HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Blood, tissue and organ screening, HC 990

Wednesday 5 February 2014

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Written evidence from witnesses:

- TaintedBlood
- The Haemophilia Society
- UK Primary Immunodeficiency Network
- Christine Lord
- Advisory Committee on the Safety of Blood, Tissues and Organs Prion Group
- UK Blood Services Prion Working Group
- Advisory Committee on Dangerous Pathogens
- UK Blood Services Joint Professional Advisory Committee

Watch the meeting

Members present: Andrew Miller (Chair); Jim Dowd; Stephen Metcalfe; Stephen Mosley; David Tredinnick

Questions 1-66

Witnesses: GRO-A and 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, gave evidence.

Q1 Chair: Can I thank everyone for coming in this morning? I know for some of you it has been an incredibly difficult journey and you can see that we are short of a couple of people who are still travelling as well.

You have seen the terms of reference, and we have had some illuminating evidence from all of the witnesses and many other organisations as well. I am sure you will have read some of it. We have a number of questions that we want to table to you that have stemmed from the evidence that we have read, the previous sessions and the visit we have undertaken to Filton. That may not be all you want to say in the short time we have available, but please let me

assure you that any subsequent evidence you submit that you feel you have not been able to get across today—please do it in writing—will be absorbed into our considerations.

We are on a fairly tight schedule, as you know, but can I start off by asking you all this? I am trying to establish the effectiveness of measures taken to protect UK blood supply now. Do you think that UK blood supply is currently as safe as it realistically can be?

Christine Lord: I don't think so. I think the UK blood supply is not free of the rogue prions that cause vCJD. The Department of Health's safety measures are not sufficient. How many members of the public know that anybody who has lived, travelled, worked or resided in the UK from 1980 to 31 December 1996 is unable to donate blood in any other country abroad because we are all deemed at risk of vCJD? How many members of the public realise that all UK blood banks and blood products since July 2007 carry the warning statement "at risk of adverse reaction infection, including vCJD"? How many people in the UK know that tens of thousands of the UK public could be silently carrying vCJD and pass it on through blood or operations? I am hopeful that this inquiry can raise awareness of these issues and many more which we will be discussing today and over the next few weeks. We face a ticking health time-bomb, which must be addressed and tackled.

I have brought along some photographs of my son and I would like to hand them over to the inquiry for you to have a look at and to keep, because *this* was my healthy young son, and *this* was him six months later. These will be the consequences of the Department of Health not screening blood and not bringing in some more safety measures. Could I pass those over to you?

Q2 Chair: By all means. The Clerk will take them and pass them round. From the perspective of the other witnesses, can I ask you to answer the same question, if you can?

GRO-A Yes, certainly. The short answer is no, we do not think it is as safe as it could be. If you look at the emerging viruses—or re-emerging viruses—such as hepatitis E, which is not screened for, I think that is a case in point that demonstrates that.

Liz Carroll: I think the answer is similar: no, we can't say the UK blood supply is safe. There are some particular areas—obviously I am representing people with bleeding disorders and particularly around fibrinogen replacement—where we could be doing much more to ensure a really safe supply. So, no, we can't say it is safe.

Dr Buckland: My main perspective is the care for patients who are receiving plasma-derived products, clearly immunoglobulin and C1 esterase. The current situation of sourcing plasma from overseas is the step that has ensured improved safety of plasma products, and I think it is key that that is maintained. For our patients with C1 esterase inhibitor deficiency who receive a concentrate that is from a cryoprecipitate, that is also sourced for the commercial products from European or US plasma, which is the step which, certainly for plasma-derived products, ensures safety for those patients. The key thing is that we feel, in terms of plasma, the supply is safe, and therefore any changes could only be made if they maintained the current level of safety for patients.

Q3 Chair: In a way, Ms Lord, you have answered it from your perspective, but again I will ask the witnesses which pathogens do you think currently pose the biggest threat to UK blood recipients? Perhaps you can start, Dr Buckland.

Dr Buckland: There are the known knowns and the known unknowns. That is always the problem in counselling patients to receive blood products. We know the things which we can screen for and mitigate out that risk, so most of the lipid-borne viruses fall into that category, and we are effective at screening out both at the donor stage and then by testing of donated samples for cellular products. However, we know that there remains a theoretical risk, for prion diseases—theoretical—but we also have evidence before leucodepleted blood of patients who are likely to have been infected. We know that that continues to be a present but low risk.

Of the things that we know, prion diseases in particular are a concern. But, of course, with all blood products, there is an appropriate screening programme to look for the other infections, including common bacterial and viral infections, which can be transmitted in blood, and as many steps are taken to remove that risk. But the giving of blood products is a risk benefit, as is the sourcing of your blood supply, so we need to have independence in our blood supply within the UK to be able to safely treat patients. If someone is bleeding, they will need red cells; they may need fresh frozen plasma in cryoprecipitate and so on. There are the major viruses or other bacteria, as to which occasionally there are historically sporadic cases of people with undiagnosed infection and rare transmission through blood donation, but the unknown unknowns are clearly the greater problem—the things we either can't screen for currently, like prion diseases, or the things that we yet don't know to worry about.

GRO-A There are certain diseases that are not known about still that you can test for such as West Nile virus. These are becoming an issue, certainly in terms of immigration and travel, but they are only tested where somebody points out, if they are honest, that they have actually travelled to an area that may have been affected. Again, those types of viruses are potentially a risk.

Christine Lord: The Health Protection Agency's latest research is that one in 2,000 of us in the UK is probably silently carrying vCJD. The great difficulty I am finding again and again in my research is that the British Government—the Department of Health—hold all the keys regarding validation of a screening test. They also control the samples from vCJD victims and many aspects of scientific research, not allowing international and foreign scientists to take their place. These few select scientists and Government officials hold a monopoly over validation.

Q4 Chair: We are going to come on to that in a minute, but you are specifically saying, in answer to my question, that vCJD—

Christine Lord: I think there is an under-reporting of cases, which I know that you are quite interested in, and there is a particular case that I brought up in my submission that you are interested in, yes.

Liz Carroll: It is the fact that there are the prion viruses that we know about, but we know there is the potential for other things that we cannot yet screen for. That is the risk, particularly for people who are having pooled products, where you get a donation of lots of different people's blood products into one thing that you receive. When you are pooling lots of different people's blood products together, your risk of then going on to develop things is much greater.

Q5 Chair: Specifically to you, Ms Lord, in your written evidence you say that you know of at least one case in which vCJD was transmitted via a blood transfusion after leucodepletion was introduced in 1999. Could you tell us a bit more detail about that, please?

Christine Lord: I will just backtrack a bit. I went to a SaBTO meeting not so long ago where Professor Marc Turner, who is going to give evidence later on today, actually declared that leucodepletion, at best, is only about 37% effective anyway. If he wants to, he can expand on that later. He talked at length about how leucodepletion, when Frank Dobson brought it in, was great, but obviously technology has moved on.

Let me tell you, a few years after Andrew was killed by vCJD I was contacted by a man called GRO-A whose middle-aged wife was dying of vCJD. The CJD Unit and the UK Government had fully recognised this lady—whom I will call Sue—as a victim but were extremely reluctant to name the origin of the disease, despite Sue having a blood transfusion at a south of England hospital in 2002, which is well after leucodepletion. The husband had been quizzed by the CJD Unit and also various members of the Department of Health, who had visited the family home. Government officials demanded to know every scrap of medical information about Sue and were particularly interested in the fact that she had had a blood transfusion in a south of England hospital in 2002. Department of Health officials took copious amounts of blood samples from Sue for their research. These included Professor Collinge's team at the Prion Unit and the CJD Unit as well.

The husband and I spoke to each other over a few years as he nursed his increasingly disabled and desperately ill wife. The husband GRO-A told me, "Sue is much older than all the other victims and she must have got human BSE from somewhere. They keep asking me about blood transfusions she had in hospital in 2002." The CJD Unit then told GRO-A that it must have been Sue eating beef from a local farm shop that caused her to develop the disease. Now, this was never backed up by facts and never backed up by information, such as why it was this particular farm shop. It was all very ad hoc and very vague. This almost throw-away suggestion of the origins of Sue succumbing to vCJD seemed to have no basis in fact at all or any concrete evidence that they could provide to her husband or the family. GRO-A, the husband, was not convinced that his wife had been infected from the shop as she rarely used it and he remained very confused. He wanted to have answers and believed it was the blood transfusion that had caused his wife to develop human BSE. Every time he challenged the beef hypothesis, life would become much more difficult for Sue and the family. Care would suddenly be limited and GRO-A, who was a self-made businessman, would get unexpected visits and calls from the taxman, which only added to his huge stress. Sadly, because the care provided for Sue became very patchy, she had to be admitted to a care home, where she died in October 2011.

Q6 Chair: Can I ask you—not necessarily in public—if you are in a position to let the Committee know more details about who that person is?

Christine Lord: Yes, I am. Obviously, I have to be a bit careful for family members because I walk between two places really.

Q7 Chair: Indeed. Obviously, we are a scientific Select Committee. We need to cross-reference all evidence as best we can. If you would be kind enough to provide that to us privately, then we can do the necessary cross-checking.

Christine Lord: Yes, of course. This husband did talk to some members of the media off the record as well.

Chair: Thank you very much.

Q8 David Tredinnick: Good morning. I want to ask you a bit about the sourcing of plasma products, please. I am going to ask Mr GRO-A a specific question in a minute and Dr Buckland can follow up on that. For several years now many plasma products have been sourced from outside the UK to reduce the risk of variant CJD transmission. What do you think are the risks and disadvantages of having to import these products?

