HOUSE OF COMMONS

# Science and Technology Committee

## Oral evidence: Clinical trials transparency: follow-up, HC 139

Tuesday 29 October 2019

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Watch the meeting

Members present: Norman Lamb (Chair); Bill Grant; Darren Jones; Stephen Metcalfe; Graham Stringer; Martin Whitfield.

Questions 1 - 212

### Witnesses

I: Professor Jane Eddleston, Joint Group Medical Director, Manchester University NHS Foundation Trust; Professor Nigel Brunskill, Director of Research and Innovation, University Hospitals of Leicester NHS Trust; Mark Cranmer, Director, Joint Research and Enterprise Services, St George's, University of London and St George's University Hospitals NHS Foundation Trust; Professor Rupert Pearse, Clinical Director of Research and Development, Queen Mary University of London and Barts Health NHS Trust; and Dr Síle Lane, Head of International Campaigns and Policy, Sense about Science.

II: Dr Martin O'Kane, Head of Clinical Trials Unit, Medicines and Healthcare products Regulatory Agency; Dr Fiona Godlee, Editor in Chief, *British Medical Journal*; Juliet Tizzard, Director of Policy, Health Research Authority; and Professor Sir Terence Stephenson, Chair, Health Research Authority.

Written evidence from witnesses:

– Sense about Science

# Examination of witnesses

Witnesses: Professor Eddleston, Professor Brunskill, Mark Cranmer, Professor Pearse and Dr Lane.

Q1 **Chair:** Welcome, all of you. Thank you very much for coming along this morning. Can we start by doing very quick introductions?

***Professor Pearse:*** Good morning. My name is Rupert Pearse. I am the clinical director for research and development at Queen Mary University of London and Barts Health NHS Trust.

***Professor Eddleston:*** Good morning. I am Jane Eddleston. I am the joint group medical director for Manchester University NHS Foundation Trust.

***Mark Cranmer:*** Good morning. I am Mark Cranmer, director of joint research and enterprise services at St George's University and St George's NHS Trust.

***Professor Brunskill:*** Good morning. I am Nigel Brunskill. I am a renal physician and director of research and innovation at University Hospitals of Leicester NHS Trust.

***Dr Lane:*** Good morning. I am Síle Lane. I am head of international campaigns and policy at the charity Sense about Science. We run the AllTrials campaign for clinical trials transparency.

**Chair:** You are just back from a rather interesting and traumatic visit to Santiago, I hear.

***Dr Lane:*** It was interesting, yes. I am back safely.

Q2 **Chair:** I am glad you are back safely. Thank you all for being here.

I will start with some questions for you, Dr Lane. In your opinion, what were the main reasons for the non-compliance we saw back in January when we wrote to universities and hospital trusts? Incidentally, I am conscious that there is a significant gap between commercial organisations—drug companies—and NHS trusts and universities. We now have pretty much full compliance among drug companies for reporting trials, but not among universities and hospital trusts. What do you think are the main reasons for that?

***Dr Lane:*** Large companies and large commercial sponsors are doing very well. That showed the gap back to where the non-commercial sponsors were. We saw in January that trials sponsored by UK universities were only about 60% compliant and those from NHS trusts were around 35% compliant, although both those figures have progressed nicely. There has been a good increase in both of them now.

It became apparent from the institutes' replies to the letters that the Committee, we at AllTrials and others sent to them, when they asked for

help, raised barriers that they face when trying to report and made excuses for why they had not reported already, that there was a very broad lack of awareness of their obligations—legal, ethical and scientific.

Q3 **Chair:** Both at the institution level and at the individual research level?

***Dr Lane:*** Absolutely. At the institution level, the problem was that, broadly, there was no one person at an institution who was taking responsibility and control for the reporting rates and record of their institution. Dozens of them wrote back to us saying, "We don't sponsor that trial. It says on the register that we do, but that shouldn't be ours," or, "This trial never actually started," or, "This trial ended early, and there shouldn't be full results for it." There were all these things that nobody in the institution was aware of until the letters you sent, when you flagged all of it up to them, suddenly made people aware of them. There wasn't anybody there in control. There has been lack of control.

Q4 **Chair:** Do you think there was lack of recognition of why it is important to register everything and to report everything at the end? Our report made the point that there is a risk to human health from non-reporting, because it gives a distorted picture of the research undertaken. Do you think that there had not been full recognition of the importance of that?

***Dr Lane:*** Yes.

**Chair:** Apart from the fact that it is public money.

***Dr Lane:*** Yes, of course. I know you did not say this, but it would not be fair to say that these researchers and institutes did not think this was important, and were blasé about it and dismissed the scientific, ethical and moral reasons for doing it. They just had not made it part of their day-to-day work. It was not part of the process of running a piece of research. It was not part of the process of ensuring that you fulfil your funders' terms and conditions for funding, although it should have been. It was not part of what they did day to day.

Then, when they suddenly became aware that they had to do it, it was difficult. They did not know how to start, because they had not tried to do it before and were suddenly coming up against barriers that had not been identified. It is important to say that in doing all of this—we must congratulate the Committee on making it happen—we have been able to identify some real barriers and problems.

Q5 **Chair:** Talk us through the barriers quickly.

