House of Commons

Science and Technology Committee

After the storm? UK blood safety and the risk of variant Creutzfeldt-Jakob Disease

Second Report of Session 2014–15

Report, together with formal minutes relating to the report

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Science and Technology Committee

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In the late 1990s, few diseases were as high profile, or as poorly understood, as variant Creutzfeldt-Jakob Disease (vCJD): the 'human form' of bovine spongiform encephalopathy (BSE). Invariably fatal and seemingly impossible to control, vCJD was an unusually enigmatic threat, leading prominent figures to warn of hundreds, even thousands of potential deaths, prompting widespread speculation that the handful of cases seen at the time were merely the tip of the iceberg.

Twenty years on, the feared epidemic has not materialised and vCJD has, to an extent, slipped from public consciousness. However, there remains much that we do not understand about vCJD and little to suggest that it should be dismissed as a threat.

While cases of vCJD are now rare, recent studies indicate that tens of thousands of people in the UK might be 'silent' carriers of the prions responsible for the disease and could perhaps transmit those prions to others. The most likely form of onward transmission is through blood transfusion. Cases of transfusion-transmitted vCJD are known to have occurred in the past, and, while it remains to be seen whether or not widespread transmission via the blood supply is probable, evidence suggests that it is possible. In the absence of a validated test capable of detecting the presence of prions in blood, we simply cannot know how significant a threat to public health vCJD might be.

The Government acknowledges this risk and claims that, like its predecessors, it has taken a precautionary stance in response. However, while administrations in the late 1990s assumed the worst and took steps to prevent it from happening, the Government recently appears to have adopted a more optimistic approach in which the low incidence of identified cases of vCJD is used as justification for inaction. This is particularly evident in the Government's less than enthusiastic response to emerging vCJD risk mitigation technologies such as prion filtration and the prototype vCJD blood assay recently developed by the MRC Prion Unit.

In this report we remind the Government that no evidence of harm is not the same as evidence of no harm. Cases of vCJD appear to be falling but, given the level of uncertainty regarding the potential for blood-borne transmission, precaution must remain the guiding principle in decision-making. Research intended to reduce this uncertainty should be pursued as a priority and, in the meantime, measures to reduce the risk of blood-borne transmission should be strengthened wherever possible.

The Government's casual attitude to vCJD transmission is not confined to blood transfusion: it is also evident in its response to the risk of surgical transmission. It is known that classical CJD can be transmitted via contaminated surgical instruments and there is reason to believe that vCJD may also be transmissible via this route; however, development of a commercial technology capable of eliminating this risk has ceased in the absence of Government support and as a result of the NHS's apparent lack of appetite for such technology. Without a technological solution, we cannot be confident that CJD is not being

transmitted through surgery and we are disturbed by the Government's apparent lack of concern about this issue.

Failure to adequately mitigate these risks means that some people have inadvertently been exposed to CJD or vCJD and may be at increased risk of developing the disease. This inquiry has exposed deficiencies in the level of support provided to these individuals and the system of surveillance through which they are monitored; both of which, in many cases, have effectively been outsourced. We consider this arrangement to be unacceptable and urge the Government to take greater care of, and responsibility for, those who have been accidentally exposed to CJD or vCJD. We were also disappointed to find that so few 'at risk' individuals have been asked for their consent to participate in research and recommend that the Government takes immediate steps to remedy this situation.

At the conclusion of this inquiry we are unconvinced that the Government has done all that it potentially could do to ensure that the UK blood supply is, and continues to be, free of dangerous pathogens. We therefore conclude by recommending that the Government commission a full assessment of the key risks, known and unknown, that the UK blood supply currently faces and might face in the future, so that it can identify and fill relevant knowledge gaps and support the development of appropriate risk reduction measures and technologies.

1 Introduction

Background

1. The UK's first voluntary blood service was founded by the British Red Cross in 1921, paving the way for the establishment of a pioneering military service shortly before the outbreak of war in 1939. Over the following years, blood transfusions played an important role in the treatment of servicemen and civilians alike and the benevolent spirit which motivated thousands to donate blood during the war persisted after its conclusion, leading to the creation of the UK Blood Transfusion Service in 1946.[1] Today, approximately 2.2 million whole blood donations are made in the UK each year and are screened, tested, processed and distributed by one of the country's four Blood Services.[2]

2. Despite these altruistic foundations, the story of blood transfusion in the UK is not unblemished. Throughout the 1970s and the first half of the 1980s, many UK haemophiliacs were treated with blood and blood products which carried the hepatitis C virus; some 4,670 became infected as a result. Between 1983 and the early 1990s, contamination of the UK blood supply with HIV led to a further 1,200 infections and it is estimated that these incidents together have led to over 2,000 deaths.[3] Since 1991, all UK blood donations have been tested for both HIV and hepatitis C; however, the 2009 public inquiry investigating these events stated that it was "dismayed" by the time taken for Governmental and scientific agencies to "become fully alive to the dangers" of these emerging infections.[4]

3. Today, we find ourselves facing another potential threat to blood safety. Variant Creutzfeldt-Jakob Disease (vCJD) is a rare neurodegenerative disease thought to be caused by an unusual infectious agent known as a prion. First characterised in 1996, vCJD is considered to be the human form of bovine spongiform encephalopathy (BSE), another infectious prion disease believed to have entered the human food chain in the 19070s or 1980s.[5] Cases of vCJD are extremely rare: official statistics state that 229 people worldwide—177 in the UK, where the BSE crisis primarily took place—have died of the disease since it was first identified nearly 20 years ago.[6] However, in October 2013, a paper published in the *British Medical Journal* suggested that approximately 1 in 2,000 people in the UK could be unknowingly carrying the prions responsible for the disease, raising the

1 NHS Blood and Transplant, *History of blood transfusion*, blood.co.uk, accessed 12 June 2014; *The Army Blood Transfusion Service*, British Medical Journal, Volume 1, Issue 4297, 15 May 1943, pp.610-11

2 BTO30 para 2 [JPAC]

3 *Independent Public Inquiry Report on NHS Supplied Contaminated Blood and Blood Products*, 'The Archer Inquiry', February 2009, pp.5-6; *HIV and Hepatitis C infection from contaminated blood and blood products*, Standard Note, SN/SC/5698, House of Commons Library, July 2011

4 *Independent Public Inquiry Report on NHS Supplied Contaminated Blood and Blood Products*, 'The Archer Inquiry', February 2009, p.104

5 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002

6 National CJD Research and Surveillance Unit, *Creutzfeldt-Jakob Disease in the UK (by calendar year)*, cjd.ed.ac.uk, accessed 30 June 2014

possibility that hundreds of blood donors could potentially be passing the infection on to others through the blood supply.[7] This gave us cause for concern and in November 2013 we held a one-off evidence session examining the ongoing risk posed by vCJD.[8] During this session, we heard evidence from leading experts suggesting that the risk of secondary transmission of vCJD—through both blood and contaminated surgical instruments—remained "significant".[9] We therefore decided to explore these issues further in an inquiry focused on blood safety and the continuing public health risk posed by vCJD.

Our inquiry

4. In December 2013, we issued a call for written evidence addressing the following points:[10]

a) Are UK policies governing who can donate blood and blood products, tissues and organs sufficiently evidence-based? Is NHS Blood and Transplant overly restrictive about who can donate, or should greater precautions be taken to further reduce risk?

b) Is the Government and its scientific advisory structure sufficiently responsive to the threat posed by emerging diseases being transmitted through blood and blood products, tissues and organs?

c) Has the threat of ongoing transmission of vCJD through the blood and blood product supply been adequately mitigated?

d) What are the strengths and weaknesses of NHS Blood and Transplant's strategy, "Taking Organ Transplantation to 2020"? What further changes could be made to safely increase the supply of blood and blood products, tissues and organs?

e) What lessons could be learnt from the screening and donation practices of other countries?

We received 55 written submissions and took oral evidence from 27 witnesses, including:

- Individuals personally affected by the issues under consideration, including patient representatives and the mother of a victim of vCJD;
- Members of relevant scientific advisory bodies, including UK Blood Services' Joint Professional Advisory Committee, the Advisory Committee on the Safety of Blood, Tissues and Organs and the Advisory Committee on Dangerous Pathogens;

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7 O. Noel Gill et al, *Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey*, British Medical Journal, Volume 349, Issue 7929, 2013. BMJ2013;347:f5675

8 Science and Technology Committee, 'Inquiry: variant Creutzfeldt-Jakob Disease', press release, 27 November 2013

9 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q4 [Professor John Collinge]

10 Science and Technology Committee, *MPs launch inquiry on blood, tissue and organ screening following vCJD fears*, press release, 3 December 2013

- Publicly- and privately-funded researchers working in the fields of blood safety and prion disease;
- Representatives of the National CJD Research and Surveillance Unit;
- Representatives of NHS Blood and Transplant (NHSBT) and Public Health England; and
- The Government, represented by Jane Ellison MP, Parliamentary Under-Secretary of State for Public Health, Department of Health (hereafter "the Minister") and Professor Dame Sally Davies, Chief Medical Officer, Department of Health.

We would like to thank those who contributed to this inquiry, with particular thanks to NHS Blood and Transplant for hosting the Committee's visit to its Filton blood processing facility in February 2014.

5. While focusing primarily on issues relating to blood safety, we also took the opportunity during this inquiry to consider the Government's new strategy for organ donation, launched in July 2013.[11] We heard evidence on this topic from the Government and NHSBT and also held one dedicated evidence session during which we heard from representatives of several medical charities.[12] As a result of this work, in July 2014 we wrote to the Minister urging her to maintain close scrutiny over the strategy's implementation in the coming months.[13] This report does not further detail this aspect of our inquiry.

6. In this report, we ask whether the Government and UK Blood Services are doing enough to protect patients from the risk of vCJD and other blood-borne infections. We begin in chapter 2 by considering the types of infectious risks faced by the UK blood supply and the controls currently in place to mitigate these. In response to evidence received on the risk of surgical transmission of CJD, we also extend this analysis beyond blood to consider the risk posed by contaminated surgical instruments. In chapter 3, we move from current risk reduction measures to possible future ones and consider three emerging vCJD risk mitigation technologies. We particularly examine the challenges that researchers have faced in bringing these technologies to market and consider the role of the scientific "gatekeepers" standing between these new technologies and their adoption by the NHS. In chapter 4, we consider the current landscape for national CJD risk management and surveillance and, finally, in chapter 5, we draw some conclusions about the Government's attitude to blood safety and vCJD risk mitigation.

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11 NHS Blood and Transplant, *Taking organ transplantation to 2020: a UK strategy*, July 2013

12 Oral evidence taken on 28 April 2014, HC (2013-14) 990

13 Correspondence from the Chair of the Science and Technology Committee to the Minister for Public Health, 9 July 2014, parliament.uk/science, accessed 14 July 2014.

2 Current infection risk and mitigation

The UK blood supply

7. Across the UK, blood donation and transfusion is made possible by one of four devolved Blood Services, each accountable to its own Department of Health: NHS Blood and Transplant (serving England and North Wales), the Welsh Blood Service, the Scottish National Blood Transfusion Service and the Northern Ireland Blood Transfusion Service.[14] Sensibly, despite this devolved structure, policies governing donor selection, testing and manufacturing are UK-wide, with recommendations provided by a variety of scientific advisory bodies, including:

- The **Advisory Committee on the Safety of Blood, Tissues and Organs** (SaBTO), an independent scientific advisory committee[15] (SAC) responsible for advising "UK ministers and health departments on the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion/transplantation";[16]
- The **Advisory Committee on Dangerous Pathogens**, an SAC responsible for providing "scientific advice on the risks to exposure to pathogens and risk assessment advice on transmissible spongiform encephalopathies" such as CJD and vCJD;[17]
- The **National Expert Panel on New and Emerging Infections**, an SAC which "assesses the threat from new and emerging infectious diseases" and advises the Government on prevention and control measures;[18] and
- The **UK Blood Services Joint Professional Advisory Committee**, a coordinating body which provides advice across UK Blood Services to ensure that the UK has "a common set of guidelines for blood transfusion services".[19]

8. In recent years, the UK has maintained a strong blood safety record and the likelihood of a patient suffering harm as a result of an infection transmitted through donated blood is extremely low.[20] According to Dr Paula Bolton-Maggs, Medical Director of the Serious Hazards of Transfusion (SHOT) scheme, a professionally-led blood safety monitoring system, recent UK figures for transfusion-transmitted infections compare favourably with

14 BTO30 para 2 [JPAC]

15 Government Office for Science's *Code of Practice for Scientific Advisory Committees* (2011) refers to SACs as "advisory committees providing independent scientific advice, regardless of their specific structure and lines of accountability; whether reporting to a Ministerial Department, Non-Ministerial Department or other public body, and whether an advisory NDPB or an expert scientific committee".

16 Advisory Committee on the Safety of Blood, Tissues and Organs, 'Homepage', Government.uk, accessed 30 June 2014

17 Advisory Committee on Dangerous Pathogens, 'Homepage', Government.uk, accessed 30 June 2014

18 National Expert Panel on New and Emerging Infections, 'Homepage', Government.uk, accessed 30 June 2014

19 Q30 [Dr Sheila MacLennan]; Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee, 'Welcome to JPAC', transfusionguidelines.org.uk, accessed 30 June 2014

20 See, for example, Q146 [Dr Paula Bolton-Maggs] and 'Annual SHOT report 2012', July 2013, accessed 30 June 2014

previous periods and UK blood safety is currently "equivalent [to], if not better" than that of other developed countries.[21] However, cases do continue to occur. In 2012, the SHOT scheme recorded three instances of transfusion-transmitted infection, all of which caused "major morbidity".[22] Some witnesses saw such cases as evidence that UK defences against blood-borne pathogens remained fallible, surmising that the UK blood supply was still not as safe as it reasonably could be.[23]

9. Blood transfusions save lives and we should be proud, as a nation, of our long tradition of altruistic donation. In recent years, the UK blood supply has proved to be extremely safe and, in the vast majority of cases, the benefits of receiving a transfusion will far outweigh the risk of acquiring a transfusion-transmitted infection. However, we urge against complacency and stress the need for UK Blood Services to remain vigilant to the threat posed by blood-borne pathogens.

In the following paragraphs we consider some of the key risks facing the UK blood supply and the measures in place to mitigate them.

Risks to the UK Blood Supply

10. Transfusion-transmitted infection risks can be divided into three categories:

i) Known risks that can be well mitigated;

ii) Known risks that cannot be well mitigated; and

iii) Unknown risks.

Viruses and bacteria, the pathogens responsible for most common infectious diseases, make up the bulk of the first category. The second category is currently dominated by a more unusual type of infectious agent known as a prion, the biology of which is discussed briefly below. The composition of the third category is, by definition, unknown, but could feasibly include all of the above and potentially other, as yet unidentified, types of pathogen.

Known risks that can be well mitigated

11. Existing blood safety measures are largely focused on mitigating the known risks posed by certain well-characterised pathogens. These currently include a wide range of bacteria, viruses and parasites, including hepatitis B and C, HIV, syphilis and the micro-organisms responsible for malaria and Chagas' disease.[24] Of course, these pathogens were themselves

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21 Q146

22 According to the Summary of the 2012 SHOT report (see previous footnote): "A child with sickle cell disease developed proven transfusion-transmitted parvovirus infection. There was a case of hepatitis E transmission [...] and two patients were infected with hepatitis B from a single donor" [counted as a single instance of transfusion-transmitted infection]. Note: the 'Annual SHOT report 2013' was released shortly prior to publication of this Report and is available at shotuk.org.

23 See, for example, Q1 [Christine Lord], Q2 [Joseph Peaty], Q2 [Liz Carroll]

24 BTO31 para 20 [Government]

once unknown; a blood safety strategy based on known risks is therefore largely retrospective, with risk mitigation measures only being implemented once a pathogen has been identified as a threat, often through instances of transfusion-transmitted infection. Current measures to protect the blood supply from hepatitis C and HIV, for example, were only implemented after the mass infection events of the 1970s, 80s and 90s.[25]

Known risks that cannot be well mitigated

12. In most cases, once a pathogen has been identified as a potential threat, it is possible to put measures in place to prevent that threat from being realised. However, some pathogens are invulnerable to standard risk mitigation measures and may therefore continue to pose a threat even after they have been identified. The most noteworthy type of pathogen currently in this category is the prion.[26]

13. A prion is an infectious agent comprised of protein folded into an abnormal form. Unlike other pathogens, prions contain no genetic material and closely resemble naturally occurring proteins, making them extremely difficult to detect, remove or selectively inactivate.[27] As a consequence, prions are largely invulnerable to many of the methods used to mitigate the risk posed by other known pathogens. Prions are responsible for a family of fatal brain diseases known as transmissible spongiform encephalopathies (TSEs). Examples include livestock diseases such as bovine spongiform encephalopathy (BSE) and scrapie[28] and, in humans, Creutzfeldt-Jakob Disease (CJD), a debilitating disease caused by a build-up of abnormal protein in the brain. Symptoms of CJD are similar to those of dementia and include loss of balance, coordination and mobility, loss of memory, slurred speech, personality change and progressive loss of brain function. CJD is invariably fatal and most people die within a year of first experiencing symptoms.[29]

14. Prior to the mid-1990s, three types of "classical" CJD had been characterised:

- an **inherited** form that runs in families (typically 5–10 cases per year in the UK);
- an **acquired** form, transmitted through contact with human tissue contaminated with prions (2–3 per year), and
- a **sporadic** form of unknown cause, historically responsible for the majority of cases (50–100 per year).[30]

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25 *Independent Public Inquiry Report on NHS Supplied Contaminated Blood and Blood Products*, 'The Archer Inquiry', February 2009

26 See, for example, Q3 [Dr Matthew Buckland]

27 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002

28 Scrapie is a transmissible spongiform encephalopathy (TSE) endemic in British sheep and found in many parts of the world. Also found in goats. Symptoms of scrapie include changes in behaviour, changes in posture and movement and skin irritation leading to repeated rubbing and scratching.