GRO-A We have talked about emerging infections. There are certainly geographical infections, and we have mentioned West Nile virus already. These are quite prevalent in certain cases; certainly north America has regular outbreaks. There is a question as to whether or not the screening within those countries, over which presumably the UK Government have very little control, is of a standard that we would wish it to be and whether it is addressed by the viral inactivation methods that are currently used. In fact, just talking about the emerging pathogens as well, I have sent a list of Susan Stramer et al. There were some 68 pathogens on there that are of potential risk to the blood supply and plasma products. We are unclear as to whether all viruses would be picked up and inactivated by these current methods. For instance, as to hepatitis E and hepatitis A, we know these are non-enveloped viruses and they are not affected by heat treatment. There is a question in my mind as to the same sort of problems they had in activating hepatitis C and HIV and finding the right temperature and length of time to treat it—whether there are weaknesses in that—that a new virus emerging may not be susceptible to those same treatments and whether they need longer periods or a different type of treatment. As to the vigilance that is required, we are not convinced that the measures are thorough enough at the moment.

Q9 David Tredinnick: Does anybody want to come in on that particular question, through you, Chair?

Dr Buckland: From a pooled normal human immunoglobulin perspective, the decision that was taken pre-emptively to source our plasma from regions of the world where CJD—and, indeed, variant CJD and BSE—was not prevalent was incredibly important in protecting patients while we have tried to establish what the risk is. We are aware that in

some parts of the world those donors are remunerated donors, and the WHO guidance is that we should all be moving towards non-remunerated donors, but I think that part of that has been essential in ensuring supply. Certainly, in the US, where much of the UK-sourced plasma is now obtained, those donor centres have very stringent systems in place, but again that is acknowledging that that is to screen for those things which we can screen for. The releasing of plasma into the pool when a donor returns three months later for their next donation—and those donations are held so that it can be clear whether or not an individual has developed a disease in the intervening three-month period—is a key step in ensuring safety, and, of course, there has to be appropriate oversight, as a medicinal product, within the UK and overseas.

You asked what the risks and the benefits are. There are clearly still risks in terms of the supply chain, if you like, which, while it sits outside the UK, is not fully within our control. However, there are other risks, which are clearly that patients within the UK are subject to the world plasma market, and that has previously caused problems. But the Department of Health does now have a demand-management project that helps ensure supply. So I think there are two issues, which are both supply and infection, but currently the sourcing of plasma outside the UK is safer for our patients than if we moved back to using UK-sourced plasma.

Q10 David Tredinnick: Thank you very much. Following up on that question, what other measures do you think can be taken to improve the safety of plasma and plasma products, and why have these not been implemented already? You have already said that you think it was safer and a good idea that we went to the United States, given what has occurred here, I think. Do you have any other thoughts about other measures that we could be taking?

Dr Buckland: The UK obviously cannot control directly the supply chain, although there can be requirements on the manufacturers of immunoglobulin, for example, as to how their product is sourced. The manufacturers have increasingly introduced additional steps, including solvent detergent treatment and pasteurisation, into the treatment of immunoglobulin, and that has now become the norm and a requirement for the licensing of the products. So, currently, we are doing what we can do. The question remains whether we can impose additional restrictions on the licensing of the products where it is known that additional pathogens can be tested for and they are not currently within that donor pool.

Christine Lord: Can I ask a question? Is anybody born before 1 January 1996 eligible for this plasma from outside the UK?

Dr Buckland: All UK plasma products, in terms of the pooled normal human immunoglobulin and other products, including C1 esterase inhibitor, are currently sourced from plasma outside the UK. We do not have a UK plasma source for those products. So even BPL, which is a UK-based company and manufactures its immunoglobulin within the UK, sources its plasma from outside the UK.

Q11 David Tredinnick: Thank you. Through you, Chair, Mr GRO-A?

GRO-A If it is possible to add to that, I think there are two aspects. In terms of the viral inactivation processes, and certainly in respect of the plasma that goes on to be used for cryoprecipitate, this product is not heat-treated but is subjected to methylene blue, I believe, so there is an element of inactivation in there. But we should be vigilant too of the fact that the USA has also had cases of vCJD. The UK still has a couple of cases—as we heard last time—per year, and, in fact, in the US they had four cases of BSE. I think the most recent case was in 2012. They have also had three cases of variant CJD, two potentially identified as being from travel to the UK. But there is a question mark over whether or not it is incubating there, and that really highlights the point that we need this variant CJD screening test developing and introducing. It is a crucial point that is going to have a major effect on safety, both within the UK and potentially imported products.

Q12 David Tredinnick: Let me ask you one more question related to what you just said and see if anyone else wants to come in on this. My understanding is that both the Haemophilia Society and the British Committee for Standards in Haematology have now recommended that the UK ceases its use of cryoprecipitate and instead uses imported fibrinogen. Do you agree with that?

GRO-A In terms of swapping over to concentrated fibrinogen, it is perhaps a little bit confusing. Reading the submission, it sounded as though it was in reference to haemophilia generally; it is not. For fibrinogen deficiency, or some people might call it haemophilia factor I deficiency, I believe there is evidence to support that swap-over; many other countries have moved over to concentrated fibrinogen, which is heat-treated, and it would appear safer. Based on that evidence, it would appear to support that case.

Liz Carroll: That is certainly one of the things that we were talking about in our evidence. There are people with fibrinogen problems who have a bleeding disorder that is not necessarily haemophilia, and there are about 412 people in the UK who are regularly receiving products that could put them at risk of CJD. If we were to move that to a source outside the UK, where it is not human plasma in the same way, it would reduce that risk dramatically for those people. They are repeatedly receiving this; it is not a one-off; it is happening a lot through their life, so their risks are being increased quite a lot, yes.

GRO-A We should point out that haemophilia on the whole is now treated with recombinant products, although there are still exceptions to that. Certainly, in terms of immune tolerance and effectiveness, there are plasma-based products that are still in use. For people with inhibitors, there are certain people who do not respond well to the current recombinant products and they are also on plasma-based prothrombin complexes, which are a number of clotting factors. So the risks are still quite prevalent in those cases.

Christine Lord: I have had countless e-mails from countless people contacting me via the website, who have received a letter to say that the medicines that they have received have been pooled from somebody who has had vCJD, most recently from a father who injected two of his sons over many years with medicines and they are now both at risk of this disease. This is not just a one-off. I am getting e-mails all the time, not just from people who have been affected through their medicines but also via contaminated instruments due to having operations in theatres in hospitals. The list of what I call "living victims" is growing and growing.

Q13 David Tredinnick: Perhaps the Committee would like to see some of these e-mails.

Christine Lord: Yes, some of them.

David Tredinnick: They might add colour—maybe that is the wrong word. They might add to our basic knowledge.

Christine Lord: Yes.

Q14 David Tredinnick: I do not know whether, Dr Buckland, you want to finish this question off and then I will hand back to the Chair.

Dr Buckland: Certainly. My expertise is not in haemophilia. My observation would be that C 1 esterase inhibitor, which is from the same faction as the clotting factors, is within the UK again sourced from non-UK plasma.

Q15 Stephen Mosley: Ms Lord, you were just talking about people who have been designated as being at risk of CJD. What sort of impact does that have on their lives?

Christine Lord: It is absolutely devastating. This particular father said, "I've got to turn round and tell my sons, when they are of sufficient age, that they are now at risk of vCJD." Also, another young man called GRO-A got in touch. He is actually recovering from brain cancer, is in his 20s and now is at risk of CJD as well. Can you imagine coming to terms with and trying to get over brain cancer and getting a letter saying that as well? The impact is absolutely devastating because there is a sword of Damocles hanging over these people's heads when they have had medicines and had operations which should be safe.

I just so want the inquiry to move this forward so that the Department of Health pushes forward and validates screening tests. There are and have been blood screening tests; I and family members have tried to support especially outside independent screening tests and we have been thwarted and blocked every way. Me, GRO-A and GRO-A all tried to access our late sons' blood to send it over to a Canadian company that had developed blood screening tests. We were blocked and thwarted and stopped at every phase. As parents and next of kin, we cannot access our late loved ones' blood samples to send them out of the country to push forward tests. The Department of Health—a small group of scientists—hold a monopoly of everything, and it blocks and stops a lot of things.

I am here today to be Andrew's voice, my late son's voice, and to be all the victims of vCJD's voices as well, but also the voice of one in 2,000 of the UK public who may be carrying this deadly disease. I have no other agenda. I'm not worried about my funding; I'm not worried about my status; I'm not worried about my career. I am here as Andrew's mum and as the voice of truth really.

To go back on that, to get a letter to say that your son, your daughter or you may be at risk of vCJD because you have had medicines or you have had an operation under the

Department of Health or the national health service—I can't put it into words, but these people obviously do to me. I speak to them regularly; they phone me; I've got e-mails, and that list is growing. So we have to do something, otherwise we are going to see many more "Andrews," and I don't want that. I want to protect other families and other parents throughout the UK. That is my only agenda.

Stephen Mosley: Okay.

Liz Carroll: As Ms Lord was saying, there were over 3,000 people who had haemophilia who were sent a letter to explain that the treatment they had had 10 to 15 years ago from now could well have put them at risk of CJD and they are living with the risk that they have that now. Our experience is that that has an impact on their everyday life all the time. It is not just the anxiety of knowing that this could happen and having read what happens to people if they develop the disease, but also every time you go for a medical procedure you have to tell everybody, "I'm at risk of this." It has had an impact on people in the past certainly being able to get access to medical procedures like endoscopies because the instruments then have to be quarantined. You have to tell your family and friends. That comes on the back of lots of people having already lived through the experience of receiving contaminated products that gave them HIV or hepatitis. So the families are living with these risk factors every day. It has a huge impact on people's lives. It is not just, "Well, it might happen to me; it might not." It is a real, everyday living thing for those people. If there is something we can do that will reduce the risk for anybody in the future, then we should do it.

GRO-A I was one of those patients living with the threat, multiply contaminated with multiple, multiple viruses—the list you have been given. I am into double figures on that. So I definitely have the "unclean" bell.

As to the impact of CJD on your life, we seem to be caught in the middle. You have doctors on one side saying it is theoretical, and yet everything else going on around you is not theoretical. For instance, when paperwork from one department in the hospital goes to another, I have AIDS—my status is AIDS—hepatitis C and hepatitis B. They are highly infectious viruses which we know will infect. They are not flagged up; my haemophilia is not flagged up; but in big block capitals across the top of the paper is "AT RISK FOR vCJD." I had an operation in 2009, and in big bright red letters on the white board at the end of the ward was my name, my bed number and again "at risk." So that meant that every person who walked into the ward, including the tea lady, who used to just throw the cup at me, all knew that I was this dangerous thing lying in there.