***Dr Lane:*** Researchers can only interact directly with their records on the European database when adding results to it. If they need to do anything else to their public information, they have to go through the national competent authority. In this country, that is the MHRA, of course. They were finding a bit of a backlog there. There were problems getting their information on the public record updated, which made them seem non-compliant.

Q6 **Chair:** Were there problems correcting errors as well, perhaps?

***Dr Lane:*** Correcting errors and changing dates—just making sure that everything was accurate. The obligations on researchers are not merely to report results at the end of a trial, but to ensure that their information on the register is accurate and up to date. That is part of the whole package. Some of them were finding it impossible or very difficult to do that because of the backlog and, possibly, lack of capacity in the national competent authority, the MHRA. There are also some real problems with the European register itself.

Q7 **Chair:** We will be talking to the MHRA later. Do you think that those problems have now been resolved, or do we need to question the MHRA on that?

***Dr Lane:*** I would like to hear what the MHRA has to say. We understand that they have put some more capacity into it and have caught up a lot. Of course, if it happens again for some reason that a lot of researchers decide that they need to publish their results going forward from now—we hope they will, and we will make sure that happens—we need to make sure that there is the ongoing capacity in the MHRA so that can take place.

Q8 **Chair:** Are there other barriers?

***Dr Lane:*** There are some real problems with the database itself, which the EMA administers. For example, if a clinical trial is given approval to begin by the HRA and the MHRA here and is added to the register, but it does not begin for some reason—lack of funding, a change in the research strategy at the institution, or whatever—there is no way of marking it as not having begun.

Q9 **Chair:** It just looks like a trial that has not been reported.

***Dr Lane:*** Therefore, it looks like it is overdue, and it is a stain on the institute's record.

Q10 **Chair:** Is this an administrative thing that the EMA could sort out or does it require some European legislation, which would take years?

***Dr Lane:*** I do not know the answer to that. We have asked, and they are aware of the problem, but I do not know what they are going to do about it. As we know, the EMA is building a new database right now, which will become live when the new European clinical trials regulation becomes the law, which we now expect in 2020. I do not know whether that is going to be an issue going forward in the new database.

Q11 **Chair:** Presumably, you have lobbied them to sort this out.

***Dr Lane:*** Of course. We have written to them a number of times. Some researchers have been able to find a workaround—I am looking at my colleague Nick, who is behind us—that may be useful going forward, but it is a workaround.

Q12 **Chair:** We ought to be making it as simple as possible to comply.

***Dr Lane:*** It is part of getting researchers to do it and making sure that everybody can comply. It is not just the push to do it but removing the barriers and making it as easy as possible. Yes, that will need to change.

Q13 **Chair:** Are there any other barriers? Have we covered the key things?

***Dr Lane:*** We have covered the barriers. As I alluded to at the beginning, researchers and sponsors are still a little bit unsure about their obligations and so on. The bottom line is that institutes should have 100% of their trials reported on the register. If they do not, it is their own fault for not keeping their registry information up to date and accurate, or the MHRA's or the EMA's fault for not doing what is needed to keep the registry information up to date or accurate, or the institution's fault for not reporting its results.

Q14 **Chair:** Given the importance of this, provided that we have a system that works properly and is easy to use for researchers and institutions, should there be consequences for the failure to comply?

***Dr Lane:*** Yes, there should. I think that is a good idea. They should be complying. These are the rules in the EU, and there is an overriding ethical and moral obligation on researchers and clinical trial sponsors to do it. We think that it is a good idea that there be sanctions. There are two parts of it, aren't there? In practice, do sanctions for non-compliance work? In this particular case, the organisations, the international bodies like the FDA in the US, that have the power to levy financial fines for non-compliance have not done it yet.

Q15 **Chair:** They never do, do they?

***Dr Lane:*** We have not seen it in practice, so we do not have evidence of whether it works.

Q16 **Chair:** Do you have a view on the sorts of sanction that would be most effective?

***Dr Lane:*** We have seen large global funders—non-governmental funders like the Wellcome Trust, the MRC, the Bill & Melinda Gates Foundation, Médecins Sans Frontières and so on—bring in new policies that say that, when a researcher applies for new funds to run new research, the funders will look at the researcher's past record in reporting results.

Q17 **Chair:** Should UKRI be doing that?

***Dr Lane:*** Yes, I think so.

Q18 **Chair:** Has anything else emerged since January as an issue that needs to be addressed, or are the issues still primarily the same as they were then?

***Dr Lane:*** They are probably still the same as they were then. We have really felt the lack of a forum for sharing best practice and learnings

around this. As we know, some institutes have done really well. They have put in place new processes and systems for reminding their researchers of their obligations and so on. That is just a number of them. There is not really a forum to share, although we think that HRA has taken its role and responsibility seriously and is looking to set itself up as a forum for sharing learnings. That will be a really important thing to do.

Q19 **Chair:** A forum for sharing, raising awareness and training.

***Dr Lane:*** Yes.

Q20 **Chair:** Earlier, you made the point that lots of institutions had come to you to ask for advice.

***Dr Lane:*** That's right.

Q21 **Chair:** That suggests a gap in the market. Are you suggesting the HRA as the obvious body to lead and perform that role?