29 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002

30 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002; National CJD Research and Surveillance Unit, *Creutzfeldt-Jakob Disease in the UK (by calendar year)*, cjd.ed.ac.uk, accessed 30 June 2014

Following the BSE epidemic of the late 1980s and early 1990s, the first cases of a new form of CJD were identified. Variant Creutzfeldt-Jakob Disease (vCJD) shared some symptoms with classical CJD but tended to affect younger people and led to a longer period of illness before death.[31] Primary transmission was thought to be caused by exposure to BSE-infected material, such as contaminated meat. Since vCJD was first identified in 1995 it has been attributed to 177 UK deaths, the majority occurring between 1996 and 2003.[32]

15. Secondary transmission of a disease occurs when an individual carrying the infectious agent passes that infection on to another person. This has been demonstrated to occur both in acquired forms of classical CJD, for example through the use of contaminated surgical instruments (see paragraphs 27–29), and in vCJD, which has been shown to have been transmitted via blood transfusion. Dr Lorna Williamson, Medical and Research Director, NHS Blood and Transplant (NHSBT), explained that in the late 1990s and early 2000s:

> three patients developed variant CJD between six and eight years after a blood transfusion, and their donors also went on to develop variant CJD, suggesting that their transfusion may have been the source of the infection. There was a fourth recipient who had no symptoms during life but who at post-mortem showed signs of variant CJD.[33]

According to Dr Simon Mead, Association of British Neurologists, this constitutes "hard evidence that variant CJD has been transmitted [via] blood transfusion".[34] However, the UK Blood Services Prion Working Group stated that there was "considerable uncertainty as to the magnitude of the risk" posed by this mode of transmission: for example, with regard the level of infectivity in blood and the likelihood that infected individuals would go on to develop disease.[35] Nevertheless, several international advisory bodies, including the US Food and Drug Administration, do not recommend that donations be taken from people who spent time in the UK between 1980 and 1996 due to the perceived risk of vCJD.[36]

16. In October 2013, the *British Medical Journal* published the results of a large study intended to provide further information on the potential public health risk posed by

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31 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002.

32 National CJD Research and Surveillance Unit, *Creutzfeldt-Jakob Disease in the UK (by calendar year)*, cjd.ed.ac.uk, accessed 30 June 2014

33 Q241. In addition, in 2009 a case of presumed transmission was described in a patient with haemophilia who had received batches of Factor VIII prepared from plasma from a donor who subsequently died of vCJD. The patient died of unrelated causes but was found at post mortem to have evidence of vCJD prion accumulation in his spleen. It is unclear whether the vCJD infection arose from transmission from the infected donor, transmission from another batch of UK Factor VIII or oral transmission via the food chain (i.e. through eating BSE-infected meat). See BTO14 para 6 [UKBS Prion Working Group].

34 Q149

35 BTO14 para 20, para 24 [UKBS Prion Working Group]

36 See, for example: U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, *Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products*, May 2010

vCJD.[37] The study, led by Public Health England, looked for the presence of prions in 32,441 samples of archived appendix tissue in order to estimate the rate of "subclinical infection": that is, the approximate number of individuals who carry prions—and could potentially transmit them to others—but do not knowingly suffer from prion disease. The study detected the presence of prions in 16 of the samples, suggesting that around 1 in 2,000 people in the UK could be 'silent carriers' of vCJD. The implications of these results remain uncertain. According to Professor Richard Knight, Director of the National CJD Research and Surveillance Unit:

> We do not know for sure whether the appendix data really mean that these people are infected. Even if they do, we do not know whether these people are infectious. If they are infectious, we do not know for what period of time they are infectious, so there is another uncertainty.[38]

Dr Williamson, NHSBT, agreed that there remained "a good deal of uncertainty" about the risk of blood-borne vCJD transmission but stated that it was desirable to "keep and, if possible, improve the preventative steps that we take" to prevent transmission from occurring.[39] Dr Paul Cosford, Medical Director, Public Health England, likewise stated that "the most precautionary steps" needed to be taken in order to minimise risk.[40] The Minister stated that she considered the Government's approach to be "extremely precautionary"; however, several witnesses stated that blood-borne vCJD remained "a concern" and Christine Lord, mother of vCJD victim Andrew Black, called the issue "a ticking health time-bomb, which must be addressed and tackled".[41]

17. The evidence that we have heard suggests that we cannot be confident that prions are not present in the blood supply. There remains considerable uncertainty about the potential implications of such contamination. We consider it imperative that a precautionary approach to this risk be maintained until further evidence becomes available.

Unknown risks

18. According to Dr Matthew Buckland, UK Primary Immunodeficiency Network, while known pathogens such as "the major viruses" continue to cause occasional infections in transfusion patients, "the unknown unknowns are clearly the greater problem […] the things that we yet don't know to worry about".[42] Pathogens are constantly emerging, evolving and colonising new areas and the campaign group TaintedBlood described the UK blood supply as "highly susceptible" to these emerging risks.[43] Other witnesses agreed

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37 Noel Gill et al, 'Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey', *British Medical Journal*, 15 October 2013. BMJ2013;347:f5675

38 Q150

39 Q241 [Dr Lorna Williamson]

40 Q241

41 Q295 [Jane Ellison MP]; Q3 [Dr Matthew Buckland]; Q1 [Christine Lord]

42 Q3

43 BTO18 para 24 [TaintedBlood]

that emerging pathogens remained an issue.[44] A 2009 study published in the journal *Transfusion* identified 68 emerging infectious agents that potentially posed a threat to the blood supply. The majority of these risks were not, at the time, mitigated by existing measures.[45] However, Dr Sheila MacLennan, Chair of UK Blood Services Joint Professional Advisory Committee, stressed that one of her group's main responsibilities was to conduct "external horizon scanning" to identify such threats and she added that she personally sat "on a European committee that looks at emerging infectious diseases".[46] Dr Bolton-Maggs, SHOT, also highlighted the "very good" global screening processes in place to identify emerging infections.[47]

Risk mitigation measures

19. Several controls are currently in place across UK Blood Services which are designed to mitigate both known and, to an extent, unknown infection risks.

Donor selection

20. Not everyone is accepted as a blood donor. Before making a donation, all potential donors complete a donor questionnaire (or 'health check') during which "a number of confidential questions" are asked in order to establish whether or not that individual meets the selection criteria.[48] These criteria are intended to protect both donor and recipient and include several measures to reduce the likelihood of transfusion-transmitted infections from occurring. For example, people are asked not to donate if they are suffering from a chesty cough, sore throat or active cold-sore, or if they are currently taking antibiotics or have had any infection in the two weeks prior to donation.[49] In addition, according to UK Blood Services' Joint Professional Advisory Committee (JPAC), "as donation testing for infectious agents cannot be 100% effective, it is important to retain policies which defer donors with lifestyle factors which increase infection risk".[50] As such, temporary and, in some cases, permanent deferrals are in place for people participating in certain activities, detailed in table 1.

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44 See, for example, Q4 [Liz Carroll]; Q142 [Nigel Talboys]

45 Stramer et al, *Emerging infectious disease agents and their potential threat to transfusion safety*, Transfusion, Volume 49, August 2009 supplement.

46 Q32

47 Q149

48 NHS Blood and Transplant, 'What happens when I give blood?', blood.co.uk, accessed 30 June 2014

49 NHS Blood and Transplant, 'Who can't give blood?', blood.co.uk, accessed 30 June 2014

50 BTO30 para 10 [JPAC]

Table 1: Behavioural deferrals for potential blood donors[51]

Behavioural risk	Donor deferral period
Accepting money or drugs for sex	Permanent
Intravenous drug use	Permanent
Sex with a sex worker	1 year from last sexual contact
Sex with an intravenous drug user	1 year from last sexual contact
Sex with anyone who may ever have had sex in parts of the world where HIV/AIDS is common	1 year from last sexual contact
Sex with anyone infected by HIV, Hepatitis B or C	1 year from last sexual contact
Sex with a man (if the potential donor is male)	1 year from last sexual contact
Sex with a man who has had sex with another man (if the potential donor is female)	1 year from last sexual contact
Sex with anyone with haemophilia or a related blood clotting disorder who has received clotting factor concentrates	1 year from last sexual contact

21. Witnesses pointed out several weaknesses associated with the use of donor selection as a tool for infection risk mitigation:

- **Reliability of information**: Whether errors are accidental or due to deliberate non-compliance, not all of the information provided during donor screening is likely to be accurate. According to the Health Protection Agency (now Public Health England, PHE), in 2011, 290 blood donations tested positive for either hepatitis B, hepatitis C, HIV, HTLV[52] or syphilis. Of these, "11% should not have been made if donors had disclosed relevant information at the time of their donation".[53] The most common reason given for non-compliance was the belief that the information "did not matter".[54] PHE is currently conducting a survey of UK donors in order to better understand compliance levels.[55]

- **Donor pool reduction**: Over 10% of attendances at UK blood sessions result in the potential donor being deferred and, according to Dr Sheila MacLennan, JPAC, "about 30% […] do not return".[56] Changes to donor selection policies have led to a reduction in the referral rate in recent years; however, according to Terumo BCT,[57] "the increased use of donor deferrals […] has been a major strand of NHSBT policy" and could lead to

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51 Information taken from Advisory Committee on the Safety of Blood, Tissues and Organs, *Donor Selection Criteria Review*, April 2011, table 4 (p.34) and NHS Blood and Transplant, 'Who can't give blood?', blood.co.uk, accessed 30 June 2014.

52 Human T cell lymphotropic virus, a usually asymptomatic virus endemic in the Caribbean, Japan, South America, and parts of Africa.

53 Health Protection Agency/NHS Blood and Transplant, *Safe supplies: new horizons*, October 2013, p.iii. Note, compliance information was only available for 257 of the 290 positive donations.

54 Health Protection Agency/NHS Blood and Transplant, *Safe supplies: new horizons*, October 2013, p.11

55 NHS Blood and Transplant, 'UK blood donor survey launched', press release, 1 October 2013

56 Q35; BTO47 [JPAC supplementary]

57 Terumo BCT is a developer of pathogen reduction technologies.

a problematic reduction in the size of the donor pool if widespread outbreaks of blood-borne pathogens were to occur in the future.[58]

- **Potential for discrimination**: Donor selection policies are currently based on population-level rather than individualised risk factors, leading to potentially inaccurate or even discriminatory assessments being made. Men who have sex with men are currently deferred from donating blood for 12 months following last sexual contact (see table 1);[59] however, as Stonewall pointed out, "gay and bisexual men are not automatically at a higher risk of contracting sexually transmitted infections"—"heterosexual people can engage in risky sexual behaviour too".[60] Stonewall stated that it was "concerned" that "gay and bisexual men engaged in low-risk sexual activity" were excluded from giving blood "while heterosexual people engaged in higher risk activity" were not.[61] Professor Mark Turner, Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), agreed that individualised risk assessment was "an ideal" but stated that there were "practical problems and issues" that would need to be resolved before this could be implemented.[62]

22. **We echo concerns that population-level risk assessment could lead to inaccurate and potentially discriminatory judgements being made about the risk posed by individuals, particularly men who have sex with men.** ***We recommend that the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) reconsider the feasibility of a move to more individualised risk assessment as part of its 2015 work programme, following completion of the current UK blood donor survey.***

Blood sample testing

23. According to the Government, "all blood donations are tested on every occasion" for evidence of infection with five known pathogens:

- human immunodeficiency virus (HIV);
- hepatitis B virus;
- hepatitis C virus;
- human T-cell lymphotropic virus (HTLV); and
- syphilis.[63]

In addition, "donors who may have been exposed to certain infections found outside the UK", that is, malaria and Chagas' disease[64], "undergo specific testing before their blood is

58 BTO47 [JPAC sup.]; BTO15 para 11 [Terumo BCT]

59 NHS Blood and Transplant, 'Who can't give blood?', blood.co.uk, accessed 30 June 2014

60 BTO17 para 6 [Stonewall]

61 BTO17 para 3 [Stonewall]

62 Q34

63 BTO31 para 20 [Government]

released for use".[65] In 2011, of the 2.4 million donations tested throughout the UK, 290 (0.012%) tested positive for one of the five infections universally screened for.[66] Of the 44,103 donations tested for malaria, 1,495 (3.4%) were positive.[67] Tests for cytomegalovirus (CMV)[68] are also carried out on a subset of donations "to meet the specific clinical needs of patients with depressed immunity".[69]

Leucodepletion

24. Leucodepletion is the process by which white blood cells are removed from whole blood, usually through use of a specialised filter. It confers several benefits on recipients[70] but was initially implemented in 1999 because of its presumed ability to reduce the risk of prion transmission. The lack of confirmed cases of transfusion-transmitted vCJD since 1999 has led the Advisory Committee on Dangerous Pathogens to speculate that leucodepletion "may have had a substantial impact on blood-borne transmission risks" and witnesses praised the Government's "prescient" decision to introduce this measure at a time when the prevailing scientific view was that blood transfusion would not prove to be a source of prion transmission.[71] However, for many years leucodepletion's utility as a vCJD risk reduction measure was unconfirmed and Dr Williamson, NHSBT, stated that the measure's "high effectiveness" in removing prions had only recently been established.[72] Chief Medical Officer Dame Sally Davies stated that leucodepletion "probably" removed "about 40%" of prion infectivity, at an estimated cost, according to Dr Williamson, of "£4 million to £4.5 million per year".[73]

Other pathogen reduction steps

25. In addition to leucodepletion, additional "pathogen reduction" measures may be applied to certain blood components to further reduce the risk of transfusion-transmitted infection, including of unknown pathogens. Nigel Talboys, Director of Blood Safety at Terumo BCT,[74] explained the advantages of this approach:

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64 Chagas' disease is a tropical disease caused by a parasitic protozoan (*Trypanosoma cruzi*). It is marked by prolonged high fever, edema (excess of fluid) and enlargement of the spleen, liver, and lymph nodes.

65 BTO31 para 20 [Government]

66 Public Health England, 'Surveillance of Infections in Blood Donors', hpa.org.uk, accessed 29 May 2014

67 Public Health England, 'Surveillance of Infections in Blood Donors', hpa.org.uk, accessed 29 May 2014. No donations were found to be positive for Chagas' disease.

68 Cytomegalovirus (CMV) is a form of herpes virus and is extremely common. It causes few symptoms in most people but can act as an opportunistic infection in immunosuppressed individuals; for example, AIDS patients, people undergoing chemotherapy or those taking immunosuppressive drugs following organ transplant.

69 BTO31 para 20 [Government]

70 See Q256 [Dr Lorna Williamson]

71 BTO31 Annex G [Government]; Q161 [Dr Simon Mead]; BTO14 para 5 [UKBS Prion Working Group]. See also Q161 [Professor Richard Knight].