Recently, within the last two months, I have been asked what treatment I am receiving for my vCJD and who is actually in charge of my vCJD—and there isn't anybody because I have not got an official diagnosis that I am positive. Therefore, nobody is prepared to talk to you; nobody will give you any information, and I actually have nobody looking after me. Also, there is a UKHCDO surveillance study going on and I have had doctors deny in writing any knowledge that they know that this surveillance study is ongoing, so you can't get any answers.

In our case, the three of us are severe haemophiliacs, all with the "at risk" status, and two of us are the only known haemophiliacs in the country that have pushed to get genotype-tested. The way I managed to get genotype-tested was because the hospital I am under

actually broke Health Protection Agency protocol. They are supposed to send a sample, if they can access your spinal fluid, to the CJD Surveillance Unit. I had a lumbar puncture performed. I actually requested that action to be taken and they did not, as far as I am aware, although the card does say "store." When I questioned and said, "The protocol says you have to send it," I was palmed off to the neurological hospital. They did not want anything more to do with me. So the two people in this country right now that we know of are sitting here. We are here, and we have done everything that we possibly can to assist in the validation process of the test, because, as Liz just said, with HIV and all those other things, you are walking around with a loaded gun pointing to your head. 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.

Christine Lord: Can I come in here because you talked a little bit about, almost, stigmatisation as to the fact that you are vCJD "at risk"? You will know that the CJD Support Network submitted evidence with case studies where people were a bit nervous about divulging the fact that they had vCJD or were vCJD "at risk." There is a lot of support out there with the public and in the media. There is a lot of support out there for people with vCJD or at risk of vCJD. Family members, including myself, have had bullying and intimidation not to talk out about our sons or daughters having vCJD, "Don't tell your neighbours. Don't tell this; don't tell this," or, "Your son was a blood donor. Don't tell the public because you'll have vigilantes at the door; you'll have the press putting their foot in the door." My experience has been that the actual stigmatisation has come through the CJD Unit and the Prion Unit trying to keep family members quiet, and this, in a way, has actually fed the myth of the mad cow disease. I hate that term but everybody knows it. The cows weren't mad; they were distressed. My son wasn't mad.

I think we need greater transparency. We need to be able to say, "I am suffering from vCJD," or "I am at risk of vCJD." The general public have been absolutely wonderful towards me and the families, but it is Westminster—sorry about that—Whitehall suits, the CJD Unit and officials that descend on families who are affected by the disease and they intimidate them into not speaking out. Greater transparency could lead to GPs, medics and the public knowing more about the disease, and then they are going to be less afraid, aren't they, GRO-A? That is what I have always tried to push forward.

Q16 Stephen Mosley: I want to come back to Mr GRO-A and Mr GRO-A, but can I just explain it a bit because I know, Ms Lord, that you said that people just had a letter coming through the post to say they were at risk? Was that your experience or was it better handled than that?

GRO-A: The picture for haemophiliacs was very mixed. The UKCDO—is it 10 or 13 years on?—still can't actually tell us how many people are aware of having been given this "at risk" status, so the follow-up has been less than adequate as far as everyone is concerned. It is almost the worst of both worlds. We have been given this status based on a theoretical risk, but we know that there is a test that is available and it is being used in kind of a trial way at this moment. Professor Collinge talked about it in the previous hearings.

As a haemophiliac myself, I spoke about three years ago, I think it was, at the Haemophilia Alliance to explain experiences I had had where, to all intents and purposes,

it looked very much as though I had the onset of variant CJD. It was unclear. The mechanisms that we were meant to access to clear up this whole point were not clear to the doctors I was under at the various clinics. Did my HIV consultant take it up, my haemophilia consultant, or whatever?

My two colleagues have had the genotype-testing, and, as I say, we know there is a screening test now. It would have been incredibly helpful if we had had access to that 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. I could not remember a thing. I am still under support for techniques to manage the impact on my memory even now, and, although I have improved a little from that time and we think perhaps there were effects of HIV medicines on the process that I was going through, there is still an apparent underlying effect on me in terms of cognitive disorders.

In BSE, the variant CJD arises through ingestion of an infected product. In haemophiliacs, this product is not necessarily ingested but injected directly into the blood. My concern is whether it would, therefore, circulate among the lymphatic tissues and may manifest itself in some other way, perhaps even in a slower progressive way, where you will see these symptoms but they will not necessarily be recognised as the classical variant CJD. That is a reason, again, why we think we need this test. We know that GPs are able to refer people who are exhibiting symptoms. We think that should be extended to people who are "at risk," to clear up this whole theoretical "at risk" process so that people can either come to terms with it if they want to or they can get the "at risk" status removed and stop having their lives blighted.

Finally, there is one other thing. There is a definite difference in the way that people are being treated over this "at risk" status, and, although I am not privileged to name specific people who have been affected for reasons of confidentiality, we know that there are people who have needed surgery and have elected—they were so desperate—to go down a private route and been told at the last moment that they cannot do that because of the problems with scopes, equipment and the cost. If they go back on to the NHS waiting list, that side is taken care of, but, if it is private, of course, the private company is expected to reimburse the NHS for the loss of scopes and surgical instruments.

Q17 Stephen Mosley: Lastly, I want to ask very quickly whether everyone who is at risk has been informed.

GRO-A In the table that we provided in our submission, in the bleeding disorder community, 3,872 were notified and, as yet, the UKHCDO, 10 years on, has not provided the Health Protection Agency with that data. It is a very easy process because it was the haemophilia centres that sent out the warning letters. Effectively, when you then go for your review—because we have to go at least every six months, but with HIV it is every three—the first time you walk in the door they should have said, "Did you receive the letter? Do you understand it? Do you have any questions?" It did say on the letter if you had any questions to contact your centre, but it appears that the follow-up either has not happened or it has happened and, for a reason unknown to us mere patients, the UKHCDO

are doing whatever they do with it. I personally don't believe that you could send out those letters and not follow it up.

Christine Lord: I think genotype is very important as well because there has been a definite under-reporting of vCJD cases and also cases where people have been recognised with vCJD but not necessarily attributed to blood.

There was a man called GRO-A who died in 2000, who had actually received a blood donation but was reported as dying because of infected beef. I have all the details here. Also, there is another man who died in 2009—somebody called GRO-A He was recognised by the CJD Unit as dying of vCJD and was found to be a different genotype—MV. He has never been officially recognised on any Government stats as dying of vCJD. Subsequent Ministers have been questioned in the House about it and they have denied it. There is a flexible protocol when somebody is diagnosed with vCJD and these flexible protocols can be moved about, whether it is definite or positive, but this young man, GRO-A, was diagnosed with vCJD. I have letters from the CJD Unit which the family have given me. I interviewed the family. I actually met the young man before he died. He died from the MV genotype.

There was also a young lady called GRO-A back in 1996, who died of vCJD, and then that was suddenly overturned to "vCJD with signs of sporadic CJD." Professor Ironside told GRO- GRO-'s grandmother, "Your daughter couldn't possibly have had vCJD because she is MV, a different genotype, and they don't get it."

So there has been an unreporting of cases, and I come across this again and again and again. These families have received compensation and have been officially recognised, but they are not recognised, if you see what I mean.

Liz Carroll: Following up what GRO-A was saying, my understanding was that everybody with a bleeding disorder who was thought to be at risk was written to, but that was the extent of what happened really. Everybody was written to. Some centres may well have followed people up, but it was not part of a protocol that everyone would be followed up. So we don't know for sure that everyone received those letters. They were sent to them, but we don't know whether they all received them or what happened to everybody after that. There is a belief that most people will know, but we can't be 100% sure and what that means for them.

Q18 Chair: Before we move on from that, I have one quick follow-up question—a yes/no answer if you can. Are there parts of the UK where the practice is better than others?

Christine Lord: My experience with e-mails from various family members is no.

GRO-A It is very patchy, I would say.

Q19 Stephen Metcalfe: Good morning, everyone. I would like to return, if I may, to the point you were just making about under-reporting, Ms Lord. One of our starting points for this inquiry is that there have been 177 sad deaths associated with vCJD, and that is as

reported by the National CJD Research & Surveillance Unit. Obviously you are sceptical of that and think there has been a high level of under-reporting, that people have been kept off official lists and so on. You have given us some examples, and obviously those are personal examples of individual cases.

Christine Lord: They are not personal examples but are fact because there are letters to say that these people did die of vCJD.

Q20 Stephen Metcalfe: I am sorry. What I meant was they are sad individual cases. What do you think the scale of that under-reporting is, and how can we ascertain whether that is correct or not?

Christine Lord: I would like to backtrack a little to when we talked about cases in America, and I know GRO-A was talking about cases there. The cases of sporadic CJD in America and across Europe and the UK have gone through the roof. Sporadic CJD is the spontaneously occurring part of the disease, which usually affects elderly people. I understand from Professor Collinge now that, instead of being one in a million, it is now one in 33,000 in the UK. There needs to be thorough investigation into just how many people are dying. Also, as I say, the CJD Unit and the Prion Unit have obviously almost got the monopoly in that when somebody is diagnosed with or suspected of having vCJD it should go through those routes and get to either of those two units. What seems to be happening is that families are at first intimidated, "Don't tell neighbours; don't tell this; don't tell that," and they then obviously keep that a secret and get a bit frightened. There are many families that I probably don't even know about. Then, after a while, they perhaps go on the internet, see my website and come on and talk to me. Then I find out that, yes, they have been interviewed by the CJD Unit, they have been bombarded with questions about, "What did your loved one eat? When did they eat it? Did they eat beef? Did they eat that?" I think there needs to be a thorough investigation into the process of diagnosing and recording people in this country.

Q21 Stephen Metcalfe: I think that is a sensible way forward, but, from your own experiences of families and the people who have contacted you, and from that 177, to what degree is that under-reported in your view? I am not going to hold you to it, but just give us an idea.

