevalent infectious carrier state of vCJD in the population. In the worst-case scenario, we have already missed some cases of blood transmitted vCJD, and we will continue to see a small number of cases (highly likely <10/year) every year for many years to come because 1 in 2000 donors are silent carriers. For more precision on the risks, modelling would need to be done along the lines of that discussed in **PHEN0000601** using up to date figures.

11. ***The Inquiry understands that you are a member of the Advisory Committee for Dangerous Pathogens Transmissible Spongiform Encephalopathies Risk Assessment Subgroup "ACDP TSE Assessment Subgroup", to the best of your ability please outline: a. The current and future risk of vCJD in the blood supply. b. Any advice given to the UK Government or Blood Services. i. In 2011, at the first ACDP TSE Risk Assessment Subgroup meeting (PHEN0000601), the evidence presented suggested the models used have "over-predicted the potential number of clinical cases and that risk assessments will be revised to reflect the current number of cases", As to this Is there agreement amongst the professions that there has been over-prediction? ii. What has brought this over-prediction to light? iii. Have the risk assessments now been revised?***

The Advisory Committee for Dangerous Pathogens Transmissible Spongiform Encephalopathies Risk Assessment Subgroup no longer meets, the last meeting was in 2019.

I have nothing further to add beyond information in the minutes of ACDP Transmissible Spongiform Encephalopathies Risk Assessment Subgroup meetings.

I think all professionals agree that the original models have over-predicted the number of vCJD blood transmitted cases. This has come to light because over time we have not diagnosed any new clinical cases of blood transmitted vCJD since the first three cases were reported around 2004-2006. I have a reasonable expectation that we should diagnose at least 50% of new cases.

Attempts have been made by the Department of Health modelling team to reconcile up to date case data with their models. These data have been presented at ACDP Transmissible Spongiform Encephalopathies Risk Assessment Subgroup meetings but not since 2019 when this committee was disbanded. It is possible that further modelling has been done, but I am not aware of the results.

Section 4: Actions and Decisions

12. ***Please provide an outline of any proposals, whether accepted or not, that were made by yourself or the organisations you were a part of in an effort to protect the blood supply from the risk of vCJD, including but not limited to: Development of screening or diagnostic tests; Filtration policy, the Inquiry is aware that you were a member of the MRC prion unit team, led by Professor Collinge in 2011. You may wish to refer to DHNI0000164, specifically pages 4 and 5; c. Donor selection and exclusion policies; and d. Surveillance. In answering these questions, you may wish to refer to the following document: NHBT0033626.***

Whilst I am a researcher at the MRC Prion Unit and Clinical Lead of the National Prion Clinic, proposals to develop screening or diagnostic tests were not my remit to lead. Professor Collinge is better placed to respond to this question. I am not aware of any proposals to study donor selection and exclusion policy. Surveillance is the remit of the National CJD Research and Surveillance Unit, so Professors Knight and Ironside should respond about their proposals. The National Prion Monitoring Cohort study has recruited from a very small group of individuals who received blood from donors who went onto die from vCJD, so we do have a specific and ongoing role for the identification of clinical signs in this small group.

13. ***In providing this outline, please state: a. When and by whom any proposals were made; b. The factors considered when deciding whether to implement these proposals; c. Decisions made on such proposals, including the date on which they were made or rejected; and d. How any such measures were implemented in practice, including efforts made to monitor their effectiveness.***

See responses to question 12. I was not responsible for proposals, or if these were made by organisations I am a part of, others are better placed to provide details.

14. ***In addition, please provide the following: a. Your opinion as to whether the risk of secondary transmission via blood and blood products was adequately mitigated in the UK in line with what was known about the potential risks of vCJD at that time. b. Your view as to whether any decisions or actions could and/or should have been made earlier and how this might have impacted the number of individuals considered to be at risk of developing vCJD.***

In the past, for example, at the time I spoke to the House of Commons Science and Technology Committee in 2014, I took a view that the risks of vCJD transmission by blood were not being taken seriously enough. I thought that a prevalence study using a prototype blood test should be done, as a route to the development of a commercial blood screening assay.

Since then, the discordance between the model predictions based on Appendix data (1 in 2000) and the observed cases has become particularly extreme. I remain quite uncertain and open-minded about how to reconcile this discordance. I have certainly become more sceptical that there really is a prevalence carrier state for vCJD infection and have looked to find other explanations for the Appendix I-III study data. A further consideration is that precautionary measures put in place have been more successful than expected. The fact that we haven't seen an outbreak of blood transmitted vCJD doesn't in my view retrospectively justify decisions not to take this risk seriously and mitigate, including support the development of screening assays.