72 Q250

73 Q325 [Dame Sally Davies]; Q256 [Dr Lorna Williamson]

74 Terumo BCT is a developer of pathogen reduction technologies.

> Many new pathogens come along. One of the issues is: can you test for every single one? The answer to that is, probably, no. By implementing a pathogen-reduction technology, you are able to inactivate not only the known pathogens […] but also give a level of protection against those emerging or unknown pathogens.[75]

Plasma imported for UK use is currently treated with methylene blue which, according to Professor Turner, SaBTO, "will inactivate most, [but] not all, bacteria and viruses".[76] Professor Turner acknowledged, however, that "the vast majority of blood components" do not currently undergo such pathogen reduction measures as there are "currently no licensed pathogen inactivation systems" that can be used on whole blood.[77] In December 2013, SaBTO recommended that novel technologies for pathogen reduction in platelets should not be implemented, in part because of their poor cost-effectiveness.[78]

26. **Pathogens are constantly emerging and evolving; novel pathogens will therefore always pose a threat to the blood supply. In the past, it has often taken multiple cases of transfusion-transmitted infection before these threats have been recognised and mitigated. This will remain the case as long as risk mitigation measures remain pathogen-specific. *We urge the Government to take steps to support the development of broader spectrum technologies with the potential to mitigate the risk of both known and unknown pathogens.***

Surgical transmission of prions

27. Blood transfusions are not the only source of secondary prion infection; transmission can also occur via other forms of medical intervention, notably surgery. The prions thought to be responsible for both classical and variant forms of CJD are known to be present in parts of the body that are accessed during surgical procedures.[79] According to Professor John Collinge, MRC Prion Unit, prions are known to "stick very avidly to metal surfaces", meaning that contaminated surgical instruments could potentially act as "a very efficient route" of person-to-person prion transmission.[80] This is more than just a theoretical risk: Professor Richard Knight, Director of the National CJD Research and Surveillance Unit, confirmed that "a handful" of cases of classical CJD appeared to have been transmitted in this way.[81] Professor Collinge added that there was "epidemiological evidence from several countries now that patients developing classical CJD are more likely to have had abdominal surgery beforehand", suggesting a potential link between the procedure and the disease.[82] Professor Collinge also considered it possible that some cases

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75 Q140

76 Q40

77 Q46

78 Q257 [Dr Lorna Williamson]

79 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q43 [Professor John Collinge]

80 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q43 [Professor John Collinge]

81 Q164

82 Q112

of vCJD had "been related to" surgical exposure, but members of the Department of Health's Decontamination Science Working Group stated that these concerns were "exaggerated".[83] To date, there have been no cases in which it has been conclusively demonstrated that vCJD has been transmitted via surgery, although scientific evidence suggests that this would be possible. [84]

28. Speaking on behalf of the Government, Chief Medical Officer Dame Sally Davies, stated that she was "concerned about the transmission of disease" via surgical instruments and claimed that the Government had applied the precautionary principle in its management of this risk.[85] The Government highlighted two key steps that it had taken:

- Since the mid-1990s, the Advisory Committee on Dangerous Pathogens (ACDP) has issued guidance on "the decontamination, quarantining and appropriate use of surgical equipment (including endoscopes), and on pre-surgical assessment of patients to identify and act on those with, or at risk of, all forms of human prion disease".[86]

- In 2006, the National Institute for Health and Care Excellence (NICE) issued guidance on "patient safety and reduction of risk of transmission" of CJD via surgical procedures.[87] This made several suggestions relating to the management and tracking of surgical instruments and recommended the use of new, unused instruments for certain groups, such as children undergoing high-risk procedures.

We did not receive any evidence on current levels of compliance with the ACDP guidance but, according to NICE, following publication of its 2006 guidance, the Department of Health became aware that implementation "had not proceeded satisfactorily".[88] A number of activities took place to address this and in 2008 NICE published additional resources to aid implementation, including "a checklist for acute Trusts to self-assess current practice against the guidance".[89] NICE does not perform implementation audits for this type of guidance. However, a 2011 academic study examining decontamination procedures across a sample of NHS centres found that the guidance had only been "fully implemented" in ten (19%) of the organisations audited.[90] Dame Sally stressed the importance of NICE's "significant" guidance and stated that she was "not aware" that it had not been fully implemented and would consider it "unacceptable" if this were the case.[91]

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83 Q112 [Professor John Collinge]; BTO20 para 12 [DH DSWG]

84 Q164 [Professor Richard Knight]; Q112 [Professor John Collinge]

85 Q296 and Q300 [Dame Sally Davies]

86 BTO31 para 23 [Government]

87 NICE, *Patient safety and reduction of risk of transmission of Creutzfeldt–Jakob disease (CJD) via interventional procedures*, IPG196, November 2006

88 BTO45 para 9 [NICE]

89 BTO45 para 9 [NICE]

90 Sjogren, G., *Creutzfeldt-Jakob Disease: A study into the changes in surgical instrument decontamination made by decontamination managers following the introduction of NICE interventional procedure guidance 196*, 2011. Available at the UHI Millennium Institute or from the Committee on request. Note: this study has not, to our knowledge, been subject to peer-review.

91 Q296

29. **The Government has acknowledged that contaminated surgical instruments are a potential source of prion transmission and states that it has taken a precautionary approach in its response to this risk. However, this response appears to rest heavily on guidance which, based on the available evidence, may not have been fully implemented.** ***We recommend that the Government work with the National Institute of Health and Care Excellence (NICE) and the Advisory Committee on Dangerous Pathogens to better understand the extent to which the precautions recommended by these bodies have been implemented across the NHS. We ask the Government to provide us with an update on this work well before the dissolution of Parliament, together with an indication of the steps it will take if preliminary findings suggest that implementation has been incomplete.***

3 Technology evaluation and the role of the scientific gatekeeper

30. Given the risk posed by prion transmission and the inability of existing measures to fully mitigate this risk, efforts are continuing, both in the public and private sectors, to develop new technologies for prion detection, inactivation and removal. The primary customers for these technologies are UK Blood Services and the NHS, access to both of which is typically mediated by one of several scientific bodies responsible for assessing the evidence to support technology adoption. Through the discussion of three case studies, this chapter examines the Government's approach to the evaluation of vCJD risk mitigation technologies, with particular focus on the role played by these scientific gatekeepers.

Case study 1: decontamination of surgical instruments

The technology: DuPont's Rely+On Prion Inactivator

31. According to the Department of Health's Decontamination Science Working Group, the risk to public health posed by surgical prion transmission is "not thought to be great".[92] However, "as it is known that a substantial number of people in the UK are carrying the abnormal prion protein that is responsible for the transmission of vCJD […], it cannot be assumed that there is no risk".[93] In response to this threat, the Government has dedicated significant funds to the field of decontamination science, valuing its current programme of research into this area at approximately £3.4 million.[94] This includes work focused on the development of new coatings for surgical instruments and "novel decontamination processes such as plasma technology", as well as "a substantial research project" looking at "novel ways to detect protein on surgical instruments".[95]

32. According to Professor John Collinge, Director of the MRC Prion Unit, this investment follows on from a similar "directed programme" of decontamination research, worth "I think […] over £10 million", initiated in the mid-2000s.[96] This was intended to encourage research groups to develop novel ways of removing prions from the surface of surgical instruments and resulted in the creation of "several solutions and products", one of which was based on a technology developed by the (publicly-funded) MRC Prion Unit itself. This technology was later commercialised by DuPont.[97] Dr Kelly Board, a Technical Specialist at DuPont, explained how this partnership came about:

92 BTO20 para 3 [DH DSWG]

93 BTO20 para 3 [DH DSWG]

94 BTO55 [Government supplementary]

95 BTO20 paras 7-9 [DH DSWG]. See also BTO55 [Government supplementary]

96 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q43

97 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q43

> Our former technical director at DuPont [Dr Crout] approached Professor Collinge's group after seeing their research demonstrating prion inactivation on surgical instruments using surfactants and a blend of enzymes. Our company has marketed a high-level disinfectant for surgical instruments called Rely+On Perasafe since 1998, and Dr Crout saw an opportunity to incorporate this disinfectant technology with that of the MRC Prion Unit.[98]

According to Dr Board, the resulting product, the Rely+On Prion Inactivator, "rapidly reduces the potential risk of prion transmission in biosurgical instruments through use of a manual pre-soak product prior to the usual decontamination methods".[99] Dr Board added that the product's performance had been validated multiple times and had been shown to reduce the risk of infection "by greater than 1 million fold".[100] Rely+On was launched in May 2007 and was subsequently evaluated by the Government's Rapid Review Panel during 2008 and 2009.[101]

The gatekeeper: The Rapid Review Panel

33. The Rapid Review Panel (RRP) is an "independent arms-length" scientific advisory committee hosted by Public Health England (PHE).[102] It is responsible for providing "a prompt assessment of new and novel equipment, materials and other products or protocols that may be of value to the NHS in improving hospital infection control and reducing hospital acquired infections", including those caused by prions.[103] According to Dr Paul Cosford, PHE Medical Director, the RRP was set up "in the early 2000s at the specific request of UK chief medical officers" as "a specific means of rapidly reviewing new technologies and new ways of providing for hospital infection control".[104] The Government stressed that, despite its mandate to assess and make recommendations about the potential value of new technologies, it was not within the RRP's remit to "influence procurement and the 'uptake' of products into the NHS".[105]

34. Following assessment by the RRP, a new technology can receive one of eight recommendations. To obtain recommendation 1, the highest level of endorsement, the RRP must conclude that scientific evaluation of the product has "shown benefits that should be available to NHS bodies to include as appropriate in their cleaning, hygiene or infection control protocols".[106] In 2008, DuPont's Rely+On Prion Inactivator received the second highest level of recommendation, recommendation 2, which recognised that "basic research and development" had been completed and that "the product may have potential

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98 Q67

99 Q67

100 Q67

101 Q67

102 Public Health England, 'Rapid Review Panel', hpa.org.uk, accessed 30 June 2014

103 Public Health England, 'About the Rapid Review Panel', hpa.org.uk, accessed 30 June 2014; BTO31 para 53 [Government]

104 Q263

105 BTO31 para 52 [Government]

106 Public Health England, 'Recommendation statements by the Rapid Review Panel', hpa.org.uk, accessed 30 June 2014

value", but recommended that further "in-use evaluations/trials" take place "in an NHS clinical setting".[107]

35. Despite receiving this recommendation, DuPont put further development of its product "on hold" in 2010.[108] It gave two main reasons for this decision:

- **Difficulties trialling the product in an NHS setting**: DuPont stated that it experienced difficulty in fulfilling the RRP's recommendation that it conduct further evaluation of its product in an NHS setting, as arranging "meaningful NHS trials" proved to be "incredibly challenging".[109] According to Dr Board, "it was very difficult for us to obtain approval to trial the product in healthcare settings" and, although the company made "several attempts" to conduct such trials, "only one materialised".[110] (Dr Board stated that this trial was "successful".[111]) The obstacles involved in initiating a UK clinical trial were well-documented in our own 2013 report on the subject.[112]

- **Poor likelihood of NHS uptake**: According to DuPont, while acknowledging that Rely+On "may have potential value", the RRP nevertheless "indicated that a pre-soak decontamination method would not obtain widespread use [in the NHS] while the prevalence of vCJD in the population remained unclear".[113] This was partly a result of the product's incompatibility with existing processes: as a pre-soak product, use of Rely+On would involve introduction of "an additional step to the decontamination process".[114] An Infection Prevention Product Specialist assigned by the Government to work with RRP applicants advised DuPont that "unless a much higher risk to the public" became apparent, such a change in procedure was "unlikely to be recommended in authoritative guidance" and DuPont's product was "therefore unlikely to be widely used".[115] Dr Board stated that this lack of a regulatory driver for product use was the "primary" barrier to further investment and development.[116]

Professor Collinge stated that it was "perhaps not surprising" that DuPont's product had not been adopted by hospitals, as the NHS was "notoriously resistant to change".[117]

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107 Q73 [Dr Kelly Board]; Public Health England, 'Recommendation statements by the Rapid Review Panel', hpa.org.uk, accessed 30 June 2014

108 Q67 [Dr Kelly Board]

109 BTO44 [DuPont]

110 Q117

111 Q117

112 Science and Technology Committee, Third Report of Session 2012-13, 'Clinical Trials', HC104

113 BTO44 [DuPont]

114 Q117 [Dr Kelly Board]

115 BTO44 [DuPont]

116 Q117

117 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q43. Note: the NHS's slow uptake of new technologies has also been documented in several other reports, including: Science and Technology Committee, Eighth report of session 2012-13, 'Bridging the valley of death: improving the commercialisation of research', HC348; The King's Fund, 'Technology in the NHS: Transforming the patient's experience of care', 2008; The Medical Technology Group. 'Medical technology: can we afford to miss out?', 2009. See also: 'NHS is "resistant to change" and "difficult to work with", says survey', *PF Discovery*, 19 November 2011 and 'Resistance to change in NHS "has cost thousands of lives", *The Times*, 1 July 2014.

Nevertheless, he said that he considered it "quite extraordinary" that a product which was the result of research directly funded by the Government, and which successfully tackled a problem acknowledged by the Department of Health, had not been put to use.[118] DuPont stated that it had not received any return on the investment that it made in this product and that there would need to be "significant justification" for it to re-start development.[119]

36. The Minister stated that she was aware of Professor Collinge's criticism of the Government's handling of this issue but that there was "nothing to stop" DuPont from "taking matters further [by] going back to the rapid review panel and doing further development and further tests".[120] She added:

> As far as I can see, no barriers have been put in the way of this product, but there is still some way to go for the people behind it to prove that it can be effective and cost-effective.[121]

Dame Sally repeated the RRP's view that "in-use evaluation trials" were now needed "in an NHS clinical setting" and stated that it was "for the company to do that".[122]

37. **Given the NHS's resistance to change and the well-documented challenges associated with initiating a UK clinical trial, the Minister's assessment that "no barriers" were put in the way of DuPont's prion inactivation product does not reflect the reality of the situation. Where technologies are developed in direct response to Government need—and on the back of Government funding—the Government must be prepared to take steps to help companies overcome barriers to adoption.** ***We ask the Government to set out how, in future, it will ensure that the directed research that it funds is better supported through the technology readiness pathway. In particular, we ask the Government to set out how it will ensure that promising clinical technologies are promptly trialled in an NHS setting, so that potential adoption challenges can be quickly identified and resolved.***

38. **We also question the value of a scientific review panel which has no mandate or power to ensure that the products that it recommends can be tested in, and eventually adopted by, the NHS. We see this as further evidence of the Government's passive approach to technology uptake.** ***We propose that the Rapid Review Panel (RRP) be given stronger powers to ensure that its recommendations open the door to in-use evaluation and stimulate NHS uptake.***

The Code of Practice for Scientific Advisory Committees

39. As a Scientific Advisory Committee (SAC), the RRP falls within the scope of both the Government Office for Science's 2011 *Code of Practice for Scientific Advisory Committees*

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118 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Qq43-44. See also Q125 [Professor John Collinge]

119 Q73; Q123 [Dr Kelly Board]

120 Q303

121 Q303

122 Q302

("the Code") and its 2010 *Principles of scientific advice to government* ("the Principles").[123] The Principles, which set out the "rules of engagement" for the relationship between the Government and its scientific advisers, highlight the need for "transparency and openness" and state that "scientific advice to government should be made publicly available unless there are over-riding reasons[124] […] for not doing so".[125] The Code likewise states that "SACs should operate from a presumption of openness" and sets out several measures to achieve this.[126] These include publishing, "as a minimum, programmes of work, meeting agendas, minutes, final advice (where appropriate) and an annual report".[127] The Code also stipulates that "Chairs and members should declare any interests they have that are relevant to the remit of the SAC" and that these should be published as part of the annual report.[128] With the exception of brief statements communicating the results of individual technology assessments, none of this information currently appears to be available for the RRP.[129] In particular, there was no evidence of any annual report having been prepared or published and no declaration of interests from the RRP's Chair or members. (We did not receive evidence from the RRP as part of this inquiry.)

40. **In our view, all Scientific Advisory Committees should adhere to both the 2010 'Principles of Scientific Advice to Government' and the 2011 'Code of Practice for Scientific Advisory Committees'. We were disappointed to find that the Rapid Review Panel (RRP) failed to do so.** ***We recommend that the Chief Medical Officer takes action to rectify current weaknesses. We request a progress report be sent to us well before the dissolution of Parliament.***

Case study 2: prion filtration

The technology: ProMetic's P-Capt prion filter

41. Prion filtration is a process through which prions are physically removed from blood through the use of highly specific resin ligands, in order to "provide increased protection against the transmission of vCJD via blood and blood-derived products".[130] One group heavily involved in the development of this technology is the UK-based company ProMetic BioSciences ("ProMetic"). In 2002, ProMetic established a joint venture with the American Red Cross aimed at developing materials "with the ability to capture and remove prion proteins from a wide variety of biological source materials including blood, red cells,

123 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011; Government Office for Science, *Principles of scientific advice to Government*, 2010

124 "Such as national security of the facilitation of a crime".

125 Government Office for Science, *Principles of scientific advice to Government*, 2010

126 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011, para 72

127 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011, para 116

128 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011, para 49

129 Based on a review of Public Health England, 'Rapid Review Panel' (and associated pages), hpa.org.uk, accessed 30 June 2014

130 BTO12 [ProMetic]; A biological ligand is a molecule that bind to a protein with a high degree of specificity. Examples are the substrate of an enzyme and a hormone binding to a cell receptor.

plasma and plasma proteins".[131] Four years later, following what ProMetic termed "extensive performance and safety testing", the P-Capt prion filtration device obtained its CE mark,[132] making it "the world's first prion-filtration product acknowledged to increase the safety of red blood cell concentrate".[133] At this point, the product became subject to further scientific evaluation, led by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO).