Christine Lord: I think past, present and even current, it is always untrue. I have been talking to family members and they just don't appear on the list. My son Andrew appeared the year after he died, and it was only because I pushed and said, "Was that my son?" Most families will see that number, whatever that number is in that column, and automatically assume it is their child—and it may not be.

Stephen Metcalfe: I see; I follow.

Christine Lord: Does that make sense?

Q22 Stephen Metcalfe: Yes, it does, because you are saying the list is anonymised.

Christine Lord: Yes, yes.

Q23 Stephen Metcalfe: So one person appearing could represent a cluster—

Christine Lord: A thousand or a hundred, yes.

Stephen Metcalfe: —of families who believe that is their child being reported.

Christine Lord: Yes, because they have had multiple visits from the CJD Unit and the Department of Health officials, and they have all come in and said, "Don't tell anybody. If your neighbours know, if the press know, you will have them putting their foot in the door. You will have people saying 'mad cow disease.'" Coming back again, we need to educate. We need to say, "The people who get the human form of BSE are innocent victims. Food and medicine should have been safe, and it wasn't." My experience of the public is that they want to know and they need to be aware. I have supporters behind me now who have never been personally affected by vCJD, but, as they said, "Andrew could be my son or daughter." So I think we are doing a disservice, or Whitehall is doing a disservice, to the public. The public want and need to know, and we need to raise awareness, educate and not frighten people. My book and the website are not about frightening people; they are about giving people information and then they have choices.

Q24 Stephen Metcalfe: Can I ask the other panel members whether you think there is an under-reporting of vCJD?

Dr Buckland: I suspect there is an under-reporting because we know when we do prevalence surveys of other diseases—and we do anonymous prevalence surveys—that there is often under-reporting of disease. But I don't think we have the evidence currently that there is an order of magnitude; it is not a log difference in terms of under-reporting. I think we are handicapped by still having a lack of understanding of the disease pathogenesis and the link between genotype and exposure. So, while we know that the reported cases of individuals who are affected are usually MM genotype, we don't know—and I think the Prion Unit will also concur with that—what the natural history will be for the other individuals who are MV or VV genotypes in terms of their susceptibility and how that interacts with infection, because, clearly, from the surveys of infected appendices we know that we have at least a handle on what the level of exposure and asymptomatic carriage is. How could we improve that? We are handicapped by a coronial system that does not allow the remit other than to find the mode of death. So, if an individual dies of a myocardial infarction, you find a myocardial infarction and you do not proceed to examine the brain. Therefore, with the current coronial system, we will always run into these sorts of problems.

Q25 Stephen Metcalfe: Can I pick up on something you said there about the tests on the appendix, the 32,000 which ended up, I think, with one in 2,000 being identified? Was the genotype identified first or after the tests were carried out? Were they all of the MM group?

Dr Buckland: They are unaffected individuals, and my understanding is that they are either MV or VV genotypes, but the MV genotype is associated predominantly with asymptomatic carriage.

Christine Lord: There are at least 18 victims of vCJD who were never genotyped, and also family members. I know a couple of the haemophiliacs have had their genotype tested. I tried for six years to have my genotype tested and I was refused. Everything led back to Rome, to the CJD Unit or the Prion Unit, and Professor Collinge told me that it would have no value for me to know my genotype. So I had to go outside the UK and have my genotype tested, and other family members have had their DNA mapped as well, which I alluded to in my statement to the inquiry. Some of the results that are coming back are very interesting. I am waiting for more corroboration about those results, but the very fact that family members also have to go outside the UK to have quite a non-invasive test absolutely emphasises the secrecy and the monopoly in the in-house stuff that is going on regarding this disease and which is creating the myths and the worries about vCJD.

GRO-A The point I was going to make has partly been made that the cause of death could potentially be linked with variant CJD, but it is not always followed up. Apparently, the primary and most obvious thing that is glaring them in the face is the one that is put down.

The other thing I was going to mention on that—and I think you may have heard it in the last hearing as well—is that Alzheimer's and variant CJD seem to follow a common pathway in the way that the receptors work. So, potentially, there is room for confusion in that respect and the under-reporting may be impacted by that.

I was going to mention as to haemophiliacs that not only do we have this "at risk" status for people who have used plasma products in this so-called danger period, which amounts to some 3,876 people, but, of those, there were people who received implicated batches, and of course the risk is perceived to be higher for these people because the donors related to those batches either went on to develop variant CJD or died from it. So it adds emphasis to the need for people to be given access to a test. In terms of myself, after everything that I went through, and the turmoil and the distress as to whether it was actually vCJD that was developing, I still, to this day, have not been offered a genotyping or even a screening test just to put my mind at rest. I understand that not everybody may want that, but I think people should at least be given that option.

GRO-A That is how we got our genotypes because we had named batches. We have the batch numbers and know how many thousand units we were injected with. When we were passed through to the neurological hospital, it was almost a trade-off; we gave our blood to help with the validation process and they told us our genotype. I will be completely honest that being told I was MV gave me a slight bit of reassurance. Okay, I might live to be 175 and then start showing symptoms—we don't know—but it does give you that tiny little bit of, "Okay, so it's possibly not the end right now."

GRO-A There was one other thing. It is not necessarily captured by these figures, but we heard at the Haemophilia Alliance, I think around three years ago, that, while you may be perceived to have a higher risk from having received an implicated batch, what may actually happen if you are on prophylactic plasma products is that the volume of these products each time increases your risk just a tiny bit. If, like myself, you were on very substantial amounts for immune tolerance purposes, your risk profile is substantially raised to the point where you do not necessarily need to be associated with an implicated batch because the chances are that there was someone within that donor pool.

Q26 Stephen Metcalfe: Did you want to add anything to whether or not under-reporting—

Liz Carroll: I don't know enough about the under-reporting. I think there were over 800 people who received—

GRO-A 802.

Liz Carroll: —implicated batches who had haemophilia, so it is a lot of people. That thing about pooled products is the thing that I was talking about earlier. That really increases your risk dramatically.

Q27 Stephen Metcalfe: Yes, I understand that. Thank you for that. It has been suggested that the "at risk" individuals should be subject to a mandatory post mortem to identify whether or not they were carrying vCJD. Do you agree that that would be a way of ascertaining prevalence or not?

Christine Lord: I think there should be an automatic test at post mortem if a person has died—a suicide or an accident, really. I have pushed for that in the past because it is just another test—

Q28 Stephen Metcalfe: Regardless of whether "at risk" or not.

Christine Lord: Yes. It is just another test to add. It is quite simple and it is not that expensive.

Liz Carroll: I think it should be choice. It should be available for those who want and need it, but, if you have been through so very much, some people would not want it for themselves or family members. The stress of a post mortem is huge for many families. I think it should be available for anybody who wishes it to be offered it, but making it mandatory could be difficult for some families.

GRO-A: We are pretty much of the same mind there. We don't believe that the mandatory route is the right way to go. People should have their freedom to choose to opt in or opt out. We would want to know a little bit more about the nature of this testing and whether or not it would be perceived as a small needle biopsy on tonsils, spleen, appendix and so on, or whether, given our past experiences and suspicions of information not being disclosed to us, potentially they could be removing whole organs for storage, testing and potential assay validation and so on. As to the impact of this on the families who may

want to know whether the person has died from variant CJD, it may have implications if they feel that there was some sort of negligence involved. Would it impact upon their legal rights to have a post mortem and autopsy done that will give them answers? This may supersede that. Could it undermine their ability to take legal action if that was what they felt was necessary? We have a question in our mind. We know that in the UKHCDO minutes of, I think it was, 1982 there was this importance mentioned of autopsies on haemophiliacs, and there was mention of a lost opportunity for central analysis. We have a suspicion and we are actually wondering whether or not such analysis is already under way given the keenness of central authorities.

There is also another question in here that bringing this about has almost been attempted several times before and it has failed on coroners not wanting to do this because they perceive that they are there to identify the cause of death as opposed to carrying out research on subjects. Now, I don't know if they have managed to get past that—I suspect not—and I don't think it would be right just to force that through again without anybody's consent.

Stephen Metcalfe: Thank you. There are some useful questions there.

Dr Buckland: Within the UK study for patients with primary immunodeficiencies for prion surveillance, there have to date been eight patients who had died, who had previously consented during life for a post mortem, but, unfortunately, post mortems only occurred on five of those patients. Two of those were cremated before post mortem, before it was realised by their local practitioners that they had been consented ante mortem for a post mortem examination. As to the third patient, the local pathologist refused to perform a post mortem due to a lack of understanding that these were individuals who were deemed to be not at greater than 1% risk. They could not be convinced that they were able to perform an autopsy under those circumstances and that patient did not have a post mortem or autopsy examination. I think that, when we have a voluntary surveillance scheme, as we do currently, and with a lack of information sometimes still within certain pathology practitioners, we will not get a full estimate of prevalence. However, we do have to respect the rights of patients, including after death, and our current system, as has already been highlighted, does not allow an enforced post mortem. Clearly, if we believe there is unnatural death or the cause of death is not known, then a coroner's post mortem is performed, but within certain remits. So, although there is precedent for post mortems, we do not normally segregate. I think it clearly adds to the stigmatisation of those patients, and that comes back to better identifying those who really are at risk ante mortem.

Christine Lord: Can I say something? I agreed for my son to have a tonsil biopsy while he was still alive. I did not have to go through with that, but, as his mother, I had to be really sure that Andrew had vCJD and that it was not some disease for which I could have sold my house and made him better from. Andrew was quite ill by that time so I had to make that decision for him, and I have never regretted it because I know, without doubt, that he died of vCJD. Although that is an awful thing for a mother to have to say—because I wish he was here, alive and well—it helped me because it meant there was no doubt that he died of that disease. It is a great comfort to families to actually have some sort of resolution.

Stephen Metcalfe: Thank you for that.

GRO-A Could I add a couple of points? There are a couple of things we would also like to understand. What is the outcome that they are hoping to see from this? If it is just spread—how prevalent it is in the population—potentially a screening test could provide the same answers. They talk about high-risk groups, and we would like to know whether or not they would consider haemophiliacs to be within those groups. At present it is all theoretical risks and theoretical, but we would want to understand that before we would take part, I think.