As we have seen no clinical cases of blood transmitted vCJD since 2006 I do not see how further decisions or actions could have prevented cases. Prescient action was taken by leukodepletion in 1998, and prototype blood tests or filtration methods were not developed until much later than these clinical cases.

The development of an effective screening test for vCJD might conceivably have resulted in more confidence in the safety of blood transfusion and therefore reduced the need to inform blood recipients that they are at-risk of vCJD. However, no test is perfect, so the introduction of a screening test for vCJD would reduce risk, not eliminate it completely. It is reasonable to speculate that substantial risk reduction (an effective screening test) might have led to less of a need to notify recipients that they are at-risk.

One ongoing concern I do have is that we now conduct far fewer post-mortem (PM) examinations that in the past. The risk here is that we miss cases of blood transmitted vCJD because a diagnosis could not be established in life. The National Prion Clinic used to fund research PMs, but we no longer have the resources to offer this to more than the most exceptional cases.

Section 5: Counselling and Support

15. ***The Inquiry seeks to gain an understanding into the kind of support that was offered to individuals diagnosed with vCJD, in your capacity as a member of the CJD Support Network, could you outline the support that was offered to patients once they were notified of their vCJD status? You may wish to refer to point 2 in HCDO0000681_002***

The diagnosis of a rapidly fatal condition like vCJD is a devastating moment for patients and their loved ones. There are of course different reactions and needs at different times. In the first instance the priority is usually to establish with as much certainty as possible the correct diagnosis and that "no stone is left unturned." This entails clinical work by the National Prion Clinic in

collaboration with local teams and our colleagues at the National CJD Research and Surveillance Unit.

Once a diagnosis is made, a key priority is providing the time as an expert to explain the causes and prognosis and respond to questions from the patient and their family, loved ones and carers.

All the way through the illness, whilst the progression cannot be stopped, support can be provided by managing symptoms. Some are easier to treat than others, and for full details see information on our website www.nationalprionclinic.org. Uncontrolled muscle jerks (myoclonus), behavioural disturbance, psychiatric disturbances, sleep disorder, pain, incontinence, for example, can not necessarily be prevented but management strategies can help.

We provide access to research studies. Some patients and families feel that contributing to research is “at least doing something” that might help others in the future. This may include access to post-mortem examinations to provide a formal and final confirmation of diagnosis.

Undoubtedly a diagnosis leads to considerable psychological distress for patients and their families, loved ones and carers. The National Prion Clinic nurses (currently four employed) all have experience in listening and helping to manage distress using psychological support strategies, and including helping to set up and coordinate work with local counselling teams. In addition, for particularly complex situations we have available an experienced Clinical Neuropsychologist who can contribute to management. In the past we had a funded counsellor at the National Prion Clinic.

The National Prion Clinic runs an annual open day event (all cases we see are invited by our nurses) which aims to provide information, and allow us to receive feedback and respond to questions in small groups. Families may also get support from other participants they meet at breaks in the day, over an informal buffet lunch, or in small groups sessions.

The CJD Support Network runs a 24-hr helpline to provide support for patients and carers. In addition, they maintain a website with helpful advice and run an annual Family Support Meeting that provides an opportunity to meet experts and other families with shared experiences.

16. ***What kind of counselling and support does the National Prion Clinic offer patients who are either infected with or at risk of vCJD?***

We may not be aware of healthy people at-risk or infected with vCJD. Such people would need to be referred to the National Prion Clinic before we could offer specific help (i.e., other than general information sharing via website, papers etc.). As far as I am aware, there is no-one in the UK who is known to be infected with vCJD, only people at-risk. Once referred we would see people in the NHNN out-patients department for a detailed consultation with neurologist and nurse that may last 1-2 hours, and could be repeated if needed. Sometimes only an initial consultation and responses to questions are wanted. At other times we have continued to see people in clinic and helped to provide psychological support by counselling and clinical neuropsychology involvement.

Statement of Truth

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

Signed GRO-C

Dated 23rd April 2022

Table of exhibits:

Date	Title	Exhibit no.
March 2020	Gill O N et al. Prevalence in Britain of abnormal prion protein in human appendices before and after exposure to the cattle BSE epizootic. Acta Neuropathologica 2020; 139(6):965	RLIT0000725