The gatekeeper: the Advisory Committee on the Safety of Blood, Tissues and Organs

42. SaBTO is an independent scientific advisory committee responsible for advising "UK ministers and health departments" on "the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion/transplantation".[134] As part of its remit, SaBTO is specifically tasked with considering the "cost-effectiveness of interventions, including the introduction of new safety measures" such as prion filtration.[135]

43. In 2006, SaBTO initiated its evaluation of ProMetic's P-Capt device.[136] This consisted of three stages:

i) **UK Blood Service studies.** According to Professor Marc Turner, SaBTO, in 2006 UK Blood Services were asked to "commission and carry out a number of independent studies" to demonstrate the P-Capt filter's safety and efficacy "in the real word".[137] This included a series of laboratory studies and the PRISM A trial, which was intended to detect any adverse effects from use of prion-filtered red blood cells in a clinical setting.[138] Professor Turner stated that these studies "broadly showed that the filters were safe and were not causing any adverse impact to patients".[139]

ii) **First set of efficacy evaluations**. An initial set of efficacy evaluations, conducted by the Health Protection Agency (HPA, now Public Health England) and completed in 2009, showed that the P-Capt filter "removed infectivity" from test samples,

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131 BTO12 para 3 [ProMetic]

132 CE marking is required for many products traded across the European Economic Area and "attests the verification by a manufacturer that these products meet EU safety, health or environmental requirements". See 'CE marking', gov.uk for more information.

133 BTO12 para 6 [ProMetic]

134 Advisory Committee on the Safety of Blood, Tissues and Organs, 'Homepage', Government.uk, accessed 30 June 2014

135 Advisory Committee on the Safety of Blood, Tissues and Organs, 'Terms of Reference', Government.uk, accessed 30 June 2014

136 According to NHSBT, ProMetic, alongside another prion filtration developer, was also invited to meet regularly with the UK Blood Services Prion Removal Working Group, a group set up in 2005 to evaluate new commercial filters (BTO14 para 26 [UKBS PWG]).

137 Q49

138 Q124 [Dr Steven Burton]; BTO53 [ProMetic supplementary]

139 Q49

"though not to the same extent as in the studies reported by the manufacturer".[140] Nevertheless, SaBTO concluded that the study supported the hypothesis that "prion infectivity" could "be removed by the filter" at levels high enough to confer protection on transfusion recipients.[141]

iii) **Second set of efficacy evaluations**. The second set of efficacy evaluations consisted of two studies; one, in hamsters, conducted by the HPA and one, in sheep, conducted by the Roslin Institute. Interim results were reported to SaBTO in March 2012;[142] to our knowledge, final results have not yet been published in a peer-reviewed journal.

Following completion of the first set of efficacy evaluations in 2009, SaBTO concluded that there was "sufficient evidence" to suggest that the P-Capt filter was effective in reducing prion infectivity and recommended that "filtered red cells be provided to those born since 1 January 1996, subject to satisfactory completion of the PRISM clinical trial".[143] The PRISM study was completed and reported positive results in March 2012;[144] however, at this time SaBTO received interim results from the second set of efficacy evaluations and decided that "no final decision" should be made until "further data on efficacy is available with respect to both the ongoing hamster and sheep studies and the final result of the current human appendix prevalence study".[145] In its evaluation of ProMetic's P-Capt device, SaBTO also drew on a cost-effectiveness analysis conducted on its behalf by the Department of Health's Health Protection Analytical Team.[146] In December 2012, having reviewed all of the available data, SaBTO decided to rescind its initial recommendation.[147] Prion filtration has therefore not been adopted by UK Blood Services and ProMetic has, to date, received no return on its $50 million (approximately £30 million) investment in this technology.[148] According to the UK Blood Services Prion Working Group, research conducted as part of this evaluation process cost upwards of £5.2 million.[149]

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140 Advisory Committee on the Safety of Blood, Tissues and Organs, *Minutes of the eighth meeting*, 27 October 2009, para 6.9

141 Advisory Committee on the Safety of Blood, Tissues and Organs, *Minutes of the eighth meeting*, 27 October 2009, para 6.10

142 Advisory Committee on the Safety of Blood, Tissues and Organs, *Final minutes of the sixteenth meeting*, 9 March 2012, para 4.19-21

143 Advisory Committee on the Safety of Blood, Tissues and Organs, *Summary of the eighth meeting*, 27 October 2009, para 3

144 See: Elebute et al, 'Transfusion of prion-filtered red cells does not increase the rate of alloimmunization or transfusion reactions in patients: results of the UK trial of prion-filtered *versus* standard red cells in surgical patients (PRISM A)', *British Journal of Haematology*, Volume 160, Issue 5, pp.701-708, March 2013. DOI: 10.1111/bjh.12188

145 Advisory Committee on the Safety of Blood, Tissues and Organs, *Final minutes of the sixteenth meeting*, 9 March 2012, para 4.22. Note: the appendix study referred to was reported to SaBTO in September 2012 and was published in October 2013. See O Noel Gill et al, *Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey*, British Medical Journal, Volume 349, Issue 7929. BMJ2013;347:f5675

146 SaBTO, *Prion reduction filters for red cell concentrates*, Eighteenth meeting, Agenda item 4, 10 December 2012

147 Q49; Q56; Advisory Committee on the Safety of Blood, Tissues and Organs, *Final minutes of the eighteenth meeting*, 10 December 2012, para 4.1-3

148 Q69-72 [Dr Steven Burton]

149 BTO14 pars 23 [UKBK Prion Working Group]

44. ProMetic criticised several aspects of this evaluation process and stated that it "strongly believed" SaBTO's 2012 reversal of its provisional recommendation "to be motivated by considerations other than filter efficacy".[150] ProMetic was particularly critical of the length of time taken to complete the PRISM A study (approximately 5 years), a technical issue in one of the hamster studies which it claimed compromised the filter's performance and the decision to test the filter in sheep, which it had previously demonstrated was "not an appropriate model" for determining the efficacy of the filter when used on human blood.[151] However, Dr Lorna Williamson, Medical and Research Director at NHS Blood and Transplant (and also a member of SaBTO), stated that these results had been "considered in the round" alongside other evidence and that she was "happy" with SaBTO's recommendation.[152]

45. **We do not wish to question the scientific decision-making of the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) and we respect its decision not to recommend adoption of prion filtration at present. However, we feel that the time taken to reach this decision was excessive and that the process, particularly in its latter stages, entailed an unnecessary level of uncertainty for the commercial developer. We have some sympathy for SaBTO's desire to wait until more evidence was available before making a decision; however, if industry is to continue to develop innovative blood safety products for the UK market, SaBTO must introduce greater speed and predictability into its evaluation process.** ***We recommend that, in future, when assessing a new technology, SaBTO agree with stakeholders at the outset what the evaluation will consist of, together with key dates, milestones and decision-points. This 'evaluation roadmap', and any subsequent amendments, should be made publicly available to ensure maximum transparency and accountability.***

46. **We also consider it important that the health technology appraisals conducted by SaBTO—and all other SACs—use the same methodology and meet the same high standards as those undertaken by the UK's centre of excellence for this activity: NICE.** ***We therefore recommend that the Government Office for Science work with NICE over the next 12 months to develop and publish a standard methodology for all SACs tasked with conducting health technology appraisal. Until this guidance is published, we recommend that a NICE representative review and, where necessary, provide input to all such appraisals undertaken by, and on behalf of, SACs.***

SaBTO's relationship with Government

47. The Government Office for Science's 2011 *Code of Practice for Scientific Advisory Committees* ("the Code") and its 2010 *Principles of scientific advice to government* ("the Principles") both highlight the importance of scientific advisors maintaining a level of

150 BTO53 [ProMetic supplementary]

151 BTO53 [ProMetic supplementary]

152 Q252-254

independence from Government.[153] The Code, in particular, states that Scientific Advisory Committees (SACs) such as SaBTO should "expect to operate free of influence from the sponsor department officials" and that members should be "professionally impartial in their activity" on behalf of the SAC.[154]

48. Under its terms of reference, SaBTO is responsible for providing advice to "Ministers of the UK Government and the Devolved Administrations as well as UK Health Departments".[155] It is not sponsored by, and its advice is not formally directed at, any of the four UK Blood Services. However, SaBTO's Code of Practice acknowledges that its advisory role extends to "UK Blood Services […] and to the NHS more widely" and many of its recommendations are implemented by these organisations.[156] At present, two members of SaBTO also hold senior management roles in UK Blood Services: Dr Lorna Williamson, Medical and Research Director of NHS Blood and Transplant (NHSBT), and Professor Marc Turner, Medical Director of the Scottish National Blood Transfusion Service (SNBTS). NHSBT is an NHS Special Health Authority and, as such, "can be subject to ministerial direction".[157] SNBTS is a division of NHS National Services Scotland, a non-departmental public body of the Scottish Government.[158]

49. As well as being members of SaBTO, Dr Williamson and Professor Turner are also members of UK Blood Services' Joint Professional Advisory Committee (JPAC), which is responsible for developing UK-wide operational policies, often drawing heavily on SaBTO's advice.[159] According to JPAC, this advisory relationship between SaBTO and UK Blood Services also operates in reverse, as "much of the detailed evidence on which SaBTO deliberates is the result of work by Blood Services staff" and other Blood Service advisory committees reporting in to JPAC.[160] During the period in which ProMetic's prion filtration device was being evaluated, Professor Turner was also Chair of both SaBTO's prion sub-group and the UK Blood Services Prion Working Group.

50. **Scientific Advisory Committees should be—and be seen to be—independent of the bodies to which they are providing advice. At present, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) comprises members who are both contributing to, and acting on, the advice that it formulates. We consider that this could be damaging to its perceived independence and a source of potential conflicts of interest. *We recommend that SaBTO's terms of reference be amended to reflect the fact***

153 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011; Government Office for Science, *Principles of scientific advice to Government*, 2010

154 Government Office for Science, *Code of Practice for Scientific Advisory Committees*, 2011, paras 31-32

155 Advisory Committee on the Safety of Blood, Tissues and Organs, *Terms of Reference*, Government.uk, accessed 30 June 2014

156 Advisory Committee on the Safety of Blood, Tissues and Organs, *Code of Practice*, para 7, Government.uk, accessed 30 June 2014

157 NHSBT. 'Home', nhsbt.nhs.uk. NHS Choices, 'The NHS in England', nhs.uk. Both accessed 1 July 2014

158 SNBTS, 'About us', scotblood.co.uk. NHS National Services Scotland, 'About us', nhsnss.org. Both accessed 1 July 2014

159 See, for example: JPAC/Health Protection Agency, *Position Statement: Blood donor selection to minimise risk of transfusion transmissible infectious agents entering the blood supply*, 14 November 2012 and *Position Statement: Creutzfeldt-Jakob Disease*, 12 November 2012, transfusionguidelines.org.uk, accessed 30 June 2014

160 JPAC. 'About JPAC', transfusionguidelines.org.uk, accessed 30 June 2014

that it does, in effect, provide advice to UK Blood Services as well as the Government. We suggest that SaBTO's current membership be reviewed and potentially revised in light of this change.

Case study 3: vCJD blood testing

The need for a vCJD blood test

51. A key strand in UK Blood Services' strategy for preventing transfusion-transmitted infections is the use of blood tests to enable those donations carrying known pathogens to be identified and discarded.[161] Unfortunately, this is not currently a viable strategy for mitigating the risk of vCJD transmission because no suitable high-throughput test currently exists. Witnesses were unanimous in their support for the development of such a test. Professor Sheila Bird, MRC Biostatistics Unit, expressed concern that the absence of a vCJD blood test meant that we could not protect the blood supply from prions in the same way that we can protect it from other pathogens, such as hepatitis B and C and HIV, and stated that development of a validated test should "undoubtedly" be a research priority.[162] Professor Richard Knight, Director of the National CJD Research and Surveillance Unit ('the surveillance unit'), agreed that development of a test was "extraordinarily important" and "would be a great boon in all sorts of ways".[163] In addition to its potential screening applications, witnesses highlighted the role that a blood test could play in providing certainty to patients thought to be at risk of vCJD. Joseph Peaty, TaintedBlood, told us that, some years ago, it had "looked very much" as though he was suffering from the early signs of vCJD.[164] He explained:

> It would have been incredibly helpful if we had had access to [a test] at that point to identify, "Is this the onset of variant CJD, or is it where these viruses overlap and you've got HIV? Perhaps the medication, or perhaps hepatitis C, is affecting the brain in some way." I had to go through brain scans and vigilance for a number of months. I had insomnia, where I hardly slept for three months. I was incredibly depressed and anxious.[165]

The Government did not explicitly state its support for the development of this technology but acknowledged that a test "may be advantageous".[166]

52. The number of research groups working to develop a vCJD blood test has fallen in recent years. According to Professor Marc Turner, Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), "looking back a decade or so ago, there were probably […] a dozen or more different research groups and commercial companies working" in

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161 BTO30 para 8 and para 11 [JPAC]

162 Q147; Q175

163 Q178

164 Q16

165 Q16

166 BTO31 para 33 [Government]

this area. Now, however, "there are really only two or three".[167] Professor Turner stated that the "most advanced test by far" was the one currently being developed by the MRC Prion Unit, a publicly-funded research group led by Professor John Collinge.[168] In addition, Prionics AG, a Swiss company, has continued to conduct work in this area, as has the Scottish National Blood Transfusion Service, working in partnership with the national surveillance unit.[169]

The technology: the Prionics blood test

53. Prionics AG is a developer of diagnostic tests for major livestock diseases.[170] In 2001, when surveillance programs for BSE became mandatory in the European Union, Prionics "pioneered" the use of in-situ rapid diagnostic tests and, today, the company continues to develop diagnostic tools for prion diseases such as vCJD.[171] According to Prionics, it has made a "significant investment" in this area, spending "€5 million to €10 million" on the development of prototype vCJD blood tests since 2002.[172] In 2009, NHS Blood and Transplant (NHSBT) issued a tender for the development of a diagnostic test for use in vCJD blood screening. Following a successful bid, Prionics was awarded a framework contract pending further evaluation of its test by the National Institute of Biological Standards and Controls (NIBSC), the body tasked with maintaining and managing the distribution of rare vCJD blood samples.[173]

The gatekeeper: the National Institute of Biological Standards and Controls

54. The National Institute of Biological Standards and Controls (NIBSC) is a body of the Medicines and Healthcare Products Regulatory Agency, an Executive Agency of the Department of Health.[174] It hosts the CJD Resource Centre, which exists to "help research scientists obtain characterised materials for studying and developing diagnostic tests" for all forms of CJD.[175]

55. In order to develop a diagnostic blood test, it is necessary for researchers to have access to blood samples from people who have suffered from the target infection. In the case of common blood-borne pathogens such as hepatitis B and HIV, such samples can be easily obtained. However, because vCJD is such a rare disease, patient samples are extremely scarce.[176] In the UK, the majority of samples from confirmed vCJD cases are initially

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167 Q62

168 Q62; MRC Prion Unit, 'About the Unit', prion.ucl.ac.uk, accessed 30 June 2014

169 BTO14 para 28 [UKBS Prion Working Group]

170 BTO39 [Prionics]

171 BTO39 [Prionics]

172 BTO39 [Prionics]; Q73 [Dr Alex Raeber]

173 BTO39 [Prionics]

174 National Institute for Biological Standards and Control, 'About us', nibsc.org, accessed 30 June 2014; Medicines and Healthcare Products Regulatory Agency, 'About us', mhra.Government.uk, accessed 30 June 2014

175 National Institute for Biological Standards and Control, 'CJD Resource Centre', nibsc.org, accessed 30 June 2014

176 BTO05 para 3 [NIBSC]

collected and stored at either the surveillance unit or the MRC Prion Unit.[177] According to the NIBSC, following requests for access to these samples from several test developers in the mid-2000s, the Government concluded that access should be "controlled" and only granted to those developers whose tests were most likely to be successful.[178] In 2007, an Oversight Committee was established within the CJD Resource Centre to "perform evaluations" of prototype tests and "manage the distribution of samples" according to a standard protocol.[179] According to Dame Sally Davies, Chief Medical Officer, the NIBSC currently holds samples from 16 individual vCJD patients: equivalent to approximately "one and a half tablespoons" of blood.[180]

56. In order to gain access to these samples, test developers require NIBSC approval. However, according to the NIBSC, "it was agreed at the start of the [CJD Resource] Centre's existence" that the two primary centres of UK prion research—the national surveillance unit and the MRC Prion Unit—should be exempt from this process in order to avoid "unreasonably" restricting their research work.[181] Additional samples are therefore currently held and used by these units and, on occasion, are provided directly to other test developers without recourse to the NIBSC evaluation process.[182]

57. Several witnesses expressed concern about the way in which access to vCJD samples was controlled in the UK. Christine Lord, mother of vCJD victim Andrew Black, pointed out that the Government held "all the keys" to vCJD test development and claimed that a "few select scientists and Government officials" held "a monopoly" over this research area.[183] Mrs Lord added that relatives of victims had been "thwarted and blocked" in their attempts to share blood samples with foreign research groups.[184] Dr Alex Raeber, Head of Research and Development at Prionics AG, agreed that, "as a foreign company", Prionics was "not treated in the same way as other stakeholders" and had faced "big challenges" in obtaining access to samples.[185] According to Dr Raeber, while the NIBSC had done "an excellent job" in setting up the test validation process, the number of samples made available through this process was "very limited".[186] Prionics' test was evaluated on the basis of two samples from known vCJD patients and, on the basis of this evaluation, was deemed "not sufficiently fit for purpose".[187] The test was never used by UK Blood Services.