***Dr Lane:*** It could be. That is certainly the case for sharing learnings and setting and sharing best practices. When it comes to literally training people to use the EudraCT—the EMA database—perhaps that is a role for the EMA, but I think the HRA is in a good place to be the forum for sharing best practice, which is what people often ask AllTrials to be.

Q22 **Chair:** Presumably, it ought to be part of the training of any researcher that this is a fundamental part of the research you undertake.

***Dr Lane:*** What seems to work for institutes that are doing well now is that there is one person, or a couple of people—a small team—within the institute who know how to do this and have broad oversight of all the clinical trials and pieces of research going on.

Q23 **Chair:** There should at least be training of researchers in the fundamental importance of this happening.

***Dr Lane:*** There you go. It is a two-stage thing. It is knowing that you have to do it, that it is part of your research cycle and you have to spend some of your funds on doing it, and there is no excuse for not finding the time, the space and the resource to report and then having someone in the institute who has the capacity, capability and technical knowledge of using the database to be able to do it properly.

Q24 **Chair:** Are you confident that we are partway to cracking this?

***Dr Lane:*** I think we are. The UK is still far ahead of the pack. The letters that the Committee, AllTrials and others sent were successful in that they increased reporting rates among universities and NHS trusts, so we see that that works. We saw that it makes institutions conscious, aware of their obligations and of what this is going to take, in a way that they never were before. That is another way of cracking it.

Q25 **Martin Whitfield:** Dr Lane, you talked about almost identifying a specialism in reporting. Do you think that we are reaching the stage, or

are at the start of the stage, where the skill of reporting and disclosure has the potential to become a self-standing job, profession or skill that is part of teams that are doing research, so that confidence can be given that, in essence, you have someone who is almost independent of the trial, but responsible for the reporting? We could then have confidence in the reporting being accurate because of their specialism.

***Dr Lane:*** If that is what would give research groups confidence that they would be able to do that at the end of their clinical trial or piece of research, we could ask them. I am not sure. What I would like to underline is that what seems to work is it being someone's job in an institute to ensure that it happens. It is also everybody's responsibility to ensure that it happens. It is the researcher's responsibility to make sure that, before the beginning of the clinical trial, they know what they are going to have to produce at the end to be able to report fully. It is still the job and responsibility of the person who is running the research day to day.

Q26 **Martin Whitfield:** You are still satisfied that that skill rests at a research individual's level, irrespective of the subject of research. It is an additional skill.

***Dr Lane:*** There needs to be knowledge and awareness of it. You must make sure that you are prepared to do it at the end and that you have the right information that you need to report at the end, even if it is somebody else who actually interacts with the database.

Q27 **Darren Jones:** I want to flesh out the question of sharing best practice. Could our university colleagues here give us some examples of the networks you might use to collaborate with other universities in sharing best practice on this issue?

***Professor Brunskill:*** I can give you a concrete example. I am talking from the NHS perspective, rather than from the university perspective. One of the difficulties is the lack of a senior forum for people who are senior leaders in research, innovation or development in NHS trusts to get together to chew the fat about problems and talk through potential solutions.

About two years ago, a group called UKRD leaders was established. It is the UK R&D leaders group, of which I am a member. We now provide a forum for senior discussion of just that kind of issue. We have picked up one or two different workstreams. It seems to me that this might be something we ought to think about. That would be one way of trying to share best practice.

Q28 **Darren Jones:** Are the rest of the panel part of the UK research leaders group?

***Professor Eddleston:*** No.

***Mark Cranmer:*** No.

***Professor Pearse:*** No.

Q29 **Darren Jones:** Which groups do you use?

***Professor Pearse:*** There are some informal groups, but there are no go-to forums for very senior R&D managers for clinical R&D. There is an R&D managers forum for research governance specialists that my colleagues are part of, and they have certainly shared some of our learning through that forum. It is fair to say that we are quite disconnected in terms of sharing experience. When I meet colleagues in other forums who happen to be R&D directors, there is a lot of sharing of anguish and particular challenges of the job, which are manifold, but I do not think that there is a formal go-to place for that.

***Professor Eddleston:*** We have an R&D group in Shelford where the research clinical directors meet. Some good practice has been shared at that level.

Q30 **Darren Jones:** An internal one.

***Mark Cranmer:*** There are operational groups. On the university side, there is the Association of Research Managers and Administrators. On the NHS side, there is the NHS R&D Forum. They are more for the operational level, rather than the director level.

Q31 **Darren Jones:** I do not understand the difference between the need for senior and the need for operational. Why do there need to be separate networks for both if we already have an NHS research and development forum? Is there a need for a separate network? Could the existing ones not do the work?

***Professor Pearse:*** In my view, a well-functioning R&D department will have experts in governance, which is a very highly qualified and specialist role. It will also have clinical researchers working with that team to help it to liaise with clinical researchers who are perhaps less familiar with the rules and help them to resolve areas where there is a bit of tension. There are all sorts of things that come up all the time. Without that joint, more strategic role of a clinical director alongside the R&D manager specialist, you have a less well-functioning system.

***Professor Eddleston:*** I concur with Rupert. It is important for any sponsoring organisation to have that infrastructure, which guides its researchers and checks its governance. It needs to be an integral part of the sponsoring function.