Then there is the value of these tests. What are they looking for? Are they looking for prevalence or, as someone suggested in the last meeting, it might be useful to know how quickly the virus propagates itself within appendices, lymph tissue and so on? It is not going to find that.

Q29 Chair: You have been giving evidence for over an hour now and we have a couple more questions that we need to drill into very quickly if we can.

Can I first of all ask what is a fairly complicated question in several parts? The first is, in terms of vCJD, tests obviously need developing; we all accept that. If there is a test that is only, let's say, 70% accurate, should individuals who have been told they are at risk be offered such a test? Ms Lord, we have seen from your evidence both today and previously in your written evidence that you have argued in favour of families having access to vCJD samples. How would you want to improve that, and, finally, what else do you think the Government ought to be doing to drive things forward in the right direction?

Christine Lord: I think the blood supply should be screened for vCJD, and this includes blood donors and patients about to receive invasive medical procedures, and anonymised data regarding prevalence is then released to the public. My view is very much that we get this test, and it is very much "chicken and egg." When HIV tests were first introduced, the prognosis for that disease was terminal and was not so good, but within a very short time we had treatments and now a lot of people with HIV live reasonable, productive lives. Family members of victims of vCJD should have the choice and the right to medical tests, including DNA mapping and genotype-testing and screening for vCJD. They must have that choice.

The next of kin should have the right and the freedom to access and send samples from their late loved ones who died of vCJD to foreign scientists, researchers and international companies who have developments, treatments and cures. For example, the Amorfix tests, which I tried to support but was thwarted throughout by the Department of Health and its officials, had a specificity of 99.9%. There were a lot of problems with them actually accessing samples. I was not allowed to send Andrew's over; Professor Collinge and his team sent some samples over in the end and it didn't go anywhere. I would like family members to have easy access to these samples so that we can send them to companies that we feel are moving forward with research on vCJD, whether it is screening tests, treatments or cures. There is no commercial financial gain for our families at all. This is about protecting families across the UK so that they don't go through the heartbreak that I do every day.

GRO-A If I can add to that, we saw with the introduction of leucodepletion that there was a perceived benefit there. It is uncertain to what extent and whether it is even effective or necessary, but it was introduced because there was a perceived benefit and people may feel safer because of it. If you introduce a test but you still only think it is 70% effective, it is still 70% more certainty than we have at the moment. That would possibly offer an element of comfort to some people—an element of reassurance.

You asked what more can be done by the Government. I think that is very simple. There is a whole minefield of problems with this funding. Professor Collinge talked about only needing something like £750,000 to move this test on to trials where you might start to get commercial interest. In terms of the Government budget and the £750,000 required to move on what is a very important public health issue, it is atrocious that they have not found that money. Apart from anything else, the introduction of a test such as that could potentially stop re-infection or recirculation of vCJD within the blood supply. I do not know if it would be exactly the same, but we saw the fall-out from Ireland when women who were infected with viruses through anti-D were perceived to have re-infected the blood supply there and it forced the Government into looking at support for them because they were perceived as not having done all that they could. I think there is a question mark here. The longer that the Government procrastinate over this issue, there will be questions asked about whether or not they have taken the most supportive route that they could have done to address this issue.

Dr Buckland: I concur. I would say that a test with a 70% sensitivity which could aid risk stratification and harm reduction has to be a good thing. This is a first-generation test, and the natural history of developing these sorts of assays is that, once you have overcome this hurdle—and, clearly, the Government hurdle is the funding—once in use and there is greater commercial interest, the normal sequence of events is that these tests become refined and the sensitivity may be able to be increased. It is an important step in continuing to improve blood product safety.

GRO-A Can I add one thing to that about pushing through a test if it was 70%? In certain groups like the haemophiliacs, because of, literally, the suffering and the pain that we have all gone through, it is cruel that we have got to a point now where there is a test sitting there? I think, as Professor Collinge said, we are in death valley, and the people with the money are on both sides. It is £750,000 to bring some form of reassurance to a really desperate group of people who do honestly live in fear, and I do have problems about the ethics of it. It should and has to be pushed and developed.

Chair: The last word.

Liz Carroll: I would absolutely say that we have to give people the chance to have the test that we have. We need to put the money in to improve it where we can, and we need to start where we know there is a product that is less likely to put someone at risk, like the fibrinogen replacement. We need to be using it.

Christine Lord: I don't want vCJD being recycled through our blood supply, and at the moment that is a very real possibility. We do face a ticking health time-bomb regarding future generations with vCJD. I see it all the time, with families phoning me up, and I have sat with so many victims in various stages of the disease—not just my son. We face looking at more "Andrews" unless we have a blood screening test for vCJD, but we should

embrace outside and foreign scientists and researchers as well. I am not very pleased and I don't think it is acceptable that there is so much of a stranglehold of in-house involvement in the Department of Health and various scientists monopolising things. As I said before, I tried to send samples to other scientists outside the UK and I was stopped repeatedly. The international scientific community should work together on this because it is not just about the UK. We exported BSE worldwide.

Chair: Can I thank you all for your evidence today, and I know particularly in your case, Ms Lord, you were reliving difficult circumstances again and again? This is obviously a hugely important piece of evidence, and, if you do have further information and especially some of that stuff that you might want to give us confidentially so that we can track it across, it would be very, very helpful. Thank you very much for your attendance this morning. We will now move straight on to the second panel, if we can.

Examination of Witnesses

Witnesses: **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, gave evidence.

Q30 Chair: Thank you very much for joining us this morning. It would be helpful if you could start off by briefly describing the remit of each of your bodies, explaining how this scientific advisory structure fits together.

Dr Salmon: Shall I start, Chair, as I seem to be back here? I am Dr Roland Salmon. I am a retired medical epidemiologist and I am currently acting as the chair of the Advisory Committee on Dangerous Pathogens. That is a long-standing committee. It dates from the 1978 Birmingham smallpox outbreak and has a remit to look at really all infectious disease threats that may affect the country. Its initial focus was on laboratory safety and it is responsible for the document by which the safety of organisms worked at in laboratories is categorised, but it now has a broad horizon-scanning remit. Finally, it has migrated from being a tripartite body with employers, employees and experts under the Health and Safety Executive for a number of years to being an expert committee of the Department of Health.

Dr MacLennan: Good morning, everybody. My name is Dr Sheila MacLennan. I am a consultant with NHS Blood and Transplant, but I am also the chair of the Joint Professional Advisory Committee of the UK transfusion services. Maybe I should explain a little bit as to what JPAC—as it is known—is about.

This committee was initially set up in 1987 with the remit to ensure that the UK had a common set of guidelines for blood transfusion services. Since that time, in addition to the guideline role, it also has developed to act as a professional advisory committee to the UK

blood services, and in that role it reports to the UK forum, which is comprised of the chief executives and medical directors of the four UK transfusion services.

Looking at what guidelines we prepare, we do prepare and regularly update them to have operational guidelines for the blood services contained in what we know as the Red Book, which is now currently in its eighth edition. We also disseminate clinical guidelines for hospitals about transfusion practice in the "Handbook of Transfusion Medicine," and we also own the donor selection guidelines. There are six donor selection guidelines currently: for whole blood and component donors; deceased and live tissue donors; cord-blood donors; and for stem cell donors. That is the range of guidelines that we manage.

The work of JPAC is conducted through seven standing advisory committees, all representing different specialist areas of blood transfusion. Members of those committees are appointed for their specialist professional advice rather than as representatives of certain organisations or blood services. Most of them are actually taken from the UK blood services, but also we have members who are from hospitals and universities as well.

The JPAC committee membership is made up of the standing advisory committee chairs, the medical directors of the four UK transfusion services, and we also have the medical director of the Irish transfusion service on JPAC. We have representation from the Medicines and Healthcare Products Regulatory Agency, from the Human Tissue Authority, a representative from SaBTO, and one from the National Institute for Biological Standards and Control. That is just a quick run through JPAC.

Professor Turner: Good morning. My name is Marc Turner. I am here representing the Advisory Committee on the Safety of Blood, Tissues and Organs this morning, of which I was appointed a member from its inception in 2008 and demitted towards the end of last year because I had fulfilled my term.

SaBTO, as the name suggests, advises Ministers and the Department of Health, both here at Westminster and at the devolved Administrations, on safety of blood, cells, tissues, organs and gametes for human use. Also, in its terms of reference it has to take cognisance of other aspects, including sufficiency of supply, effectiveness of existing or proposed methods for risk reduction, cost-effectiveness, and also, of course, give a degree of balance between the duty of care to patients and recipients, and also the duty of care to donors—particularly to live donors.

The members are appointed by the Appointments Commission. There are 15 members, including an independent chair, and they have a spectrum of backgrounds. Some are haematologists, transplant surgeons, IVF specialists, patient representatives, and so on and so forth.

Q31 Chair: You have heard the evidence session earlier today. Are you confident that the organisations you represent are sufficiently independent, obviously given that most of the funding for respective works comes from Government? Is there sufficient independence in the structure?

Dr Salmon: I think the short answer is yes. These are independent scientific committees. The appointment is done by a public competitive process. The minutes, as far as is

possible, are made available to anybody who cares to read them on the internet, and the emphasis is on getting the best scientific opinion available. I suppose I might add that none of the members are paid, so they have no particular immediate interest in protracting the deliberations or anything similar to that.[1]

Dr MacLennan: As far as JPAC is concerned, the members are appointed for their professional expertise, and in fact it is a professional advisory committee. Again, they are not paid. Their day job, as I say, is usually within the UK blood services, so within that remit I think they are as independent as they could be.

Professor Turner: Chair, I would give a similar answer to Dr Salmon for SaBTO. These are independent members appointed through a clear procedure.

Q32 Chair: Again, reflecting on the earlier evidence, how do you make sure that your best practice conforms to best practice globally? How do you integrate your scientific effort with that which is happening elsewhere?