58. Dr Raeber criticised this evaluation process, stating that it was "really not adequate" for the NIBSC to validate the efficacy of his company's test on the basis of only two samples[188],

177 Q103 [Professor John Collinge]

178 BTO05 para 3 [NIBSC]

179 BTO05 para 12; annex 4 [NIBSC]

180 Q292

181 BTO05 para 5 [NIBSC supplementary]

182 Q292 [Dame Sally Davies]; Q103 [Professor John Collinge]

183 Q3

184 Q15

185 Q102; Q97

186 Q102; Q96

187 Q96

188 These two vCJD samples were contained within a blind panel of 200 samples.

particularly given that there was no guarantee that prions were present in these particular samples.[189] Professor Sheila Bird, MRC Biostatistics Unit, agreed that the statistical significance of this evaluation was questionable and pointed out that "provision of fewer than five or six vCJD samples within a blind panel of 500" was an "inadequate—or very harsh" statistical assessment to which to submit a prototype test.[190] In contrast, the test developed by the MRC Prion Unit (discussed below) has so far been validated on the basis of 21 samples from known vCJD cases, all sourced directly from its own collection of patient samples.[191] In response to these criticisms, the NIBSC stated that its process was "open to all" and that, in fact, "most interactions" had been with non-UK developers rather than UK companies.[192] It acknowledged that it was "not ideal that only two samples were made available" to Prionics, but stressed that this decision was made only after "substantial discussion in the Oversight Committee".[193]

59. **We understand the need to carefully control access to rare vCJD samples and commend the National Institute of Biological Standards and Controls (NIBSC) for putting in place a standard protocol for test validation. However, we are disappointed that so few samples are currently held by the NIBSC and consider its process to be undermined by the fact that the two major centres of UK prion research—the National CJD Research and Surveillance Unit and the MRC Prion Unit—can each use and distribute samples independent of NIBSC evaluation.** ***All test developers should be given equal opportunity to gain access to the available samples and these should be distributed on the basis of merit alone. We recommend that access to all vCJD patient samples—including those currently held elsewhere in the UK—be managed through the NIBSC, according to a consistent set of test validation protocols.***

60. **We were also concerned by the apparent statistical weakness of past NIBSC evaluations.** ***We recommend that the CJD Resource Centre Oversight Committee add to its membership an individual with expertise in biostatistics, who can provide it with expert advice on this matter during future deliberations.***

The technology: the MRC Prion Unit blood test

61. The MRC Prion Unit was established in 1998 and is located at the UCL Institute of Neurology.[194] It was formed "to provide a national centre of excellence with all necessary facilities to pursue a major long-term research strategy in prion and related diseases".[195]

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189 Q96. See also Mead et al., *Variant Creutzfeldt-Jakob Disease With Extremely Low Lymphoreticular Deposition of Prion Protein*, JAMA Neurology, Volume 71, Issue 3, March 2014. doi:10.1001/jamaneurol.2013.5378

190 BTO51 [Professor Sheila Bird]. Note: while the Prionics test was evaluated on the basis of two vCJD samples contained within a blind panel of 200, another company that similarly underwent evaluation by NIBSC were provided with two vCJD samples in a blind panel of 500.

191 Jackson et al., *A highly specific blood test for vCJD*, *Blood*, Volume 123, pp.452-453, January 2014. doi:10.1182/blood-2013-11-539239

192 BTO50 para 4 [NIBSC supplementary]

193 BTO50 para 4 [NIBSC supplementary]

194 MRC Prion Unit, 'About the Unit', prion.ucl.ac.uk, accessed 30 June 2014

195 MRC Prion Unit, 'About the Unit', prion.ucl.ac.uk, accessed 30 June 2014

The Unit undertakes research across a wide-range of topics and aims to "seamlessly combine basic (laboratory) and clinical (patient-based) research" in order to enable "better early diagnosis, prevention, and effective treatment" of prion disease.[196] It receives approximately £6 million per year from the Medical Research Council and is led by John Collinge, Professor of Neurology and Head of the Department of Neurodegenerative Disease at the UCL Institute of Neurology.[197]

62. In February 2011, the Unit announced that it had developed a prototype blood test capable of detecting "blood spiked with a dilution of vCJD to within one part per ten billion—100,000 times more sensitive than any other method developed so far".[198] In this study, the prototype test returned no false positives from 100 control samples and accurately identified 15 of 21 samples taken from known vCJD patients as positive, indicating that the test was 100% specific and approximately 70% sensitive.[199] In a larger follow-up study published in early 2014, the prototype was tested on 5,000 control samples (from US citizens considered not to have been exposed to BSE) and a subset of the vCJD samples previously used in the 2011 study. It again demonstrated 100% specificity and 70% sensitivity.[200]

63. Professor Collinge stated that the next logical step in the test's development would be to carry out a larger 'population prevalence' study in which the prototype would be used to test 20,000 UK blood samples and 20,000 US blood samples, at an estimated cost of £750,000.[201] According to Professor Collinge, if, during this study, the test returned positive results only from UK samples, two things could be concluded:

> One is that our test is capable of detecting [vCJD] carriers, which we don't formally know yet: we have simply looked at [vCJD] patients. Secondly, we would have confirmed that there is, indeed, a problem in the British donor core. In our view, that piece of research is required to make the case to progress that test further.[202]

A proposal for this study was considered by the MRC in March 2013, but was rejected, in part because of the test's "low level of sensitivity".[203] According to the MRC:

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196 MRC Prion Unit, 'About the Unit', prion.ucl.ac.uk, accessed 30 June 2014

197 BTO31 para 20 [Government]

198 BTO27 para 21 [MRC]. See also Edgeworth et al., *Detection of prion infection in variant Creutzfeldt-Jakob disease: a blood-based assay*, The Lancet, Volume 377, Issue 9764, pp.487-493, 5 February 2011. doi:10.1016/S0140-6736(10)62308-2

199 Edgeworth et al., *Detection of prion infection in variant Creutzfeldt-Jakob disease: a blood-based assay*, The Lancet, Volume 377, Issue 9764, pp.487-493, 5 February 2011. doi:10.1016/S0140-6736(10)62308-2. Note: sensitivity refers to the ability of a test to detect an agent when present. A low level of sensitivity could lead to "false negatives"—that is, people who receive a negative result but do actually carry the agent. Specificity refers to the ability of a test to detect the absence of an agent. A low level of specificity could lead to "false positives"—that is, people who receive a positive result who do not in fact carry the agent.

200 Jackson et al., *A highly specific blood test for vCJD*, Blood, Volume 123, pp.452-453, January 2014. doi:10.1182/blood-2013-11-539239

201 Q87; Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q14

202 Q87

203 BTO27 para 22 [MRC]

> the Unit was advised to consider ways to improve the test sensitivity to provide greater confidence of identification of infected people, in order to make the test more accurate for prevalence studies and more attractive for development into a screening test.[204]

Professor Collinge disputed the MRC's decision, claiming that the recommended steps constituted "test development work" which lay outside of his unit's area of expertise.[205] He added that, in the view of his Unit's "statistical advisers", the test's sensitivity was "perfectly adequate to do the study that we propose to do" and that it may not be possible to further increase sensitivity because "it could be that only 70% of people with vCJD have prions in their blood".[206] Professor Collinge also highlighted that feedback from diagnostics companies was "very much" that they wanted to see the results of a larger study "before thinking about whether they would help us to take [the test] any further"—a view confirmed by several industry representatives.[207]

64. Expert witnesses strongly supported Professor Collinge's proposal for a UK blood prevalence study; indeed, Dr Simon Mead, Association of British Neurologists, stated that there now appeared to be "scientific consensus" on this matter.[208] Professor Marc Turner, SaBTO, agreed with Professor Collinge that the test's sensitivity was "pretty good" and considered a blood prevalence study to be "the next logical step" in its development, while Dr Roland Salmon, Acting Chair of the Advisory Committee on Dangerous Pathogens, considered there to be "a great deal of scope" for the test to be used for research purposes in its current state.[209] Dr Lorna Williamson, NHS Blood and Transplant (NHSBT), took a similar view:

> I think we are all in agreement that the next step, if there were a medium throughput test available, would be to conduct a study of the UK population using blood samples to understand what the frequency of prion infection in the blood actually is.[210]

The Government, however, stated that there were "currently no tests suitable" for this purpose and was non-committal in its support for further test development work.[211] Dame Sally Davies, Chief Medical Officer, stressed that the Government had "limited budgets for healthcare, public health and research" and that it had previously "given a lot of money to this area of prion research, particularly to Professor Collinge".[212] The Minister said that she was "open-minded to receiving advice" on this matter, but added that she was

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204 BTO27 para 22 [MRC]

205 Q90

206 Q90. See Mead et al., *Variant Creutzfeldt-Jakob Disease With Extremely Low Lymphoreticular Deposition of Prion Protein*, JAMA Neurology, Volume 71, Issue 3, March 2014. doi:10.1001/jamaneurol.2013.5378

207 Q87 [Professor John Collinge]; Q93-95 [Dr Alex Raeber; Dr Steven Burton; Nigel Talboys]

208 Q161 [Dr Simon Mead]

209 Q62 [Professor Marc Turner]; Q63 [Dr Roland Salmon]

210 Q244

211 BTO31 para 33 [Government]

212 Q288

"pretty satisfied that, proportionate particularly to the number of cases and deaths over the last 10 years or so, there is a good body of work going on at the moment".[213]

65. **The incubation period of prion diseases such as vCJD can extend to several decades and it is therefore possible that individuals infected in the 1990s might not yet have developed symptoms. We do not follow the Minister's logic that there should be a link between the number of cases seen in the last ten years and the level of resource dedicated to prion research. We simply do not know, at present, how many people have been exposed to prions and what the implications of this might be for the blood donor pool. There is an urgent need to reduce this uncertainty.**

66. **Based on the testimony that we have heard, we consider that a vCJD blood prevalence study utilising a version of the prototype test developed by the MRC Prion Unit would be of considerable value, both for test development and research purposes. We recognise that significant public funds have already been directed towards the development of this test; we view this as even more reason to ensure that a return on this investment is realised. To cut off support now would be a false economy. *We recommend that the Government ensures that a large-scale vCJD blood prevalence study be initiated in the UK within the next 12 months.***

213 Q287

4 CJD risk management and surveillance

CJD risk management and 'at risk' individuals

67. Both classical and variant forms of CJD[214] are relatively rare and precautions are in place to prevent those known to be suffering from the disease from passing it on to others. However, CJD's long incubation period—that is, the time between infection and the onset of symptoms—means that people could unknowingly carry the disease for many years before symptoms appear. During this time, they could participate in procedures which risk exposing others.[215] To date, in the UK, over 6,000 people have been identified as being at increased risk of CJD as a result of this type of retrospectively recognised secondary exposure.[216] Public Health England (PHE) divides these people into two groups:

- "individuals with a known link to a clinical case of vCJD (through donation or receipt of blood or blood products, receipt of certain pooled plasma products or following surgical exposure); and
- groups of individuals, not linked directly to a clinical case but who, on the basis of a risk assessment, are defined as likely to have been exposed to a high enough risk of exposure through their treatment with blood or plasma products to inform them about this risk, where possible, and to recommend that public health precautions concerning blood, tissues, organs and surgery are followed".[217] (These precautions are detailed in box 1.)

Incidents leading to further additions to the 'at risk' list continue to occur and, until its dissolution in March 2013, were managed under the advice of the CJD Incidents Panel, a scientific advisory committee with expertise in CJD risk management.[218] According to PHE, between January 2010 and March 2013, the CJD Incidents Panel was notified of 43 'CJD incidents' and 70 lower-risk 'CJD reports'.[219]

214 In this Chapter, the term 'CJD' refers to both classical and variant CJD unless otherwise indicated.

215 Parliamentary Office of Science and Technology, *vCJD in the future*, POSTnote number 171, January 2002

216 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

217 BTO34 [PHE]

218 Health Protection Agency, 'CJD Incidents Panel', hpa.org.uk, accessed 30 June 2014

219 Public Health England, *Health Protection Report: weekly report*, Volume 7, Number 33, 16 August 2013, hpa.org.uk, accessed 30 June 2014

Box 1: Public health advice for those notified that they are 'at risk' of having contracted CJD[220]

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 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.

Notification of 'at risk' individuals

68. Historically, cases of potential CJD transmission were managed by the CJD Incidents Panel in collaboration with several bodies.[221] These included the Health Protection Agency, now PHE, which maintains a CJD Section to provide "national advice and support to prevent the potential spread of CJD in healthcare settings",[222] and the UK Haemophilia Centre Doctors' Organisation, an association of medical practitioners working within UK haemophilia centres.[223] Since the dissolution of the Panel last year, "responsibility for actions on individual CJD incidents"—including patient notification—has passed to local teams.[224] Dr Katy Sinka, PHE CJD Section, stated that when notifying an individual of their 'at risk' status, the aim was "to provide as much information and support as possible".[225] She added that "a whole suite of written information" had been produced to achieve this and that notification usually involved the person's GP or clinical specialist, "so there is someone who is able to support them and explain the risks".[226] The written information referred to by Dr Sinka consists of two six-page leaflets which detail the reasons for a

220 Public Health England, 'Information for people who have an increased risk of CJD', May 2013, hpa.org.uk, accessed 30 June 2014

221 Health Protection Agency, 'CJD Incidents Panel', hpa.org.uk, accessed 30 June 2014

222 Public Health England, 'Creutzfeldt-Jakob disease: General information', hpa.org.uk, accessed 30 June 2014

223 UK Haemophilia Centre Doctors' Organisation, 'Introduction to UKHCDO', ukhcdo.org, accessed 30 June 2014

224 BTO31 para 57 [Government]

225 Q266

226 Q266

person having been designated as 'at risk' and the potential implications of this status.[227] Website details are provided for those who wish to obtain further information.

69. Several witnesses highlighted issues with this process. Liz Carroll, Chief Executive of the Haemophilia Society, stated many of the people with bleeding disorders who were thought to be at risk had been written to, "but that was the extent of what happened really".[228] GRO-A TaintedBlood, confirmed that he had received such a letter but agreed that there had been little further support.[229] According to the CJD Support Network, a UK charity supporting those affected by CJD:

> We currently receive around 400 helpline calls per year. Between July 2011 and October 2013 we have received 28 calls specifically from people with issues about the support and information received when they had been informed that they are at higher risk of CJD through secondary transmission. In addition to those calls we have received in the same period 15 calls from health facilities who were asking about uncertainties in dealing with CJD incidents.[230]

Nevertheless, the Government's Chief Medical Officer, Dame Sally Davies, indicated that she was "confident" that local CJD management and reporting structures were robust and that 'at risk' individuals were receiving the necessary support.[231]

70. **People who are notified that they may have been exposed to CJD will inevitably be alarmed by this information and will likely have questions that cannot be answered in the leaflets currently provided by Public Health England. We consider it totally inappropriate for this news to be communicated solely in writing.** ***We recommend that the Government put robust measures in place to ensure that all individuals assigned this designation receive the news verbally, either from a healthcare provider or from a CJD specialist with experience in patient communication.***

The impact of 'at risk' notification

71. Several witnesses stressed to us the negative impact that 'at risk' notification could have on a person's life: Christine Lord, mother of vCJD victim Andrew Black, described the designation as "a sword of Damocles hanging over these people's heads".[232] GRO-A TaintedBlood, who has himself been notified that he is 'at risk' of CJD, agreed that the experience was like "walking around with a loaded gun pointing to your head",[233] adding:

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227 Public Health England, 'Information leaflets for patients and healthcare professionals', hpa.org.uk, accessed 30 June 2014

228 Q17

229 Q17

230 BTO07 [CJD Support Network]

231 Q312-314

232 Q15

233 Q15

> you are waiting for it to go off—you don't know where and you don't know when, but because there is no information you are literally living in fear.[234]

Dr Simon Mead, Association of British Neurologists, described notification as a "concrete harm" because individuals were notified of their risk "with no opportunity for a blood test to confirm or not whether that risk is real, and with an indefinite prospect of a potentially incurable disease".[235] Dr Cosford, PHE, agreed that the "actual benefit" of telling a person that they were at risk was "very limited" and that notification was therefore "a very delicate area".[236]

72. Witnesses highlighted the potential for a vCJD blood test to minimise the harm caused by notification. GRO-A TaintedBlood, who is also 'at risk', highlighted that a blood test such as the one developed by Professor Collinge's group at the MRC Prion Unit could "possibly offer an element of comfort to some people—an element of reassurance", even if the results were not 100% reliable.[237] Liz Carroll, the Haemophilia Society, agreed that she "absolutely" thought that people should have the opportunity to utilise the existing test.[238] According to Professor Collinge:

> Many of these people want to know whether or not they are infected. They have already had their lives blighted by being told [that they are 'at risk'], and told that the risk is essentially unknown. A number of these people have come to see me in clinic and asked whether they can be tested.[239]

Professor Collinge stated that the MRC Prion Unit had not, to date, made its test available to 'at risk' individuals because he did not think enough was known about infection risk for it to be useful.[240] However, he added that if more information was gathered "it may be that we could offer the test and provide some predictive value" for people impacted by their 'at risk' designation.[241] Professor Collinge stated that the test was already "in clinical use at the National Prion Clinic", where it was used for "diagnosing variant CJD".[242]

73. **It is clear that the prototype vCJD blood test developed by the MRC Prion Unit cannot yet be relied upon for universal screening purposes. However, it could be of significant value to those people who have been notified that they are at increased risk of carrying the disease. *Until the implications of a negative test result can be more firmly established, current precautions must remain in place for those considered to be 'at risk' of vCJD. However, the results of an imperfect test may provide comfort to some. We***

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234 Q15

235 Q173

236 Q275

237 Q29

238 Q29

239 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q16

240 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q16

241 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q16

242 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q7

therefore recommend that 'at risk' individuals be given the opportunity to participate in the blood prevalence study recommended in paragraph 66.