***Professor Brunskill:*** A few moments ago, my colleague answered a question about where this function should sit and whether driving the clinical trial reporting is a research team function. It is probably not a research team function. It is a central function in the organisation, to which the researchers can refer for advice. It is a very specialised area. The research governance landscape is extremely crowded, and it

changes. To keep on top of that, you need one team that really knows what it is doing.

Q32 **Darren Jones:** Where do you go to find this information? Is it easy for universities or other organisations to ask someone? Do you just google it? How do you find the information? For example, in some of the evidence we have had, the National Institute for Health Research clinical research network was mentioned, but that has not been mentioned once today. Where do you find reliable sources of advice on where to do this work?

***Professor Eddleston:*** For this particular topic—uploading on to the European database—my teams have been going directly to the European database or to the MHRA to ask for advice.

Q33 **Chair:** Have they been helpful?

***Professor Eddleston:*** I think they have. I agree with Dr Lane that sometimes there has been a time lag. Sometimes, they may not have come up against some of the questions before and have not been able to give us solid advice. For instance, if you have a multinational, multi-centre trial that is also done outside Europe, when is the termination of that trial and how do you physically upload the reporting? Do you upload your bit, or do you have to wait for all of the multinational trial to finish? Different parts of the world may recruit at different timeframes. There are definitely some complexities that make completion of the database slightly more difficult than you might imagine.

Q34 **Darren Jones:** Does anyone want to add anything to that point?

***Professor Brunskill:*** I was not quite sure whether your question was driving at how we know that we have to report clinical trials in this way.

Q35 **Darren Jones:** It was about how you know where to go to share best practice.

***Professor Brunskill:*** I see. That's fine. I think we have covered that.

**Darren Jones:** From the answers today and the evidence we have heard, it looks like there are a few bits and bobs, but nothing that is really the go-to place, and the advice you might get is not always helpful in pointing you in the right direction. Clearly, something needs to improve. My last question, therefore, is, what do you think needs to happen for us to get to the position where we have a proper, functioning network for sharing best practice that people know exists? Is that something that requires central Government action, or is it something that you guys can organise? Does it need incentives or sanctions? What do we need to do?

***Professor Pearse:*** There is an awful lot that needs to happen. This conversation has centred around the EudraCT database for the registration and reporting of drug trials, but that represents only one third of the clinical trials we are worried about. Some of those clinical

trials are much higher risk for patients taking part than some of the drug trials we are focused on reporting today.

Q36 **Chair:** I understand that the reporting on ClinicalTrials.gov—the US one—is much worse.

***Professor Pearse:*** It is very complicated, and the quality overall is incredibly variable, both in the United States and in the UK, with the UK databases. Different countries each have their own reporting databases, which can make it complicated for international trials.

Q37 **Chair:** Do you think there ought to be a system whereby you can just report once and it gets shared with all the relevant international registers?

***Professor Pearse:*** That would make it a lot easier. I am slightly disappointed to hear words like "censure" and words that imply punishing individuals and organisations being used a lot in these conversations, and words like "incentivise", "facilitate" and "support" being used less.

Q38 **Chair:** Can I pick you up on that? First, do we all agree that there should be 100% reporting of everything?

***Professor Eddleston:*** Yes.

***Mark Cranmer:*** Yes.

***Professor Brunskill:*** Yes.

***Professor Pearse:*** Yes.

Q39 **Chair:** If there isn't—if an institution is taking public money and not reporting—doesn't that require some consequences?

***Professor Pearse:*** The analogy I would give is this. I park outside my house, and sometimes I make what seems to me a trivial infraction and get a very expensive parking ticket on my car for something that looks to me minor. In a sensible world, you could have a conversation and fix it.

Q40 **Chair:** You sound a bit bitter and twisted about this.

***Professor Pearse:*** It is incredibly hard work. We have managed to achieve 100% reporting for Queen Mary University of London. We have only managed to achieve that through the very hard work of one individual in my department, Marie-Claire Good, supported by her line manager, Mays Jawad, who is with me today. They have been working at this for four years.

In the last 18 months, we have swung in behind them as clinical directors to search the internet for published papers that were not reported on the database. They were already open access and searchable on the internet, but, technically, they were not reported. We have managed to approach individual researchers to explain to them the importance of reporting. Your letter has been incredibly helpful in that respect, because it has

allowed us to show that this is a serious issue, but it has involved a lot of hard work. It has not been easy.

Q41 **Chair:** But you have taken it seriously. Some others have not. Some others are still on 0%.

***Professor Pearse:*** I cannot speak for why some centres are on 0% and what challenges they may have. For example, in our partner organisation, Barts Health, we are at 88% at the moment. We have five trials that we cannot register. Four of those relate to individuals who have left the organisation, two of whom retired many years ago. We believe that the trials never took place, but proving it is very difficult. To be punished, censured or anything like that in that context seems inappropriate.

Q42 **Darren Jones:** Are there any other answers to the question about how we get to the right place?

***Professor Eddleston:*** It needs to be multi-layered, doesn't it? The regulators need a responsibility. Then, as individual sponsors, we need a responsibility.

I concur with what Rupert said about ease. On the database, it looks like Manchester University foundation trust is at 34%, but in actual fact we are not. If you take into account the trials that terminated early, we are up at nearly 80%. The database itself has problems in interacting with the sponsors.