Dr MacLennan: As far as JPAC is concerned, one of its main remits is to do external horizon scanning, and we have a lot of collaboration with other blood services throughout the world. I personally sit on a European committee that looks at emerging infectious diseases. That also has representation from Australia and America on that committee. I also sit on European committees. In fact, I currently chair a European committee on blood transfusion. So we do have a lot of collaboration from around the world.

Q33 Chair: As I understand it, the Australian link ties into Asia-Pacific more broadly.

Dr MacLennan: Yes, absolutely.

Dr Salmon: The Advisory Committee on Dangerous Pathogens' members are broadly chosen for the contribution they can make to introducing science to policy making. Therefore, they have considerable scientific standing in their own right. You can only acquire that by a process of research and publication, which, in a sense, requires you to be up to an international norm because it is an international pursuit. A number of the members, like Dr MacLennan, have membership of other international bodies, and I, for the sake of argument, spent nine years on the Conseil scientifique of the Institut de veille sanitaire, which is France's health protection agency. My experience is similar to many of the other committee members.

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[1] The witness later clarified that, "I do realise, however, that I have unwittingly misinformed the committee. In discussing the independence of the committee I claimed that the minutes of ACDP were made available on the web. In fact, although this is ACDP's intention and indeed we resolved to do this at our most recent meeting on 10 February, this hasn't been done hitherto. The confusion was mine. I sit and have sat on various advisory committees, some of which currently do publish their minutes and simply got muddled. That said, there have been for some time annual summaries of ACDP's work published on the web and these quote extensively from minuted discussions and the minutes are anyway, disclosable under Freedom of Information legislation. Thus, I feel that the sentiment of what I expressed, concerning the committee's independence, was perfectly accurate. Nevertheless, for the record, I recognise that the detail should be accurate."

Professor Turner: Again, my answer is going to be similar to Dr Salmon's. The members of SaBTO are appointed on the breadth of their expertise, but they are all experts in their own fields and have connectivity, therefore, into their own UK and international networks. Where required, SaBTO asks for additional expert help either from other organisations or from other specialists.

Q34 David Tredinnick: Good morning. Could you explain why it is that blood donor risk assessment is carried out at a population level rather than on an individual basis, please?

Dr MacLennan: That is probably down to me. I think you are probably referring to the policy.

David Tredinnick: "On the basis of individual risk," I should perhaps have said.

Dr MacLennan: You are probably referring to the policy on men who have sex with men donation specifically.

David Tredinnick: Yes.

Dr MacLennan: Probably two years ago, SaBTO considered the rules regarding men who have sex with men, and they did consider whether we could move to individual donor risk assessment in that review. The conclusion was that there was insufficient evidence available to be able to determine what the impact of that change would be on the level of risk. They also considered that, if there was an introduction of more extensive donor questioning, the donors may not like that and we may therefore lose some donors on that basis. If you look at policy worldwide, there are probably two countries which currently espouse individual donor risk assessment, but all other countries do it on the basis of evidence from population risk assessment. Some countries, including the UK, have moved to a temporary donor deferral on that basis, but the rest of the countries in fact still keep the lifetime ban. But this is not set in stone, and there is a European group now trying to look at what the risk might be if you did move to such a policy. Also, NHSBT is currently conducting a survey among blood donors looking at what the perception is among donors about the questions that they are asked.

So I think, in summary, this is an evidence-based decision and, if we were to have further evidence to say that we should change it, then we would look at that.

Dr Salmon: I would comment on men who have sex with men, but it is fair to say that the blood service—and indeed many other screening services—aspire to offer an individualised service. But the question is about having the tools that allow you to individualise that risk. If we consider the CJD example, the Advisory Committee on Dangerous Pathogens is very clear that the further development of a blood test so that it could be used would be enormously helpful in that regard; that would allow an individualisation of risk and would certainly reduce the need for approaching the population on a rather crude population basis, with a group of haemophiliacs here, a group of people who have had certain types of surgery there and so on. But you do need the tools to be able to do that.

Professor Turner: I would add that an individualised risk assessment is an ideal. We would require the evidential basis, as my colleagues have said, on which to build those risk assessments. There are also, I think it is fair to say, practical problems and issues. For example, we have around 200 different categories of donor deferral criteria, and we will screen, say, about 7,500 blood donors per day across the United Kingdom. Of course, many of those sessions will be taking place in the community, in village halls or community centres, where sometimes privacy is not as contained as it can be in a custom-built donor centre. So there are practical problems to an individualised risk assessment for every specific donor.

Q35 David Tredinnick: Moving on from that, how many blood donors who are temporarily deferred actually return once the deferral has ended? Of those who do return, how quickly do they do so?

Dr MacLennan: About 30%, the current data suggests, do not return. I am sorry, what was the second part of your question?

Q36 David Tredinnick: Of those who do return, how quickly do they do so?

Dr MacLennan: I am sorry I do not have that data, but I could probably find that out for you.

Q37 David Tredinnick: You can write to us, okay. Finally, are your advisory bodies currently considering any changes to blood or organ donor selection policy? If they are, what are they, and when are these decisions likely to be made?

Dr MacLennan: Changes to blood and organ—

David Tredinnick: Are your organisations currently considering any changes to blood or organ donor selection policy? Are they proposing any changes? Is there anything out there that you are about to announce? Do you have any plans that we might want to be aware of?

Dr MacLennan: We are constantly looking at changing donor selection criteria. Examples of ones that are currently being implemented are that we have just announced a change to donor deferral for people who visited the French West Indies, because Chikungunya virus has suddenly appeared in the French West Indies and we did not have a deferral in that region. In fact, we constantly monitor where diseases are and the effectiveness of our travel deferrals.

As to other ones that we are about to implement, we are removing a donor deferral criteria for patients who are now on Tamoxifen for prophylactic purposes, whereas before they would have been deferred. We are also adding a new medication to the skin disease category for donors—a new medication that can potentially cause problems in recipients. We are also reviewing the entry on mental health problems to allow donors on some medications to donate, which will mean that we get more donors. We are also planning a

study to look at the risk around body piercing, particularly acupuncture, to see if we can change and improve the donor selection criteria on that. So we are constantly looking at new donor deferral criteria changes.

Q38 David Tredinnick: Finally, on that last point, do you mean more and more people are turning to acupuncture first, very often when they do not want to have drugs that they think might have side-effects, so they will try that system? What is your experience of it and what do your studies show?

Dr MacLennan: The main potential risk is infectious disease that could be carried by needles. At the moment there is not the evidence base to say that this is definitively safe. That is what we are going to be looking at.

Q39 David Tredinnick: But most of the acupuncturists now use throwaway needles; they are not re-used at all.

Dr MacLennan: Yes, absolutely. That is the sort of risk that we are going to look at, yes.

David Tredinnick: That is almost all of them; there is no risk. Thank you.

Q40 Jim Dowd: I want to look briefly at plasma products. Since 2004, we have used foreign-sourced, overseas-sourced, fresh frozen plasma as a vCJD risk reduction measure. Can I just ask first off are we sure that the stuff we are now using for those born after 1996, while minimising the risk of vCJD contamination, does not contain other harmful viruses, such as West Nile, for example?

Professor Turner: The United Kingdom started importing plasma for the manufacture of plasma products in 1999, as the speakers earlier this morning said. I believe that we started importing fresh frozen plasma—so clinical plasma products—for those born since 1 January 1996 in 2005. I think that was an MSBTO decision. MSBTO was the predecessor of SaBTO. The plasma is sourced, to my recollection, from other European countries which will have a lesser incidence, certainly, and therefore a presumed prevalence of sub-clinical variant CJD. They should all comply with the EU Blood Directive and therefore be applying similar standards to ourselves of donor selection and screening. The plasma is also treated with a compound called methylene blue, which will inactivate most, not all, bacteria and viruses. Finally, I do not think, since 2005, that we have seen any instances of transmission of infection by FFP, including that which is imported. [2]

Q41 Jim Dowd: Can I go on then? It is only used at the moment to treat those born after 1 January 1996, and UK-derived plasma is still used for those born before that. Why the difference? Why not just use the fresh frozen imported plasma for everybody?

[2] The witness later clarified that, "In summer of 2011 there was a transmission of hepatitis B (HBV) from a donor with very low level viraemia which was not picked up in the routine nucleic acid screening. The recipients of the red cells and FFP were infected."

Professor Turner: SaBTO looked at that issue—I am sorry I can't remember the date—in around July 2009, I think, but I will clarify that for the Committee, and then again more recently in 2012 and concluded that importation of FFP, clinical plasma, for all patients was not cost-effective by most yardsticks.[3] Clearly, there is a wide confidence interval on estimates because of the uncertainties around issues such as the prevalence and infectivity of variant CJD, but in the order of magnitude it was between, say, about £250,000 per quality-adjusted life year and several tens of millions per quality-adjusted life year.

Q42 Jim Dowd: That is quite a staggering difference. Is that because of the proportions of those being treated who were born after January 1996 compared with those before? Do we have any idea what the proportions might be?

Professor Turner: I cannot give you the precise figures, but obviously people born after 1 January 1996 are still very young, and what we tend to see in terms of overall blood usage is fairly high blood usage in neonates and then it drops very rapidly, and of course in children and young adults it is low. Then it builds as we gracefully age. So, proportionately speaking, a lot more clinical plasma is used in the older population.

Q43 Jim Dowd: So it would be pre-1996.

Professor Turner: Yes.

Q44 Jim Dowd: Both the Haemophilia Society and the British Committee for Standards in Haematology have suggested that we discontinue the use of cryoprecipitate and replace it with fibrinogen, which apparently is what everybody else in Europe does. We are the only country that continues with cryoprecipitate. Do you agree with that and, if not, why not?