CJD surveillance

74. The Government described national surveillance as "the cornerstone" of its policy "to monitor and control the spread of vCJD".[243] At present, this system consists of two main strands:

i) 'enhanced surveillance' of those considered to be 'at risk' of CJD, led by Public Health England (PHE); and

ii) national monitoring and investigation of suspected and confirmed cases of CJD, led by the National CJD Research and Surveillance Unit (NCJDRSU).

Enhanced surveillance of 'at risk' individuals

In-life surveillance

75. According to PHE, individuals designated 'at risk' of CJD are "followed-up" in order to ascertain whether their potential exposure eventually leads to signs of clinical infection. It states that:

> Public Health follow-up activities include clinical monitoring, general practitioner (GP) updates, and post mortem investigations to determine whether asymptomatic individuals in these groups have been infected with the CJD agent. Some individuals also provide blood or tissue specimens for research purposes.[244]

These "enhanced surveillance" activities are coordinated by PHE but rely on data held by several other organisations which are individually responsible for monitoring different 'at risk' cohorts (see table 2). Of particular note is the UK Haemophilia Centre Doctors' Organisation (UKHCDO), which is responsible for the surveillance of 3,875 bleeding disorder patients identified as having received plasma products between 1990 and 2001—the largest single 'at risk' group.[245]

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243 BTO31 para 26 [Government]

244 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

245 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

Table 2: Summary of groups 'at risk' of CJD[246]

'At risk' group	Organisation responsible	Individuals designated 'at risk'	Individuals notified of their 'at risk' status *All (alive)*	CJD cases and asymptomatic infections
Recipients of blood from donors who later developed vCJD	Public Health England	67	27 (15)	4
Blood donors to individuals who later developed vCJD		112	107 (104)	0
Other recipients of blood components from these donors		34	32 (19)	0
Plasma product recipients (non-bleeding disorders) who received UK sourced plasma products 1980-2001		11	10 (4)	0
Certain surgical contacts of patients diagnosed with CJD		154	129 (113)	0
Highly transfused recipients		11	10 (6)	0
Total for 'at risk' groups where PHE holds data		**389**	**315 (261)**	**4**
Patients with bleeding disorders who received UK sourced plasma products 1980-2001	UK Haemophilia Centre Doctors' Organisation	3,875	National information incomplete	0
Recipients of human derived growth hormone	Institute of Child Health	1,883	1,883 (1,504)	75
Total for all 'at risk' groups		**6,147**	**>2,198 (>1,765)**	**79**

76. When questioned about its enhanced surveillance scheme, Dr Katy Sinka, Head of PHE's CJD section, stated that there were long-term processes in place to identify "any development of neurological symptoms or CJD in people who have been told that they are at increased risk".[247] However, PHE acknowledges that it only holds data on 389 of the 6,147 individuals identified as being 'at risk' of CJD and that not all patients in this larger group have necessarily been notified of their status (see table 2).[248] In particular, PHE explains that:

> The data from the UKHCDO [UK Haemophilia Centre Doctors' Organisation] are likely to be an underestimate of the true number of 'at risk'

246 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

247 Q268

248 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014. See also Q272 [Dr Katy Sinka]

> patients […], as there was incomplete reporting of identified 'at risk' patients by haemophilia centres to the UKHCDO database.[249]

Evidence from the cohort of patients managed by the UKHCDO indicated that, in contrast to the picture offered by PHE, little follow-up or support had been offered. TaintedBlood, a national advocacy organisation for haemophiliacs and others with bleeding disorders, stated that there had been a "breakdown in communication" following patients' notification of their 'at risk' status and that there had been no opportunity for patients to "discuss any concerns or fears".[250] Liz Carroll, the Haemophilia Society, agreed that there was no protocol in place to ensure that these patients were followed up, so it was impossible to "know for sure" that all patients had been notified or "what happened to everybody after that".[251] According to GRO-A TaintedBlood: "nobody is prepared to talk to you; nobody will give you any information, and I actually have nobody looking after me".[252] However, the Government's Chief Medical Officer, Dame Sally Davies, stated that she believed that clinicians were "giving good support" to those 'at risk' of CJD and were following those at highest risk "very carefully".[253]

77. **The Government claims to be undertaking close surveillance of those it considers to be 'at risk' of CJD. Yet it cannot provide reliable data either on the total number of people designated 'at risk' or the number who have been notified of this fact. This is unacceptable.** ***We recommend that the Government conduct an immediate audit of the entire 'at risk' cohort to establish whether any notifications remain outstanding and to ensure that appropriate support and follow-up is in place for all those affected. We also propose that the Government commission an independent review of the transfusion data pathway to ensure that, in the event of any future blood contamination incident, it can promptly trace, notify and provide support to affected recipients.***

78. **We were disappointed by the evident lack of support provided to those designated 'at risk' of CJD. We consider it inappropriate for the Government to have effectively delegated responsibility for the care and surveillance of a large proportion of these individuals to external bodies such as the UK Haemophilia Centre Doctors' Organisation—a charitable organisation with no formal relationship with the Executive.** ***We recommend that the Government, through its public health agencies, assume direct responsibility for the surveillance and support of all those considered to be 'at risk' of CJD, with input from other specialist organisations as required.***

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249 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

250 BTO18 para 40-41 [TaintedBlood]

251 Q17

252 Q15

253 Q314

Participation in research

79. PHE states that its follow-up of individuals 'at risk' of CJD includes the collection of blood and tissue samples and post-mortem investigation.[254] However, evidence suggests that only a small subset of individuals have been asked to provide consent for such research. Dr Katy Sinka, PHE, stated that, of the "small cohort [of 'at risk' individuals] that Public Health England follows up", "twenty-seven people were asked" for their consent for post-mortem investigation, "eleven of whom said yes".[255] These twenty-seven individuals included several patients who had received blood or blood products from donors who later developed vCJD and were therefore at particularly high risk of carrying the infection.[256] (Three of the eight patients examined from this cohort died of vCJD and the fourth showed signs of infection.[257]) According to Professor Knight, Director of the National CJD Research and Surveillance Unit, "in 2013 there were eleven deaths in the enhanced surveillance cohort"—"as far as we know, no post-mortems were done".[258]

80. Witnesses broadly agreed that data collected after death would be helpful in increasing our understanding of CJD, but disagreed about whether this justified compulsory post-mortem examination. Professor Bird stated that it was "regrettable" that "valuable evidence" from potential carriers of CJD was being destroyed and argued that those considered to be at high risk "should be subject to mandatory post-mortem" in the public interest.[259] She continued:

> I would like there to be an almost annual accounting of the types of vCJD at-risk network, how many people within those networks survived for at least five years from putative exposure, how many died at least five years out and how many post-mortems there have been, so that we can see for each of these groups what the information accrual and the loss of information is.[260]

The majority of witnesses, however, shared the view of GRO-A TaintedBlood, who stated that "the mandatory route" was not "the right way to go".[261] For example, Professor Knight stated that he "would be very opposed to mandatory autopsy" and Dr Roland Salmon, Advisory Committee on Dangerous Pathogens, did not consider this to be "a terribly practical suggestion because I do think people expect a degree of autonomy about how they dispose of their bodies".[262] Professor Marc Turner, Advisory Committee on the

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254 Public Health England, 'Creutzfeldt-Jakob Disease (CJD) biannual update (February 2014) with briefing on novel human prion disease', 14 February 2014, hpa.org.uk, accessed 30 June 2014

255 Q270

256 Qq170-173

257 Q168 [Professor Sheila Bird]; BTO14 para 3-6 [UKBS PWG]

258 Q169

259 Q174; BTO11 para 16 [Professor Sheila Bird]

260 Q174

261 Q28. See also Q28 [Liz Carroll]; Q28 [Dr Matthew Buckland]; Q60 [Dr Roland Salmon]; Q60 [Professor Marc Turner]; Q60 [Professor Sheila MacLennan]; Q169 [Professor Richard Knight]

262 Q169 [Professor Richard Knight]; Q60 [Dr Roland Salmon]

Safety of Blood, Tissues and Organs (SaBTO), agreed that mandatory post-mortem would be "a step too far".[263]

81. **In our view, the decision to participate in research should always rest with the individual or, in exceptional circumstances, their loved ones. Nevertheless, samples contributed by those potentially exposed to CJD are of immense scientific value and we are disappointed that more has not been done to obtain consent from those willing to participate in research.** ***We recommend that the Government consider ways to increase the number of 'at risk' individuals giving consent for research participation, particularly post-mortem. We ask that the Government summarise its plans for achieving this in its response to this Report.***

The National CJD Research and Surveillance Unit

82. The National CJD Research and Surveillance Unit ('the surveillance unit') was established in 1990 in response to a recommendation made by the Southwood Working Party.[264] Based at the Western General Hospital in Edinburgh, the unit was initially tasked with identifying any changes in the pattern of CJD cases which could be traced back to the BSE epidemic. It recognised such a change in 1996 and its work led to the characterisation of a new form of the disease: variant CJD (vCJD).[265] Figures for UK deaths from CJD—including both classical and variant forms—continue to be updated and published by the surveillance unit on a monthly basis and it also works on "a significant number of research projects", including studies focused on evaluating the risk of blood-borne transmission of vCJD.[266] It is supported primarily by public funds and the Government confirmed to us during our inquiry that it would continue funding the surveillance unit until "at least" 2017.[267]

Classification and reporting

83. National CJD surveillance is currently based on a "passive" system of bottom-up reporting.[268] Clinicians (most often neurologists) with someone under their care who they think may be suffering from CJD are asked to refer the case to the surveillance unit, which then investigates further.[269] If there is evidence to support a diagnosis of CJD, specialists from the unit classify that patient as either a 'definite', 'probable' or 'possible' case. Only cases receiving a final classification of 'definite ' or 'probable' are included in official

263 Q60

264 The Southwood Working Party, chaired by Sir Richard Southwood, was convened in 1988 to advise the Government "on the risks posed by BSE and the measures that should be taken to counter those risks". See *The BSE inquiry: the report*, Volume 4, 'The Southwood Working Party, 1988-1989', October 2000.

265 National CJD Research and Surveillance Unit, 'About us', cjd.ed.ac.uk, accessed 30 June 2014

266 National CJD Research and Surveillance Unit, 'Research', cjd.ed.ac.uk, accessed 30 June 2014

267 Q318 [Dame Sally Davies]

268 Q184 [Professor Richard Knight]

269 National CJD Research and Surveillance Unit, *National Creutzfeldt-Jakob Disease Surveillance Protocol*.

statistics, which, to date, state that there have been 177 UK deaths from vCJD, most recently in 2013.[270]

84. One witness challenged the veracity of these official figures. Christine Lord, mother Andrew Black, who died of vCJD in 2007, stated that there had been a "definite under-reporting of vCJD cases" and provided the Committee with several examples of deaths which she alleges to have been misclassified by the surveillance unit.[271] According to Mrs Lord, "many flexible protocols" are used to diagnose vCJD "and this means that victims can disappear from official stats".[272] Professor Richard Knight, unit director, acknowledged that there was likely to be some accidental under-reporting but denied that cases had been deliberately misclassified, as suggested by Mrs Lord.[273] He explained:

> if you ask any honest surveillance system whether there are any missing cases, there is only one answer: yes. The question is the magnitude of it.[274]

Professor Knight stated that the surveillance unit had done "various things" to try to ascertain that it had "not missed cases" of CJD, including conducting retrospective reviews of death certificates to identify potential instances of disease.[275] He added that CJD cases were classified on the basis of a "diagnostic classification protocol" which had been "published in peer review journals", "presented at a wide variety of scientific meetings" and "discussed endlessly with international colleagues".[276] Thus, while acknowledging that he could not be "absolutely confident" that no cases had been missed, Professor Knight considered it unlikely that there was significant under-reporting and stated that the UK had "as good a surveillance system" as was "practically possible".[277]

85. Other witnesses agreed that deliberate under-reporting was unlikely.[278] However, there was evidence to suggest that some cases might be accidentally overlooked due to misdiagnosis, particularly given the similarities between CJD and other more common forms of dementia. According to Professor Collinge, MRC Prion Unit, "diagnosis of dementia in the elderly is not done well in this country" and, "given the way these people are investigated", a case of either classical or variant CJD could well be misdiagnosed as Alzheimer's disease.[279] Dr Simon Mead, Association of British Neurologists[280], agreed that

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270 Q188. According to Professor Knight there have been four instances in which cases were classified as "possible" vCJD and were therefore omitted from official figures.

271 Q17. The Committee raised these cases with the National CJD Research and Surveillance Unit and requested additional information to investigate Mrs Lord's claims. The Committee found no evidence of deliberate misclassification. See also BTO03 [Christine Lord], BTO46 [Christine Lord supplementary] and BTO42 [NCJDRSU]

272 BTO03 para 8 [Christine Lord]

273 Q187-188

274 Q180

275 Q180

276 Q192

277 Q180

278 See, for example, Q24 [Dr Matthew Buckland] and Q193 [Dr Simon Mead]. See also BTO42 [NCJDRSU supplementary] and oral evidence taken on 27 November 2013, HC (2013-14) 846, Q42 [Profesor James Ironside]

279 Oral evidence taken on 27 November 2013, HC (2013-14) 846, Q28 [Professor John Collinge]

280 Dr Mead is also a member of the MRC Prion Unit.

poor diagnosis of dementia could give rise to "massive under-ascertainment" of CJD in the elderly.[281] Professor Knight stated that the surveillance unit was also interested in whether it was "missing cases in the elderly", particularly of classical forms of CJD, and that it had submitted a proposal to the Department of Health for a study to investigate this matter in more detail.[282] Dame Sally Davies, the Government's Chief Medical Officer, confirmed that there was "some discussion at the moment" as to whether the Government "could and should" fund this proposal.[283]

86. Evidence of potential under-reporting is also provided by the so-called "calibration problem"—that is, the discrepancy between the number of transfusion-transmitted cases of vCJD predicted by the available scientific evidence and the actual number of cases recorded in official statistics. In 2011, an analysis conducted by the Department of Health presented a model which attempted to solve the calibration problem.[284] Under this model, assumptions about the likely infectivity of blood and susceptibility to infection of transfusion recipients were varied in order to match the actual number of transfusion-transmitted cases reported by the surveillance unit. The amended assumptions generated by this model were used in the cost-effectiveness analysis performed on ProMetic's prion filtration device. However, according to ProMetic, "making the model fit the observed number of cases could result in a serious under-estimate of the possible future extent" of transfusion-transmitted vCJD.[285] ProMetic added that if the assumed prevalence of prions across the UK population were adjusted to 1 in 2000, as per the recent appendix study findings, then "the number of cases predicted by the model would significantly exceed the actual number of cases reported to date".[286] According to ProMetic, "this raises the question of whether a significant number of vCJD cases are currently being missed".[287]

87. **We are confident in the integrity of the National CJD Research and Surveillance Unit and have not seen any evidence to corroborate claims of deliberate under-reporting or misclassification. However, we share our witnesses' concerns that cases could be missed due to misdiagnosis, particularly in the elderly. *We recommend that the Government lend its support to research intended to give greater clarity over the causes of atypical dementia in the elderly and, through this, the potential rate of undiagnosed CJD.***

281 Q193

282 Q179-180

283 Q315; Q320

284 Department of Health, *Blood-Borne Transmission of vCJD Re-Examination of Scenarios*, September 2011

285 BTO53 [ProMetic supplementary]

286 BTO53 [ProMetic supplementary]

287 BTO53 [ProMetic supplementary]

5 After the storm?

88. Variant Creutzfeldt-Jakob Disease (vCJD) is not like other infectious diseases. Caused by a mysterious pathogen which we are still only just beginning to understand, vCJD is an invariably fatal disease of sudden onset, which has historically inflicted on its young victims a progressive dementia more often seen in the oldest and sickest members of society. When the first cases began to emerge in the mid-1990s, the tragic images of young vCJD victims worked alongside the existing narrative of 'mad cow disease' to create an unprecedented level of public anxiety, maintained over subsequent years as the number of cases gradually rose.[288]

89. Underlying this anxiety was the suggestion that these deaths were an avoidable and man-made tragedy: that the Government had mishandled the BSE crisis and was therefore to blame for vCJD. Between 1998 and 2000, the Government's role in the crisis came under increasing scrutiny as a result of the BSE inquiry, and it was during this period that the Government took its first major steps to protect the UK blood supply from vCJD. These steps were largely precautionary: in the late 1990s there were no confirmed cases of vCJD having been transmitted via blood transfusion and many scientists thought this unlikely to occur. Nevertheless, costly risk mitigation measures—leucodepletion and the importing of fractionated plasma products—were implemented as part of a "precautionary policy" which sought to "minimise" any potential risk.[289] In 2004, following the report of the first presumed case of transfusion-transmitted vCJD, a second wave of precautionary measures was introduced: the deferral of donors who had themselves previously received a blood transfusion and an extension of the existing imported plasma policy.[290] In the words of one witness:

> The climate that existed round about 2000 to 2005 was one of real concern. The UK blood agencies and the Department of Health were very concerned that there was going to be […] a growth of cases of vCJD by virtue of blood transfusion. There was, I think, a genuine desire to do something about that.[291]

90. Several witnesses told us, however, that this climate of concern, in which the precautionary principle had been at the forefront of Government policy, dissipated in the late 2000s. The initial wave of vCJD appeared to have peaked and cases were down to a handful a year, leading to a gradual diminishing of the sense of panic that had existed a decade earlier. According to Dr Steven Burton, Chief Executive of ProMetic Biosciences, at

288 See Washer, P., 'Representations of mad cow disease', *Social Science and Medicine*, Volume 62, Issue 2, January 2006, pp.457-466. DOI: 10.1016/j.socscimed.2005.06.001. Washer refers specifically to the "descriptions of the physical and mental decline of the young people who succumbed to the disease, juxtaposed mentally as they are with images […] of uncoordinated and frightened cows", which contributed to the public fear of dehumanisation: "of becoming like a maddened (rabid) animal".