There is definitely a need for the regulators to play a role and for the European database to have changes made to it. If there was only a single upload required, it would be so much easier. If it managed to fit into the statistical analysis programme that was set for that particular study, it would probably be even more valuable. It is also important for the sponsor to fulfil their duties as a sponsor and to transmit that to their clinical staff.

***Mark Cranmer:*** There are multiple issues, internal and external. What has been lacking at St George's is an internal system where we follow up and remind people. Very recently, in the last week or so, we have gone from 0% to 55%.

Q43 **Chair:** Does that have anything to do with your appearance at the Committee today?

***Mark Cranmer:*** The Committee shone a spotlight on us, but we started to act on this last March. We followed up with all our chief investigators. Unfortunately, no one responded. My team are completing the reporting, as far as they can, and we are asking the chief investigator to finish. We are on 55% now. Within the next two weeks, we should be on 91%. There is one trial where we are awaiting MHRA guidance, so we hope to be on 100% very soon. We are totally committed to clinical trial transparency, but we have fallen short of our own standards.

Q44 **Chair:** Is that for the university, the trust or both?

***Mark Cranmer:*** For both. For the university, we are now on 55%. We have posted all the results. It takes some time for that to show on the system. For the trust, we are now on 100%.

Q45 **Darren Jones:** We have deviated from my question to defence arguments. For the sake of equality, would you like to have the last shot, Professor Brunskill, before I finish my questioning?

***Professor Brunskill:*** I completely agree that this needs to be a streamlined process that is built into what is already quite a stringent reporting requirement at the end of clinical trials. There is already a necessity to report to MHRA and HRA at the end of clinical trials. We need to try to build this into a single system, so that researchers and teams need to send only one set of reports, which are then redirected to the appropriate authorities. It is very complicated for people to keep track of the system as it currently is.

I would like to make a comment about how you incentivise organisations to do this. I understand why there might be a feeling that some kind of sanction is required. Maybe it is true that it should be in some cases. My experience of dealing with researchers is that, if you try to push them around, they will just say, "I'm not doing this any more."

Q46 **Chair:** Well, they shouldn't have public money.

***Professor Brunskill:*** I agree, but they will.

Q47 **Chair:** That is a ridiculous argument, surely.

***Professor Brunskill:*** No, because we are reliant—

Q48 **Chair:** I am sure it is a human instinct to say, "I don't want to be pushed around." But can we not all agree that, if you streamline the system, and you have single reporting and a system that allows for the sorting out of trials that were never started and so forth, once it is simple to do and easy to comply with, there should be a sanction if you do not comply?

***Professor Brunskill:*** I agree with that. If you simplify it, that is fine, but there is a risk that NHS researchers will walk away from it if you make it too difficult for them.

Q49 **Chair:** I totally endorse the idea of simplified reporting, but this is public money, and we have already had evidence that human health is put at risk by non-reporting. I think there is a culture that hitherto has not regarded this as serious enough.

***Professor Brunskill:*** Yes. My point is not that people should not be encouraged to do it. It is about how you get to the position you want to be in, and whether you do it by sanctioning people or by encouraging and supporting them. I would recommend the latter.

***Professor Pearse:*** I agree with that point. It does not affect the agreement that we should have 100% reporting and that that is important. The clinical investigators who lead these studies often do a lot of that work in their own time. They are often innovative people pursuing an entrepreneurial idea to try to do something that matters. They often feel very stifled by a very regulated environment, and it does not take much to put them off.

We need to be careful about that, because it takes a very long time to develop these people. As a country, we invest huge amounts of money in developing them. We need to be careful not to disincentivise them, while getting them to do the right thing.

Q50 **Chair:** All I would say is that this Committee has been confronted by a pretty woeful system where reporting is clearly hard and there are delays and backlogs among the regulators. Performance against a legal requirement to report is woeful. What do you expect Parliament to conclude, other than that something needs to change? The idea of gentle encouragement seems to me not to have worked hitherto until one tries to name and shame and expose unacceptable failure to report.

***Professor Pearse:*** I saw your letter as gentle encouragement, and it was very helpful.

Q51 **Chair:** It is all we can do.

***Professor Pearse:*** Passing that letter on to our investigators allowed us to show that it was not just us having another moan about this week's issue but that it was being raised at a very high level.

**Chair:** It does not necessarily solve it in the longer term. It was a one-off; we cannot write letters every few months just to check that people are complying. It is not really our role.

Q52 **Graham Stringer:** Is there any difference in the willingness of researchers to report positive results as opposed to non-conclusive or negative results?

***Professor Pearse:*** In my experience, it is not so much about positive versus negative. A well-designed clinical trial on an important question cannot be negative because it gives you an answer you need to know. That is quite important, because in a lot of our research we are trying to prove things that are not needed as well as things that are. That is one area.

It is much more likely in research that did not finish. It was difficult to deliver the research; we could not recruit enough patients; the evidence base was superseded; or things moved on and the trial became obsolete. Those kinds of trials are more frequently unreported.

**Chair:** Clearly, there ought to be a basis for getting rid of those rather than it being a stain on the reputation of the organisation. I totally take

that.

Q53 **Bill Grant:** Nigel, if we can put the carrots and sticks to the side for a moment, University Hospitals of Leicester Trust has seen a massive improvement in reporting; I think it is 100%. Could you share with the Committee what processes you have installed or policies you have adopted to achieve that positive turnaround?