Professor Turner: SaBTO looked at the issue of cryoprecipitate again in 2009 and was very concerned because, generally speaking, quite a lot of cryoprecipitate is still used in not well-founded clinical indications. That is a matter of concern. Nevertheless, there are well-founded clinical indications. SaBTO was certainly, in broad terms, in favour of us using fibrinogen concentrate. Unfortunately, at that stage, at that time, commercial fibrinogen concentrate was not licensed in the United Kingdom. Now, it has subsequently become licensed in the United Kingdom. My understanding is that it is licensed for patients with congenital hypofibrinogenemia, as we call it—an inherited disorder in which you do not produce enough fibrinogen—but not in what we call acquired hypofibrinogenemia. Your fibrinogen can fall very low, for example, if you have a major road traffic accident or you have major liver disease, for example. The vast majority—not all—of cryoprecipitate is used in those acquired circumstances. So, while individual doctors can prescribe fibrinogen concentrate off licence, it becomes then very difficult for an Advisory Committee to advise doctors to do that because that is going against the

[3] The witness later clarified that, SaBTO considered importation of clinical plasma (FFP) on 14 July, 15 July 2009, and 9 March 2012.

licensing of the product within this country. So there is a legal and regulatory issue in there.

Q45 Jim Dowd: So you are saying that because it is currently available perfectly legally and properly—

Professor Turner: Yes, yes.

Jim Dowd: —you could not advise anybody not to use it. You could not say, "Just use the fibrinogen instead."

Professor Turner: I personally could as a doctor, but it is very difficult for an advisory committee or, indeed, the Government to say, "Doctors, you should use this product off licence." You are right that the vast majority of European countries do use fibrinogen concentrate. I think, apart from us, there are one or two other countries like Estonia and Latvia that use cryoprecipitate, but I am afraid I am not familiar enough with their legal and regulatory environments to know what the differences are between their European setting and ours.

Jim Dowd: Thank you.

Q46 Stephen Metcalfe: Good morning. I want to talk a bit about viral inactivation and prion filtration reduction. The Haemophilia Society has told us that UK blood products do not currently undergo any viral inactivation. Is that accurate? If so, why?

Professor Turner: The plasma products that are imported do undergo virus inactivation, but they are commercially manufactured products. The vast majority of blood components do not undergo microbiological inactivation, apart from, as I described to your colleague, fresh frozen plasma, which is imported. There are currently no licensed pathogen inactivation systems that are applicable to red cell concentrates, which of course are the majority of the products that are used. There are two, to my knowledge, pathogen inactivation systems—potentially three—which are licensed on a European level for platelets. SaBTO has recently revisited pathogen inactivation for platelet concentrates, balancing that against current methodologies, which include, of course, intensive testing of donors by both serology and nucleic acid testing, and, in terms of bacteria, stringent cleaning of the donor arms and BacT/ALERT testing. That was reviewed in December, and I believe the minute and papers of that meeting will be published very soon.

Q47 Stephen Metcalfe: Originally your committee did approve the filtration.

Professor Turner: I am sorry, but I was talking about pathogen inactivation very specifically.

Q48 Stephen Metcalfe: Okay, but that process was approved, was it not, in 2009 by your committee, and then the recommendation in December was that it was no longer approved? Is that correct?

Professor Turner: No, that is prion filtration.

Q49 Stephen Metcalfe: I am getting confused, I am sorry. Help me out here.

Professor Turner: Pathogen inactivation will deal with microbiological agents—the viruses and bacteria, for example—but it will not deal with prions, which do not have a known nucleic acid component. In terms of prion filtration, if one goes back to 2006, there were two or three companies working on so-called prion filtration technologies. So that you understand, they are not really filters in the way that you and I might think of them as size filters; they are resin ligands, which have an affinity for the abnormal conformer and bind them. So they are affinity filters, as it were, rather than size filters. One of those two companies withdrew from a CE mark filter, but the other continued to develop its filter.

In 2006, SEAC—the Spongiform Encephalopathy Advisory Committee—and MSBTO expressed concern that the CE marking process, while clearly necessary for these kinds of devices, was not sufficient in terms of either demonstrating their efficacy in the real world of removing prions from red cell concentrates or, indeed, their safety, and they asked UK blood services to commission and carry out a number of independent studies. So a series of clinical studies were carried out by UK blood services—the so-called PRISM A study—which broadly showed that the filters were safe and were not causing any adverse impact to patients. There was a complex set of independent effectiveness assessments carried out, both a primary set using crude brain homogenates, and then a secondary set using various kinds of animal models. Those were carried out by the Health Protection Agency and by the Roslin Institute respectively. SaBTO reviewed the outcome of all of that data in December 2012 and on the basis of that data decided not to recommend a prion reduction.

Q50 Stephen Metcalfe: I am not sure if it is the report that came to that meeting—it has been redacted anyway—but you talk about the two studies, one being the hamster study and one being the sheep study, presumably.

Professor Turner: Yes.

Q51 Stephen Metcalfe: It says on here that the peer-reviewed journal information will be published in due course.

Professor Turner: Yes.

Q52 Stephen Metcalfe: So at that point it had not been published, presumably, when this was being drawn up. Was there a subsequent—

Professor Turner: Correct, and, fortunately—or unfortunately—quite a lot of the minutes are quite heavily redacted because of commercial confidentiality on the part of the company itself. If the Committee want to see the unredacted minutes and papers, my suggestion would be for you to request them from the Department of Health and from the SaBTO secretariat. I am aware that the independent hamster studies have been submitted for publication, but I do not believe they are published yet. The sheep studies, I am sure, will be submitted for publication in due course.

Q53 Stephen Metcalfe: When this decision was being made, was that information available?

Professor Turner: Yes.

Q54 Stephen Metcalfe: So you have seen it; it just has not been published.

Professor Turner: That is correct.

Q55 Stephen Metcalfe: I am going to attempt to put words in your mouth, so stop me if I get it wrong. I think what you are saying is that the system is safe but it was not deemed to be clinically effective in great enough numbers. Is that right?

Professor Turner: Yes.

Q56 Stephen Metcalfe: Was, therefore, the decision to change your opinion from three years earlier unanimous at that meeting?

Professor Turner: Yes.

Q57 Stephen Metcalfe: It was; thank you. That is useful and we look forward to having a look at the redacted minutes in due course.

Are there any other ways of removing prions from blood supply and also, presumably, from instruments and anywhere else that they may be found? Are there good systems or procedures in place to do that?

Professor Turner: I will not speak to surgical instruments because they are outwith my expertise, but, in broad terms, the kind of intensity of disinfection one would need to destroy the prion agent would destroy cellular material. So, from the perspective of blood components, there is no disinfection that will not destroy the product, which is why companies worked, quite rightly, on trying to remove the product rather than disinfect it.

Dr Salmon: I will have to speak for surgical instruments, though forgive me in that I do not pretend in any way to be an expert either. You will have received some evidence from

the decontamination science working group, and this summarises quite nicely the potential things that you can do to reduce prion infectivity. It perhaps should be remembered that, although a residual prion infectivity is extremely resistant to heat, actually heat does reduce it. But in terms of reducing that residue of infection, which is what represents the risk from a number of types of surgery, it has been made clear that, if the practice could be changed to keeping surgical instruments wet before they went through the washer disinfectors, this would represent progress. Of course, this would represent something of a sea change in the way work had been done, because, historically, to reduce the risk of more conventional infections to the staff, they had been encouraged to dry them out. So you are having a process change here.

As to the systems for detecting protein so that we can have a better idea of the efficacy of cleaning processes that are being developed, I understand there is potential for developing coatings for instruments, though I think that would have to be a long-term solution, and there are some novel detergents. You will recall hearing from Professor Collinge last time about one of those. Again, with all of these, as I understand it—and, as I say, I would counsel you to talk directly to experts in decontamination and sterile supplies if you want to pursue this—the problem is not so much in getting products that may work, or work to a degree, but getting them in a way that they can be introduced into what is in effect an industrial-scale process.

Stephen Metcalfe: Thank you very much.

Q58 Stephen Mosley: Dr Salmon, your advisory committee has recently considered the fact that not everybody who is at risk of CJD has been notified of that risk. When you were discussing it, you did decide that those people should not be notified of this risk. Could you explain how your committee reached that decision?

Dr Salmon: Yes, I can. As I say, one of the many things we will have gleaned from the earlier session is that bearing news to someone that they are at increased risk of vCJD for public health purposes is not a simple task. Although some people may be very sanguine about that information, for others it has a very difficult and destructive effect. As I say, we heard some very important testimony, I think, in that regard.

There are a number of difficulties in identifying the group of the multiply transfused—those who have received large numbers of transfusions—that are really even more extensive than those of identifying haemophiliacs. They are not by and large under single centres. They may have been multiply transfused for a variety of reasons. Much of the activities would have been done locally and so there is no easy, centralised record keeping that you could go to. Of course, because we are talking about a rather heterogeneous group of people in a rather heterogeneous set of circumstances, it is even more difficult to be certain of what the theoretical risk might be. I don't like this phrase "theoretical risk," and I noticed that some of the Haemophilia Society did not like it, but I can't think of a better one. When that was weighed up, a larger proportion of the committee felt that the disbenefits of pursuing that course of action would outweigh any benefits—not theoretical benefits—from preventing infection.

As I make clear, this was not a unanimous decision and there is an important minority of the scientists involved who thought that just to remove some of the risk from some of the

people whom you could identify more easily—in effect, that would have been people with certain haemoglobin disorders who do tend to be under centralised clinics—would have been worth doing. So we felt the only scientifically honest thing to do here was to convey both sides of the argument to the Department of Health, which, after all, has scientists in-house—the chief medical officer and the chief scientific adviser. Although we accept that this, in some ways, vitiates the usefulness of an expert committee, I suppose it at least does illustrate that some of those concerns that we somehow represent a monolith that just reflects back received wisdom is not in fact the case.

Q59 Stephen Mosley: In October last year the *British Medical Journal* published some research funded by the Department of Health that showed that one in 2,000 people tested positive for the abnormal prions. Those people are at risk, they have been tested and they have the abnormal prions. Should those people be notified that they are at risk?

Dr Salmon: If it was possible to establish who they were or if we had come to know of them by some other route, the answer would have been yes. The fact is, though, in terms of the construction of that study, the samples were absolutely unlinked from the information about who the individuals were, using techniques that were originally developed to do anonymous blood surveys at the start of the AIDS epidemic. It was done precisely because there would have been no treatments that could have been offered, and the implications of this advice are rather uncertain. Even if we felt that this might be a desirable thing to do, the way the study was set up intentionally leaves us in a position where it cannot be done.