289 Spongiform Encephalopathy Advisory Committee (SEAC), *SEAC annual report 1997-98*, p.10; p.33

290 Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), *Measures currently in place in the UK to reduce the potential risk of transmitted variant Creutzfeldt-Jakob Disease via blood*, December 2013

291 Q124 [Dr Steven Burton]

this time the "spirit of collaboration" which had previously existed between the Government, UK Blood Services and research companies such as his "disappeared", making it more difficult for new risk mitigation technologies to reach the market.[292] Dr Burton stated that his company was now:

> witnessing an environment where, from our perception, road blocks were being placed in the way and things were being stretched and taking longer. As soon as we achieved one hurdle, another one was, all of a sudden, in the way.[293]

Other witnesses argued that the Government's approach to blood safety was, and remained, "a political issue" and that for many years the Government's uptake of risk mitigation technologies had been based not just on their effectiveness, but on "public sentiment and the perceived risk and need to do something".[294] ProMetic went further, stating its belief that the decision made by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) not to recommend adoption of its prion filtration technology was based not on the scientific evidence, but on "other considerations" such as cost (at a time of economic austerity) and "a widely held belief within parts of the Department of Health that the vCJD emergency has passed and there [was] no need for the implementation of additional blood safety measures".[295]

91. The Minister told us that "successive governments" had applied a precautionary approach to vCJD and that this had been maintained by the current administration.[296] However, now that the initial storm of cases has passed, we too have perceived a change in the Government's attitude to vCJD. During this inquiry, we have amassed considerable evidence to challenge the Government's claim that it maintains the precautionary approach that it has always taken. For example:

- The Government accepts that some of those who have potentially been exposed to vCJD and are therefore at increased risk of transmitting it may not have been notified of this risk. These people are therefore not in a position to take the precautions recommended to prevent further transmission. To our knowledge, the Government has taken no steps to rectify this situation and has delegated significant responsibility for ongoing surveillance to the UK Haemophilia Centre Doctors' Organisation—a body which has, for many years now, evidently failed to maintain an accurate record of this 'at risk' population. (Paragraphs 75-78).

- The Government appears unconcerned by the extremely low rate of research participation from this 'at risk' population, citing this as "a cultural issue" and failing to assure us that it is taking any steps to increase consent rates in order to preserve potentially invaluable scientific information. (Paragraphs 79-81).

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292 Q124

293 Q124

294 Q125 [Mr Nigel Talboys]; Q79 [Dr Steven Burton]. See also Q74 [Dr Alex Raeber and Mr Nigel Talboys]

295 BTO53 [ProMetic supplementary]

296 Q295

- The Government tells us that it is concerned about the risk of prion transmission via surgical instruments, but is "not aware" of evidence suggesting that national guidance intended to reduce this risk is not being followed. (Paragraphs 27-29).

- The Government has failed to ensure that a technology with the potential to render this guidance redundant—which was itself based on publicly-funded research—is adopted by the NHS. Seven years after DuPont's Rely+On product received its CE mark, neither it, nor any alternative product capable of inactivating prions present on surgical instruments, has yet been introduced. (Paragraphs 31-38).

- Despite witnesses overwhelmingly considering a vCJD blood test to be the most important prospective vCJD risk reduction measure—and despite the considerable progress made in the development of such a test—the Government has failed to declare its explicit support for this technology. (Paragraphs 51-52). Moreover, it has taken no steps to ensure that the prototype test developed by the MRC Prion Unit receives the support necessary for the next stage of its development: a blood prevalence study which could also provide valuable data on the rate of subclinical vCJD infection in the UK donor pool. (Paragraphs 61-66).

- Current assumptions about blood infectivity and susceptibility to infection appear to be largely based on an analysis conducted by the Department of Health in 2011, in which it attempted to solve the 'calibration problem' by matching these assumptions to the observed number of vCJD cases. This is despite fears, acknowledged by the national surveillance unit, that there might be under-reporting of the disease, particularly in the elderly, in whom both classical and variant forms of CJD could feasibly be misdiagnosed as others forms of dementia. (Paragraphs 83-87).

- After a lengthy evaluation, SaBTO has decided not to recommend the adoption of prion filtration: a technology with the potential to significantly reduce the risk of prion transmission. This decision was made following several years of evidence gathering and a detailed cost-effectiveness analysis, neither of which were carried out in advance of the introduction of another prion reduction measure—leucodepletion—in 1999. (Paragraphs 41-46).

92. We would draw particular attention to this final point. The decision to introduce leucodepletion in the 1990s was a genuinely precautionary step much praised by witnesses to this inquiry.[297] However, had leucodepletion been subject to the same requirements in the late 1990s that prion filtration was in the late 2000s, it would not have been recommended. In 1999, there was little evidence that prions could be transmitted via transfusion and none to conclusively demonstrate that leucodepletion would mitigate this risk. Under today's approach, it is therefore likely that leucodepletion would not have been adopted for several years, if at all.

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[297] It has been argued that other aspects of the Government's response to the BSE crisis were less in line with the precautionary principle. See, for example: European Environment Agency, *Late lessons from early warnings: the precautionary principle 1896-2000*, Chapter 15, '"Mad cow disease" 1980s–2000: how reassurances undermined precaution, 2001.

93. We may never know what the impact of such a delay in the adoption of leucodepletion would have been; whether the measure has saved hundreds of lives or wasted millions of pounds. Because now, as in 1999, there remains "a good deal of uncertainty about the risk" of transfusion-transmitted vCJD.[298] However, while the Government was previously prepared to assume the worst and take every precaution to prevent it from happening, its attitude now appears to be one of measured optimism, in which the apparently low incidence of cases is repeatedly used as a "key piece of evidence" to justify an approach which can no longer be described as genuinely precautionary.[299] We consider this change to be deeply regrettable and unjustified by the available evidence.

94. **SaBTO's decision not to recommend the adoption of prion filtration, taken alongside the other evidence that we have gathered during this inquiry, in our view signals a change from what was a genuinely precautionary approach to vCJD risk reduction in the late 1990s to a far more relaxed approach today. Much of the uncertainty surrounding prions, their potential modes of transmission and the possible rate of undetected infection and disease remains: recent evidence that subclinical prevalence could be as high as one in 2,000 people would suggest that a precautionary approach is now more warranted than ever.**

95. **Our fear is that the Government's current attitude is driven less by the available scientific evidence than it is by optimism: a hope that the storm has now passed and that vCJD is no longer the threat to public health that it once was. In the current economic environment, this attitude is not surprising. However, it is not justified. For all we know, the storm may well be ongoing. *We conclude this report by recommending that the Government take a more precautionary approach to both vCJD risk mitigation and blood safety more generally, in order to safeguard against future infections. We suggest that it begin by assessing the key risks, known and unknown, that the UK blood supply currently faces and might face in the future, so that it can identify and fill relevant knowledge gaps and support the development of appropriate risk reduction measures and technologies. The Government should initiate this work immediately and we ask that it provide us with an update on its progress well before the dissolution of Parliament.***

298 Q241

299 Department of Health, *Blood-Borne Transmission of vCJD Re-Examination of Scenarios*, September 2011, p.11. See also SaBTO, *Prion reduction filters for red cell concentrates*, Agenda item 4, 10 December 2012 and Q287 [Jane Ellison MP]

Conclusions and recommendations

Risks to the UK blood supply

1. Blood transfusions save lives and we should be proud, as a nation, of our long tradition of altruistic donation. In recent years, the UK blood supply has proved to be extremely safe and, in the vast majority of cases, the benefits of receiving a transfusion will far outweigh the risk of acquiring a transfusion-transmitted infection. However, we urge against complacency and stress the need for UK Blood Services to remain vigilant to the threat posed by blood-borne pathogens. (Paragraph 9)

2. The evidence that we have heard suggests that we cannot be confident that prions are not present in the blood supply. There remains considerable uncertainty about the potential implications of such contamination. We consider it imperative that a precautionary approach to this risk be maintained until further evidence becomes available. (Paragraph 17)

3. We echo concerns that population-level risk assessment could lead to inaccurate and potentially discriminatory judgements being made about the risk posed by individuals, particularly men who have sex with men. We recommend that the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) reconsider the feasibility of a move to more individualised risk assessment as part of its 2015 work programme, following completion of the current UK blood donor survey. (Paragraph 22)

4. Pathogens are constantly emerging and evolving; novel pathogens will therefore always pose a threat to the blood supply. In the past, it has often taken multiple cases of transfusion-transmitted infection before these threats have been recognised and mitigated. This will remain the case as long as risk mitigation measures remain pathogen-specific. We urge the Government to take steps to support the development of broader spectrum technologies with the potential to mitigate the risk of both known and unknown pathogens. (Paragraph 26)

Surgical transmission of prions

5. The Government has acknowledged that contaminated surgical instruments are a potential source of prion transmission and states that it has taken a precautionary approach in its response to this risk. However, this response appears to rest heavily on guidance which, based on the available evidence, may not have been fully implemented. We recommend that the Government work with the National Institute of Health and Care Excellence (NICE) and the Advisory Committee on Dangerous Pathogens to better understand the extent to which the precautions recommended by these bodies have been implemented across the NHS. We ask the Government to provide us with an update on this work well before the dissolution of Parliament, together with an indication of the steps it will take if preliminary findings suggest that implementation has been incomplete. (Paragraph 29)

Case study 1: decontamination of surgical instruments

6. Given the NHS's resistance to change and the well-documented challenges associated with initiating a UK clinical trial, the Minister's assessment that "no barriers" were put in the way of DuPont's prion inactivation product does not reflect the reality of the situation. Where technologies are developed in direct response to Government need—and on the back of Government funding—the Government must be prepared to take steps to help companies overcome barriers to adoption. We ask the Government to set out how, in future, it will ensure that the directed research that it funds is better supported through the technology readiness pathway. In particular, we ask the Government to set out how it will ensure that promising clinical technologies are promptly trialled in an NHS setting, so that potential adoption challenges can be quickly identified and resolved. (Paragraph 37)

7. We also question the value of a scientific review panel which has no mandate or power to ensure that the products that it recommends can be tested in, and eventually adopted by, the NHS. We see this as further evidence of the Government's passive approach to technology uptake. We propose that the Rapid Review Panel (RRP) be given stronger powers to ensure that its recommendations open the door to in-use evaluation and stimulate NHS uptake. (Paragraph 38)

8. In our view, all Scientific Advisory Committees should adhere to both the 2010 'Principles of Scientific Advice to Government' and the 2011 'Code of Practice for Scientific Advisory Committees'. We were disappointed to find that the Rapid Review Panel (RRP) failed to do so. We recommend that the Chief Medical Officer takes action to rectify current weaknesses. We request a progress report be sent to us well before the dissolution of Parliament. (Paragraph 40)

Case study 2: prion filtration

9. We do not wish to question the scientific decision-making of the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) and we respect its decision not to recommend adoption of prion filtration at present. However, we feel that the time taken to reach this decision was excessive and that the process, particularly in its latter stages, entailed an unnecessary level of uncertainty for the commercial developer. We have some sympathy for SaBTO's desire to wait until more evidence was available before making a decision; however, if industry is to continue to develop innovative blood safety products for the UK market, SaBTO must introduce greater speed and predictability into its evaluation process. We recommend that, in future, when assessing a new technology, SaBTO agree with stakeholders at the outset what the evaluation will consist of, together with key dates, milestones and decision-points. This 'evaluation roadmap', and any subsequent amendments, should be made publicly available to ensure maximum transparency and accountability. (Paragraph 45)

10. We also consider it important that the health technology appraisals conducted by SaBTO—and all other SACs—use the same methodology and meet the same high standards as those undertaken by the UK's centre of excellence for this activity: NICE. We therefore recommend that the Government Office for Science work with NICE over the next 12 months to develop and publish a standard methodology for

all SACs tasked with conducting health technology appraisal. Until this guidance is published, we recommend that a NICE representative review and, where necessary, provide input to all such appraisals undertaken by, and on behalf of, SACs. (Paragraph 46)

11. Scientific Advisory Committees should be—and be seen to be—independent of the bodies to which they are providing advice. At present, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) comprises members who are both contributing to, and acting on, the advice that it formulates. We consider that this could be damaging to its perceived independence and a source of potential conflicts of interest. We recommend that SaBTO's terms of reference be amended to reflect the fact that it does, in effect, provide advice to UK Blood Services as well as the Government. We suggest that SaBTO's current membership be reviewed and potentially revised in light of this change. (Paragraph 50)

Case study 3: vCJD blood testing

12. We understand the need to carefully control access to rare vCJD samples and commend the National Institute of Biological Standards and Controls (NIBSC) for putting in place a standard protocol for test validation. However, we are disappointed that so few samples are currently held by the NIBSC and consider its process to be undermined by the fact that the two major centres of UK prion research—the National CJD Research and Surveillance Unit and the MRC Prion Unit—can each use and distribute samples independent of NIBSC evaluation. All test developers should be given equal opportunity to gain access to the available samples and these should be distributed on the basis of merit alone. We recommend that access to all vCJD patient samples—including those currently held elsewhere in the UK—be managed through the NIBSC, according to a consistent set of test validation protocols. (Paragraph 59)

13. We were also concerned by the apparent statistical weakness of past NIBSC evaluations. We recommend that the CJD Resource Centre Oversight Committee add to its membership an individual with expertise in biostatistics, who can provide it with expert advice on this matter during future deliberations. (Paragraph 60)

14. The incubation period of prion diseases such as vCJD can extend to several decades and it is therefore possible that individuals infected in the 1990s might not yet have developed symptoms. We do not follow the Minister's logic that there should be a link between the number of cases seen in the last ten years and the level of resource dedicated to prion research. We simply do not know, at present, how many people have been exposed to prions and what the implications of this might be for the blood donor pool. There is an urgent need to reduce this uncertainty. (Paragraph 65)

15. Based on the testimony that we have heard, we consider that a vCJD blood prevalence study utilising a version of the prototype test developed by the MRC Prion Unit would be of considerable value, both for test development and research purposes. We recognise that significant public funds have already been directed towards the development of this test; we view this as even more reason to ensure that a return on this investment is realised. To cut off support now would be a false

economy. We recommend that the Government ensures that a large-scale vCJD blood prevalence study be initiated in the UK within the next 12 months. (Paragraph 66)

CJD risk management

16. People who are notified that they may have been exposed to CJD will inevitably be alarmed by this information and will likely have questions that cannot be answered in the leaflets currently provided by Public Health England. We consider it totally inappropriate for this news to be communicated solely in writing. We recommend that the Government put robust measures in place to ensure that all individuals assigned this designation receive the news verbally, either from a healthcare provider or from a CJD specialist with experience in patient communication. (Paragraph 70)

17. It is clear that the prototype vCJD blood test developed by the MRC Prion Unit cannot yet be relied upon for universal screening purposes. However, it could be of significant value to those people who have been notified that they are at increased risk of carrying the disease. Until the implications of a negative test result can be more firmly established, current precautions must remain in place for those considered to be 'at risk' of vCJD. However, the results of an imperfect test may provide comfort to some. We therefore recommend that 'at risk' individuals be given the opportunity to participate in the blood prevalence study recommended in paragraph 66. (Paragraph 73)