***Professor Brunskill:*** I can. The first was the letter that we received. When I saw that letter, I thought, "Oh, my goodness, look at that." There is nothing like being on 0% to focus people's attention. I am not going to rehearse the argument we have just had, but it is quite an important stimulus to action.

The next response was to get my team together and say, "What are we going to do to sort this out?" We had a brain-storming session about what needed to be done, and then we went away and did it. I supported my team to do that; I freed up time to make sure they had the wherewithal to deliver what was necessary. As they have been through that process, they have come across the difficulties and challenges that my colleague outlined very eloquently just now and in her report. We found our way through that. I think that my team are now experts at this—I am not—and can provide advice.

Q54 **Chair:** These are very disturbing figures. You described your reaction to the letter, but quite a lot of institutions did not reply at all.

***Professor Brunskill:*** I cannot answer for them. Obviously, they have a different mindset and you would have to ask them about that, but I can tell you that in my organisation it was a bit of a mind-blowing experience when we saw that.

Q55 **Bill Grant:** The Committee understood that one of the reasons for poor reporting was that the burden fell on the shoulders of the chief investigator. That role is still there, but I sense it is supported by other triggers and reminders.

***Professor Brunskill:*** That is exactly right. I have in front of me a new standard operating procedure that we have put in place since then. That has been ratified and disseminated. It clearly spells out the responsibilities of the chief investigator and those of the sponsor in supporting the chief investigator to deliver those responsibilities. That is what we have done internally. We share our SOPs with the University of Leicester, so we try to do all the same things together.

Q56 **Bill Grant:** Sometimes in organisations a policy was set in a previous life and placed somewhere. How do you keep momentum going? How does that continue? Will it still be as positive two years from now, and will you review that policy from time to time?

***Professor Brunskill:*** We have a system where we review all our clinical trials through our operational meetings. We will now build into that

operational system monitoring compliance with this particular metric, because we were not doing it before and now we will.

Q57 **Bill Grant:** Rupert, Professor Bailey of Queen Mary University indicated that the processes had been updated at that facility. Are you able to share with us something similar to what Nigel has achieved?

***Professor Pearse:*** It is a similar process. I think we were already working on it before we got the letter, so that gave us a lot of additional momentum. A lot of this problem is about clearing the very long backlog, so that we can get on with being fully compliant moving forward. I see those as two slightly different challenges. Where your letter was helpful was in clearing the backlog.

Moving forward, in a similar way to Leicester, we have made it a requirement of allowing us to sponsor a new study that any outstanding studies are reported before we will offer a sponsorship to an investigator. That pretty much focuses their mind. A typical investigator might be doing one or two randomised trials at a time. It could be three, four or five years since the last time they registered something. If the process is very clunky and not very user-friendly, it is hard for them to do it, so support there is an essential factor.

Q58 **Bill Grant:** Nigel and Rupert, you have come a long way and you are obviously well satisfied about where you are on that particular journey. On that journey, was there resistance or barriers that you had to overcome? You are imposing change; you are imposing compliance to existing regulations. What barriers or obstacles did you find? Are you happy to share that with the Committee?

***Professor Pearse:*** The database has come up again and again. I do not need to reiterate that, but battling with that and the support for it is a worry because, moving forward, I see us dealing with a whole load of different databases and that becoming even more complicated and confused. That is something the Committee needs to keep an eye on.

Simple hard work and taking it seriously at an organisational level is something we got right, but there are some investigators who, frankly, need to take the issue much more seriously than they do. I am not sure there is a more polite way of saying that.

Q59 **Chair:** Can you expand that? Tell us which regulators you have concerns about.

***Professor Pearse:*** Getting the EudraCT database changed via MHRA and the European Medicines Agency is the difficult thing. As Jane alluded to, timelines are often very slow. We have an online status and a real status, as St George's does, and we have to keep track of those two things to make sure about what is coming down the pipe at us. That is much more complicated than it needs to be.

Q60 **Chair:** How long is the delay between registering and it appearing on the

site?

***Professor Pearse:*** It varies, and often the problems happen around where the database simply does not allow you to put in data that you think as an investigator the public need to have. The database does not facilitate certain trial designs, for example. If it is a straightforward entry, it might be a couple of weeks, but if it is a complicated entry, it could be many weeks or months.

Q61 **Bill Grant:** Nigel, do you have similar challenges or barriers?

***Professor Brunskill:*** Before I came here today, I asked my research operations manager to list what she thought were the barriers. I am not going to go through all of them, but her No. 1 was the EudraCT back-end database. She has had to interact with a number of investigators to get information updated. Her feedback is that it takes four to six hours to perform that particular task. That is the experience we have had.

There have been other things, not idiosyncratic but maybe unusual. A group of researchers moved from our organisation to another one. Sponsorship transferred from our organisation to the new organisation, but it was very difficult to update the European database accordingly. It took a long time to get that to happen. It happened eventually, but it was quite time-consuming.

Where there were historical trials and investigators had moved away, retired or, in one case, even deceased, it was very difficult to get control of the record and update it, because retired people may not be particularly motivated to do it any more. Somehow, the host organisation has to take control of it again.