Q60 Stephen Mosley: Okay. Moving on to something slightly different, it has been suggested to us that "at risk" individuals should be subject to post mortem examinations to determine the level of abnormal prions. Do you—and I am asking all three of you now—think that would be in the public interest? Would that be useful?

Dr Salmon: Perhaps I will start. I think this was the suggestion of Dr Sheila Bird, who is a very brilliant biostatistician and very passionate about public health causes. I do not think it is a terribly practical suggestion because I do think people expect a degree of autonomy about how they dispose of their bodies or how they dispose of the bodies of their relatives. I see no problem in encouraging that group of people to come forward for post mortem. That said, I think the gentleman who was giving evidence at the far end in the earlier session made a very telling point in that, if we could arrive at the point where we had a reliable blood test, that would probably represent a simpler and more efficient route to assessing the risk of this generalised group.

Professor Turner: This is not really a SaBTO issue, so I will give a personal view, and that is that I would strongly encourage such people to agree to a post mortem. But in terms of respect for the autonomy of people, for it to be compelled would for me personally be a step too far.

Dr MacLennan: I entirely concur. Again, this is a personal opinion, but I would not want to force a post mortem on people. To encourage that to happen would be the best route.

Dr Salmon: I might say this represents partly a personal issue but it was a reflection of the Spongiform Encephalopathy Advisory Committee at the time. We felt it was regrettable that an agreement was not able to be made with the coronial system and the coroners so that where people were going to have post mortems anyway the brain tissue could not be examined for evidence of prion diseases. Much as I have a great deal of confidence in the figures that are issued by the CJD Surveillance Unit for the characteristic forms of the disease, there does exist a scientific question to what extent there might be atypical forms, particularly in older populations, and this would have been a potential way to have got a handle on that. So, as I say, the fact that an agreement could not be reached with the coroners was very regrettable, and that was an observation that the Spongiform Encephalopathy Advisory Committee, whose responsibilities we have taken over in the ACDP, made at the time.

Q61 Stephen Mosley: Expanding on that a bit, we heard in the earlier session that some family members were sometimes prevented from doing their own testing or using other testing systems on people. From your own perspective, does that sound right, should that happen, or do you think people should be able to use their own testing methods and people outside the UK to do the tests if necessary?

Dr Salmon: Let's put it this way, and let me perhaps preface these remarks by saying that I am neither a select scientist nor a Government official. As I stated at the outset, I am a retired public health doctor. I do not altogether recognise the accounts of my colleagues in the CJD Surveillance Unit and the MRC Prion Unit from the evidence session you got before. I have always found them to be extremely conscientious and committed individuals, who have given their professional lifetime to addressing these diseases. In many ways, for that reason, they would be the people, if it were my choice, I would have chosen to have sent my specimens to.

One of the problems that you have—well, it is not a problem; it is a good thing—is that, mercifully, this remains, in terms of clinical diseases, a rare disease, and where you have a rare disease, if you wish to make progress, you do have to concentrate the resources. I am kind of saddened that this is somehow perceived as a dysfunctional monopoly. I don't see many other solutions. You could not have a great proliferation of units, and I would worry if this material that will bring an understanding to us was to be widely disseminated round the world to groups that, potentially, could be of very varying standing.

Q62 Chair: Just carrying on with the question of testing, you heard the exchange about a test that may be 70% sensitive. Are there any circumstances in which you think that such a test would be useful?

Dr Salmon: I certainly can think of some, but I might let the blood services go first, if only because they are much more mindful of the practical difficulties than I tend to be; but I will come back.

Professor Turner: Thank you, Dr Salmon. First of all, I would say that the colleagues in the Prion Unit are to be credited on the test that they have developed because the difficulty

of developing assays in this field should not be underestimated. These diseases are not like, as I said earlier, microbiological agents; they do not raise an immune response, and they do not have nucleic acids associated with them. So the normal approaches we take for HIV and hep B are not, for example, applicable in this kind of context.

Looking back a decade or so ago, there were probably—I don't know—a dozen or more different research groups and commercial companies working in this space. Now there are really only two or three research groups still working, of which the most advanced test by far is the Prion Unit assay. My personal view is that 70% sensitivity in clinical variant CJD is pretty good. Would I like 99%? Yes, I would, but that is as good as the test is at the present time, and certainly no other test currently has shown the ability to detect infectivity in the blood of people with patients with clinical variant CJD.

Professor Collinge's team have also just published on 20 January, I think, a study of US samples that showed no positives among 5,000. That gives a statistical false positive rate with 99% certainty of about 0.1%, so that is repeat reactive, which is about similar to that which we see—repeat reactivity—in other tests that we use. So I think the test has moved forward a long way.

SaBTO has not taken a view on the most recent data, so I will express a personal opinion, if I may. I would have thought that the next logical step would be some form of prevalence study. There are a number of issues that need to be considered. First, the tests obviously are research-based tests currently within the Prion Unit laboratories, and if you are going to test 25,000 or 50,000 individuals it will need to be brought into an operational high-throughput format to achieve that. We need to look at, and indeed the UK blood service is looking at, what we call confirmatory assays. These are other assays that work in a different way, which can be used specifically to test those individuals who come up positive to try and determine whether they are truly positive or false positive.

I think we need to give deep consideration to the issues which, Mr Mosley, you raised around how a prevalence study would be structured. Really, I think there are two options: either the donors to the study give fully-informed consent, traceability is retained, and if they are positive they are contacted and informed, in which case I am sure they would be managed as "at risk" for public health service purposes; or it is set up as an anonymised, unlinked and unimputable study, in which case we recognise that what we are looking for is prevalence in the general population and we will not be able to re-identify and go back to those specific individuals. I think ethical consideration has to be given to which of those two strategies is appropriate.

Q63 Chair: I can certainly see the ethical issues. I want to push you a little harder on why, with its availability, a test that, let us say, is 70% is not routinely used. I presume that a test that is closer to 100% is going to generate fewer false negatives and false positives than something that is lower down the spectrum. Am I right in saying that applying this test now would inevitably produce more samples that were subsequently deferred and, therefore, would have cost implications?

Professor Turner: If we accepted the sensitivity of 70%, that means that one may miss 30% of people who are infected but not showing up in the test. My personal view would

be that it would be nice if it was better, but at least you would pick up those 70% of individuals; so that would be good. The false positive rate—that is, what we call the specificity, the 5,000 normal US samples—looks quite good. We would certainly want to have in place confirmatory assays so that, first of all, we minimise the number of people we were wrongly telling they were positive, and, secondly, that, when we did approach a person to inform them that they were positive, we were very clear that that was a true result. Studies that we have done with blood donors show in broad general terms that, if they thought we had a very good test and that when we said they were positive they were positive and when we said they were negative they were negative, they would accept that as they accept testing for HIV and hep B and so on and so forth. If they felt it was a poor test, then there would be great concern among the donors that they were being tested in that way.

From a practical perspective, right at the moment, one of the significant issues for the Prion Unit assay test, of course, is that it is a very research, labour-intensive test. UK blood services test around 7,500 individuals a day, 2 million to 2.5 million a year. We could not apply that test as it is currently formatted into that context, and I think this is principally what Professor Collinge is referring to when he says he needs to try and get across that valley of death from a research-grade test into something that is manufactured by a test-making company to the kind of scale, standards and robotics and so on that you need for that magnitude of testing.

Dr Salmon: I am glad I let Marc go first because it is precisely some of these operational issues that I did not feel unduly confident to comment on. In terms of the test as it exists now, I certainly think there will be a great deal of scope for using it in a research context, as he suggests, either as a population prevalence study or, conceivably, on a sample of blood donors. The actual detail needs quite a bit of thinking through, but we are at the stage where we ought to be thinking about how we would do that. I notice that Public Health England have what, in a sense, amounts to a précis or almost a research proposal in their evidence. While I suspect it constitutes a bit of an advert, none the less I would commend the Committee members to have a look at it because I think it sets out rather nicely the sorts of things we could do.

Before I finish on this, the Department of Health seemed to be committed to this inasmuch as on page 2 of their evidence they mention that, "A blood test for vCJD may be advantageous for both health protection and possibly prevalence study purposes." Then, on page 4, if I can find it, in paragraph 63 they regard as a key issue maintaining a balance in the costs and benefits "of additional risk reduction" and the "appropriate definition and handling" of individuals defined as "at increased risk," both of which you would have thought were things that required a blood test. So I see the commitment there, but it takes a bit of decoding, and I suppose I would just express slight regret that a statement of support for developments of this nature, whoever makes them, was not a bit more explicit.

Q64 Chair: So you would like to see more action from the Government in, specifically, the Department of Health.

Dr Salmon: I think the Department of Health have to front a lot of these things. You may recall, as I mentioned before, I consider that they are possibly constrained rather by

sections of Government that are even higher than they are, but I think this is one area where they could usefully make a very explicit statement of intent, yes.

Q65 Chair: Is that agreed across the panel? I know, Dr Salmon, in your retired position, you are feeling more comfortable—

Dr Salmon: Exactly. I was about to make the point, Chair, that I am in a privileged position.

Professor Turner: I would say it is a shared responsibility now for UK blood services, Public Health England, the Department of Health and others to look at the most recent published data from Professor Collinge's group and consider whether it is practical to run a prevalence study.

Dr MacLennan: I have to say this is not my main area of expertise at all, but, going back to your question of whether a 70% sensitive test is worth implementing, I do not see that it is an issue because it is 70%, but obviously all of the other criteria would have to be addressed first to make sure that this is a useful test within the blood services that does not create too many false positives, as outlined by Marc.

Q66 Chair: So there is a lot more to be done, and it is not just in terms of the victims and their families that there are cost-benefits in getting tests in place that can deliver the kind of answers that you as clinicians would want.

Dr Salmon: I think that is a very fair summary, Chair.

Chair: Thank you very much for your evidence today.