CJD surveillance

18. The Government claims to be undertaking close surveillance of those it considers to be 'at risk' of CJD. Yet it cannot provide reliable data either on the total number of people designated 'at risk' or the number who have been notified of this fact. This is unacceptable. We recommend that the Government conduct an immediate audit of the entire 'at risk' cohort to establish whether any notifications remain outstanding and to ensure that appropriate support and follow-up is in place for all those affected. We also propose that the Government commission an independent review of the transfusion data pathway to ensure that, in the event of any future blood contamination incident, it can promptly trace, notify and provide support to affected recipients. (Paragraph 77)

19. We were disappointed by the evident lack of support provided to those designated 'at risk' of CJD. We consider it inappropriate for the Government to have effectively delegated responsibility for the care and surveillance of a large proportion of these individuals to external bodies such as the UK Haemophilia Centre Doctors' Organisation—a charitable organisation with no formal relationship with the Executive. We recommend that the Government, through its public health agencies, assume direct responsibility for the surveillance and support of all those considered to be 'at risk' of CJD, with input from other specialist organisations as required. (Paragraph 78)

20. In our view, the decision to participate in research should always rest with the individual or, in exceptional circumstances, their loved ones. Nevertheless, samples contributed by those potentially exposed to CJD are of immense scientific value and

we are disappointed that more has not been done to obtain consent from those willing to participate in research. We recommend that the Government consider ways to increase the number of 'at risk' individuals giving consent for research participation, particularly post-mortem. We ask that the Government summarise its plans for achieving this in its response to this Report. (Paragraph 81)

21. We are confident in the integrity of the National CJD Research and Surveillance Unit and have not seen any evidence to corroborate claims of deliberate under-reporting or misclassification. However, we share our witnesses' concerns that cases could be missed due to misdiagnosis, particularly in the elderly. We recommend that the Government lend its support to research intended to give greater clarity over the causes of atypical dementia in the elderly and, through this, the potential rate of undiagnosed CJD. (Paragraph 87)

Conclusion

22. SaBTO's decision not to recommend the adoption of prion filtration, taken alongside the other evidence that we have gathered during this inquiry, in our view signals a change from what was a genuinely precautionary approach to vCJD risk reduction in the late 1990s to a far more relaxed approach today. Much of the uncertainty surrounding prions, their potential modes of transmission and the possible rate of undetected infection and disease remains: recent evidence that subclinical prevalence could be as high as one in 2,000 people would suggest that a precautionary approach is now more warranted than ever. (Paragraph 94)

23. Our fear is that the Government's current attitude is driven less by the available scientific evidence than it is by optimism: a hope that the storm has now passed and that vCJD is no longer the threat to public health that it once was. In the current economic environment, this attitude is not surprising. However, it is not justified. For all we know, the storm may well be ongoing. We conclude this report by recommending that the Government take a more precautionary approach to both vCJD risk mitigation and blood safety more generally, in order to safeguard against future infections. We suggest that it begin by assessing the key risks, known and unknown, that the UK blood supply currently faces and might face in the future, so that it can identify and fill relevant knowledge gaps and support the development of appropriate risk reduction measures and technologies. The Government should initiate this work immediately and we ask that it provide us with an update on its progress well before the dissolution of Parliament. (Paragraph 95)

Formal Minutes

Wednesday 16 July 2014

Members present:

Andrew Miller, in the Chair

Jim Dowd	Pamela Nash
David Heath	Sarah Newton
Stephen Metcalfe	Graham Stringer
Stephen Mosley	

Draft Report (*After the storm? UK blood safety and the risk of variant Creutzfeldt-Jakob Disease*), proposed by the Chair, brought up and read.

Ordered, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 95 read and agreed to.

Summary agreed to.

Resolved, That the Report be the Second Report of the Committee to the House.

Ordered, That the Chair make the Report to the House.

Ordered, That embargoed copies of the Report be made available, in accordance with the provisions of Standing Order No. 134.

[Adjourned till Wednesday 3 September at 9.00 am

Witnesses

The following witnesses gave evidence. Transcripts can be viewed on the Committee's inquiry page at www.parliament.uk/science.

	Question number
Wednesday 5 February 2014	
GRO-A Secretary and Head of Publicity, Taintedblood, **Liz Carroll**, Chief Executive Officer, The Haemophilia Society, **Dr Matthew Buckland**, Chair of Medical Advisory Panel, UK Primary Immunodeficiency Network, and Consultant Immunologist, Barts Health NHS Trust, and **Christine Lord**, freelance journalist, campaigner and mother of vCJD victim Andrew Black	Q1-29
Professor Marc Turner, Chair, Advisory Committee on the Safety of Blood, Tissues and Organs Prion Group, and Chair, UK Blood Services Prion Working Group, **Dr Roland Salmon**, Acting Chair, Advisory Committee on Dangerous Pathogens, and **Dr Sheila MacLennan**, Professional Director, UK Blood Services Joint Professional Advisory Committee	Q30-66
Wednesday 5 March 2014	
Professor John Collinge, Director, MRC Prion Unit and Professor of Neurology at the UCL Institute of Neurology, **Dr Steven Burton**, Chief Executive, ProMetic Biosciences Ltd, **Dr Kelly Board**, Technical Specialist, DuPont Chemicals and Fluoroproducts, **Dr Alex Raeber**, Head of Research and Development, Prionics AG, and **Nigel Talboys**, Global Director of Blood Safety and EMEA Director of Public Policy and Government Affairs, Terumo BCT	Q67-144
Wednesday 26 March 2014	
Professor Richard Knight, Director, National CJD Research and Surveillance Unit, **Professor Sheila Bird**, Programme Leader, Medical Research Council Biostatistics Unit, **Dr Paula Bolton-Maggs**, Medical Director, Serious Hazards of Transfusion Haemovigilance Scheme, and **Dr Simon Mead**, Association of British Neurologists	Q145-200
Monday 28 April 2014	
Dr Richard Baker, Executive Committee Member, British Transplantation Society, **Dr Mike Knapton**, Associate Medical Director (Prevention & Care), British Heart Foundation, **Ed Owen**, Chief Executive, Cystic Fibrosis Trust, and **Keith Rigg**, Chair, Transplant 2013	Q201-239
Wednesday 30 April 2014	
	Q240-281
Professor James Neuberger, Associate Medical Director, NHS Blood and	

Transplant, **Dr Lorna Williamson**, Medical and Research Director, NHS Blood and Transplant, **Dr Paul Cosford**, Director for Health Protection and Medical Director, Public Health England, and **Dr Katy Sinka**, Consultant Epidemiologist and Head of CJD Section, Public Health England

Jane Ellison MP, Parliamentary Under-Secretary of State for Public Health, Department of Health, and **Professor Dame Sally Davies**, Chief Medical Officer, Department of Health Q282-328

Published written evidence

The following written evidence was received and can be viewed on the Committee's inquiry web page at www.parliament.uk/science. INQ numbers are generated by the evidence processing system and so may not be complete.

1	Christine Lord	BTO0003
2	Lauren Clarke	BTO0004
3	National Institute of Biological Standards and Control	BTO0006
4	CJD Support Network	BTO0007
5	National CJD Research & Surveillance Unit (NCJDRSU)	BTO0008
6	The Haemophilia Society	BTO0009
7	Dr Neil Raven	BTO0010
8	Professor Sheila M Bird	BTO0011
9	ProMetic BioSciences Ltd	BTO0012
10	Anthony Nolan	BTO0013
11	UK Blood Services Prion Working Group	BTO0014
12	Terumo BCT	BTO0015
13	The British Transplantation Society	BTO0016
14	Stonewall	BTO0017
15	Taintedblood	BTO0018
16	Anita Jenkins	BTO0019
17	Department of Health in England Decontamination Science Working Group	BTO0020
18	Advisory Committee on Dangerous Pathogens	BTO0022
19	Professor Richard Tedder	BTO0023
20	Primary Immunodeficiency UK	BTO0025
21	NHS Blood and Transplant	BTO0026
22	Medical Research Council	BTO0027
23	Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO)	BTO0028
24	Serious Hazards of Transfusion Haemovigilance Scheme	BTO0029
25	UK Blood Services Joint Professional Advisory Committee	BTO0030
26	Department of Health	BTO0031
27	Human Tissue Authority	BTO0032
28	UK Primary Immunodeficiency Network	BTO0033
29	Public Health England	BTO0034
30	British Heart Foundation	BTO0035
31	Royal College of Physicians	BTO0038
32	Prionics AG	BTO0039
33	Transplant 2013	BTO0040
34	Dr Peter R Foster	BTO0041
35	National CJD Research & Surveillance Unit (NCJDRSU) (supplementary to BTO 08)	BTO0042
36	DuPont Chemicals & Fluoroproducts	BTO0044
37	National Institute for Health and Care Excellence (NICE)	BTO0045

38	Christine Lord (supplementary to BTO0003)	BTO0046
39	UK Blood Services Joint Professional Advisory Committee (supplementary to BTO0030)	BTO0047
40	CJD Support Network (supplementary to BTO0007)	BTO0049
41	National Institute of Biological Standards and Control (supplementary to BTO0005)	BTO0050
42	Professor Sheila M Bird (supplementary to BTO0011)	BTO0051
43	Cystic Fibrosis Trust	BTO0052
44	ProMetic BioSciences Ltd (supplementary to BTO0012)	BTO0053
45	Coroners Society	BTO0054
46	Department of Health (supplementary to BTO0031)	BTO0055

Unpublished evidence

The following written evidence has been reported to the House and copies have been placed in the House of Commons Library, where they may be inspected by Members. Other copies are in the Parliamentary Archives (www.parliament.uk/archives), and are available to the public for inspection. Requests for inspection should be addressed to The Parliamentary Archives, Houses of Parliament, London SW1A 0PW (tel. 020 7219 3074; email archives@parliament.uk). Opening hours are from 9.30 am to 5.00 pm on Mondays to Fridays.

Atomic Energy Commission

Advisory Committee on the Safety of Blood, Tissues and Organs

National CJD Research and Surveillance Unit

UK Blood Services

List of Reports from the Committee during the current Parliament

All publications from the Committee are available on the Committee's website at www.parliament.uk/science.

The reference number of the Government's response to each Report is printed in brackets after the HC printing number.

Session 2014–15

First Special Report	Communicating climate science: Government Response to the Committee's Eighth Report of Session 2013–14	HC 376
First Report	Ensuring access to working antimicrobials	HC 509

Session 2013–14

First Special Report	Educating tomorrow's engineers: the impact of Government reforms on 14–19 education: Government Response to the Committee's Seventh Report of Session 2012–13	HC 102
First Report	Water quality: priority substances	HC 272–I (HC 648)
Second Special Report	Marine science: Government Response to the Committee's Ninth Report of Session 2012–13	HC 443
Third Special Report	Bridging the valley of death: improving the commercialisation of research: Government response to the Committee's Eighth Report of Session 2012–13	HC 559
Second Report	Forensic science	HC 610 (Cm 8750)
Fourth Special Report	Water quality: priority substances: Government response to the Committee's First Report of Session 2013–14	HC 648
Third Report	Clinical trials	HC 104 (Cm 8743)
Fifth Special Report	Clinical trials: Health Research Authority Response to the Committee's Third Report of Session 2013–14	HC 753
Fourth Report	Work of the European and UK Space Agencies	HC 253 (HC 1112)
Fifth Report	Pre-appointment hearing with the Government's preferred candidate for Chair of the Natural Environment Research Council (NERC)	HC 702
Sixth Special Report	Forensic science: Research Councils UK Response to the Committee's Second Report of Session 2013–14	HC 843
Seventh Special Report	Clinical trials: Medical Research Council Response to the Committee's Third Report of Session 2013–14	HC 874
Sixth Report	Women in scientific careers	HC 701 (HC 1268)
Seventh Report	Pre-appointment hearing with the Government's preferred candidate for Chair of the Arts and Humanities Research Council (AHRC)	HC 989
Eighth Special Report	Work of the European and UK Space Agencies: Government Response to the Committee's Fourth	HC 1112

	Report of Session 2013–14	
Eighth Report	Communicating climate science	HC 254 (HC 376, Session 2014–15)
Ninth Report	Government horizon scanning	HC 703
Ninth Special Report	Women in scientific careers: Government Response to the Committee's Sixth Report of Session 2013–14	HC 1268

Session 2012–13

First Special Report	Science in the Met Office: Government Response to the Committee's Thirteenth Report of Session 2010–12	HC 162
First Report	Devil's bargain? Energy risks and the public	HC 428 (HC 677)
Second Report	Pre-appointment hearing with the Government's preferred candidate for Chair of the Medical Research Council	HC 510–I
Second Special Report	Engineering in government: follow-up to the 2009 report on Engineering: turning ideas into reality: Government Response to the Committee's Fifteenth Report of Session 2010–12	HC 511
Third Report	The Census and social science	HC 322 (HC 1053)
Fourth Report	Building scientific capacity for development	HC 377 (HC 907)
Fifth Report	Regulation of medical implants in the EU and UK	HC 163 (Cm 8496)
Sixth Report	Proposed merger of British Antarctic Survey and National Oceanography Centre	HC 699 (HC 906)
Third Special Report	Devil's bargain? Energy risks and the public: Government Response to the Committee's First Report of Session 2012–13	HC 677
Fourth Special Report	Building scientific capacity for development: Government and UK Collaborative on Development Sciences Response to the Committee's Fourth Report of Session 2012–13	HC 907
Fifth Special Report	Proposed merger of British Antarctic Survey and National Oceanography Centre: Natural Environment Research Council Response to the Committee's Sixth Report of Session 2012–13	HC 906
Seventh Report	Educating tomorrow's engineers: the impact of Government reforms on 14–19 education	HC 665 (HC 102, Session 2013–14)
Eighth Report	Bridging the valley of death: improving the commercialisation of research	HC 348 (HC 559, Session 2013–14)
Sixth Special Report	The Census and social science: Government and Economic and Social Research Council (ESRC) Responses to the Committee's Third Report of Session 2012–13	HC 1053

Session 2010–12

First Special Report	The Legacy Report: Government Response to the Committee's Ninth Report of Session 2009–10	HC 370
First Report	The Reviews into the University of East Anglia's Climatic Research Unit's E-mails	HC 444 (HC 496)
Second Report	Technology and Innovation Centres	HC 618 (HC 1041)
Third Report	Scientific advice and evidence in emergencies	HC 498 (HC 1042 and HC 1139)
Second Special Report	The Reviews into the University of East Anglia's Climatic Research Unit's E-mails: Government Response to the Committee's First Report of Session 2010–12	HC 496
Fourth Report	Astronomy and Particle Physics	HC 806 (HC 1425)
Fifth Report	Strategically important metals	HC 726 (HC 1479)
Third Special Report	Technology and Innovation Centres: Government Response to the Committee's Second Report of Session 2010–12	HC 1041
Fourth Special Report	Scientific advice and evidence in emergencies: Government Response to the Committee's Third Report of Session 2010–12	HC 1042
Sixth Report	UK Centre for Medical Research and Innovation (UKCMRI)	HC 727 (HC 1475)
Fifth Special Report	Bioengineering: Government Response to the Committee's Seventh Report of 2009–10	HC 1138
Sixth Special Report	Scientific advice and evidence in emergencies: Supplementary Government Response to the Committee's Third Report of Session 2010–12	HC 1139
Seventh Report	The Forensic Science Service	HC 855 (Cm 8215)
Seventh Special Report	Astronomy and Particle Physics: Government and Science and Technology Facilities Council Response to the Committee's Fourth Report of Session 2010–12	HC 1425
Eighth Report	Peer review in scientific publications	HC 856 (HC 1535)
Eighth Special Report	UK Centre for Medical Research and Innovation (UKCMRI): Government Response to the Committee's Sixth Report of session 2010–12	HC 1475
Ninth Report	Practical experiments in school science lessons and science field trips	HC 1060–I (HC 1655)
Ninth Special Report	Strategically important metals: Government Response to the Committee's Fifth Report of Session 2010–12	HC 1479
Tenth Special Report	Peer review in scientific publications: Government and Research Councils UK Responses to the Committee's Eighth Report of Session 2010–12	HC 1535
Tenth Report	Pre-appointment hearing with the Government's preferred candidate for Chair of the Technology Strategy Board	HC 1539–I
Eleventh Special Report	Practical experiments in school science lessons and science field trips: Government and Ofqual Responses to the Committee's Ninth Report of Session 2010–12	HC 1655
Eleventh Report	Alcohol guidelines	HC 1536 (Cm 8329)

Twelfth Report	Malware and cyber crime	HC 1537 (Cm 8328)
Thirteenth Report	Science in the Met Office	HC 1538
Fourteenth Report	Pre-appointment hearing with the Government's preferred candidate for Chair of the Engineering and Physical Sciences Research Council	HC 1871–I
Fifteenth Report	Engineering in government: follow-up to the 2009 report on Engineering: turning ideas into reality	HC 1667 (HC 511, Session 2012–13)