Predominantly, there were difficulties around the database. One or two investigators need to be chased quite hard for that, but again that is a sponsor responsibility. We know who they are and what we have to do to try to get them on side. Those are the main things.

Q62 **Bill Grant:** I see two common concerns. Feel free to chip in. For me, the logical question is: who or what organisation should be listening to you and implementing the changes that you appear to require?

***Professor Pearse:*** It has to be the Health Research Authority because the MHRA covers only drug trials. I am afraid it has to be the HRA. I do not wish to drop them in it.

Q63 **Bill Grant:** Please do, because we need to try to drive these changes.

***Professor Pearse:*** We have to work with them afterwards.

Q64 **Bill Grant:** You have come along the road and it is only fair that somebody else helps you continue that journey. If they block it, for want of a better word, whether it is an individual or organisation, thank you for identifying them. They should be listening to you and taking your concerns forward.

***Professor Pearse:*** I would add that the sponsors and the groups we represent need to take that seriously. We all do. All of us here take that responsibility very seriously, but the HRA will say that the sponsors need to as well. I agree.

Q65 **Bill Grant:** There are some nodding heads. Can we get Nigel and Rupert off the hook?

***Professor Eddleston:*** We have nine hospitals in our group. We have some very specialised hospitals; we have a children's specialist hospital, an obstetrics and neonatal hospital and an eye hospital. The design of some of those studies is very complicated, as Rupert alluded to earlier. To be able to lift some of those into the European database is incredibly difficult. Many of them are multinational and incorporate sites outside Europe, so it is very difficult.

Q66 **Bill Grant:** It is a common thread.

***Professor Eddleston:*** It is a common thread. I know that our own performance looks poor. It is not as poor as it looks on the database, as I mentioned before. A year ago, as executive medical director I took over responsibility for R&I. We were aware of our performance. We had just merged with another hospital, University Hospital of South Manchester, that had a large number of studies. We then had to rebuild all of our CTIP group. As Nigel said, it is a specialist job in our sponsoring function to uplift to that database, so we had to rebuild capacity to start to put the data on.

For the older studies, pre-2014, there has been a huge amount of difficulty because some people have retired; some researchers are, unfortunately, no longer with us at all. Trying to get that data has been incredibly difficult for the teams. If you look at our own performance, we are in the process of uploading another 10 studies. That may well take several months because some of it is complicated data, and I can see that we will be going back and forth, asking how to deal with a particular paediatric study, for instance, or how we can statistically put that into the database. Our statisticians have some concerns themselves about how we report, and the value of the way we are being asked to report to the database.

***Professor Pearse:*** I do not see this mentioned in any of the documents I have been reading: is the Committee aware that the research excellence framework will not credit any paper that a university wishes to submit to the Higher Education Funding Council if it has not been open access published within three months of being accepted—not published by a journal but accepted for publication by a journal? Most universities have online repositories where they put a non-copyrighted version of a scientific report in the public domain before that happens.

This is not an isolated discussion about EudraCT databases and so on; it is part of a wider culture that we have to get research into the public

domain, and it is part of our job to do that. The culture is changing very much, but the functionality of the systems that make it quick and easy to do that is lagging behind.

***Dr Lane:*** It might be useful to distinguish a little bit between the roles of MHRA and HRA.

Q67 **Chair:** That would be very helpful.

***Dr Lane:*** Do correct me, but we are talking about the EU clinical trials register.

Q68 **Bill Grant:** The regulations.

***Dr Lane:*** The EU trials tracker tool, on which we are basing the information we are talking about, interacts with the EU clinical trials register. It is the MHRA that interacts with that, and has access to the information on it, and can make the updates and changes needed. That is the organisation that interacts with the EMA on that information, so that is where their power and role is.

If we are talking about an organisation that may be able to pull different information about clinical trials centrally and make it publicly available to others, maybe that is where the HRA role is. It does not interact with the register so much and does not have that national competent authority power to do the things we have been talking about with regard to updating register entries and helping researchers to do that.

***Professor Pearse:*** But there is some linkage with the ISRCTN registry. That is a non-specific registry that does not use just drug trials and is probably one of the main non-drug trial registries in the UK. It is linked to the HRA process and is part of the National Institute for Health Research processes. The ISRCTN registry is probably an important one for the Committee to consider when we get to the much bigger problem of non-drug trials.

Q69 **Chair:** There has been reference to ClinicalTrials.gov which, as I understand it, is the American system. You record all trials of medical devices on there, but it is relevant only if there is some association with the States. Is that right?

***Dr Lane:*** One can register a clinical trial from anywhere in the world on it, but the existing law in the US applies only to a subset of trials at sites in the US that are done on a licensed medical product in the US, so it is a messier scene.

Q70 **Chair:** Will there be plenty of research being undertaken in this country that ought to be registered under US law, or do we not know that?

***Dr Lane:*** I do not know.

***Professor Pearse:*** There will be a little bit of international research, or research that is sponsored in the United States, being conducted in the

UK, for example US funders and that kind of thing, where that kind of situation will arise, but it is not a major issue. The main reason you find UK investigators using ClinicalTrials.gov is just that it is there and it is relatively easy to use. The ISRCTN register is a better register in my view, but is newer on the scene, so it has not been used as much.

Q71 **Chair:** TranspariMED say that there are about six times as many UK university trials listed on ClinicalTrials.gov alone as there are on the EU register.

***Professor Pearse:*** Part of that will be because they are not drug trials. They may not even be interventional trials at all. There will be a lot of observational studies on there. In the last 10 or 15 years, there has been a huge wave in culture because, now, if you do not register your trial before you start it, a journal will not publish it. A lot of investigators worry about that kind of thing and register everything, whether it is a clinical trial or just an epidemiological study.

Q72 **Chair:** The bottom line is the need to improve to get 100% reporting on all these registers. Whether it is for drug trials or anything else, presumably the argument is the same: it is paramount.

***Professor Pearse:*** We all agree with your principle that we need to be 100% reported.

Q73 **Chair:** It requires the regulators to get their act together.

***Professor Pearse:*** The system is chaotic. Whose fault that is I do not know.

**Bill Grant:** Thank you very much for your openness. It is fascinating.

Q74 **Martin Whitfield:** Professor Pearse, you mentioned earlier that for your sister organisation, Barts, there were five specific trials that you were having problems uploading. If you got that uploaded, do you know what it would lift Barts percentage to?

***Professor Pearse:*** One hundred per cent.

Q75 **Martin Whitfield:** Those five trials are taking it from 88% to 100%.

***Professor Pearse:*** Yes.

Q76 **Stephen Metcalfe:** Mr Cranmer, we as a Committee wrote to St George's University of London and St George's University Hospital NHS Trust. As you have heard, we wrote to a number of organisations. We were interested in the poor compliance of the organisation. Whose responsibility was it to reply to that letter?

***Mark Cranmer:*** It was my responsibility, and that of my department. The action we took earlier in the year was that my team went through all the trials and went to the chief investigators and asked them to upload. The failure in that system is that there is no mechanism to follow up. It is

a complicated system, as we have heard, and, unfortunately, none of our chief investigators did so, so that system has not worked.

We have now put in place a system where my research governance team completes the reporting as far as we can before asking the chief investigator to finish, and we have monthly monitoring to ensure that we follow up. We appreciate that we have fallen short of our own standards, as well as our legal obligations, but we have got to 55% now and expect to be at 91% by the end of next week. We appreciate that we should have acted better and sooner.

Q77 **Stephen Metcalfe:** Yes. I may want to explore a little further the progress you have made. The question was more that, if it was your responsibility to reply to us, why was there no reply forthcoming?

***Mark Cranmer:*** I apologise; it was an oversight. We took action to try to solve the problem, but it was an oversight that there was no response.

Q78 **Stephen Metcalfe:** The letter acted as the push we have heard it had in other organisations; you just did not tell us you were going to do anything with it.

***Mark Cranmer:*** That is unfortunately the case. It acted as a push. The first push did not work; the second push has worked, but we should have acted sooner.

Q79 **Stephen Metcalfe:** Errors happen. We all accept that. What system have you put in place to make sure, if there is further correspondence, not necessarily from us but perhaps other organisations, that even if it is a holding reply there is an acknowledgment of the fact that there has been some correspondence, because that does not indicate a great system either, does it?

***Mark Cranmer:*** Absolutely. We will log them and respond. We are very compliant in other areas, in things like MHRA reporting and our open access publishing. I do not think this represents St George's performance in other areas. None the less, it was an oversight in this area.

Q80 **Chair:** It is a legal requirement.

***Mark Cranmer:*** We appreciate that it is a legal requirement.

Q81 **Chair:** It is a legal requirement for a reason.

***Mark Cranmer:*** Absolutely.

Q82 **Chair:** It feels rather like, "We're great at everything, but we've just fallen short of this one little requirement." The reason we are supposed to be reporting all clinical trials is that not doing so lacks accountability for public money, puts public health at risk and distorts the research record. Your organisation has not taken it seriously, has it?

***Mark Cranmer:*** We have published our research in open access journals. I appreciate that is not the level of detail that is on the database, and I

appreciate that we have not complied with the database. The system we had in place was not robust enough; it has not worked. We have reviewed that and improved it, and we have an ongoing system to keep that up in future.

Q83 **Stephen Metcalfe:** On the ongoing review or changes to the system you have introduced, when do you expect to get to 100% compliance, and how will you ensure that you keep that up?

***Mark Cranmer:*** We expect to get to 91% by the end of next week. To get to 100%, we are waiting for MHRA guidance on one remaining trial. When we have that guidance, we will do that. In future, we will have monthly monitoring by my team to ensure that we remain at 100%, and we will chase investigators, where action lies with them, with escalation. Our research governance committee, which has oversight of trials, will review that every quarter when it meets. In terms of policy, I believe it is quite similar to what Nigel mentioned.

Q84 **Stephen Metcalfe:** What were the barriers previously to doing that? Was it something deemed not wholly necessary, or did it just fall through the gaps?

***Mark Cranmer:*** The barriers were chiefly that investigators found it hard to do it and did not do it, and we did not push them enough and follow up to do it.

Q85 **Stephen Metcalfe:** That culture has now changed.

***Mark Cranmer:*** That has now changed.

Q86 **Stephen Metcalfe:** The work is ongoing. Who is now responsible in the organisation? How high up in the organisation is the responsibility for ensuring this stays in place and continues to work?

***Mark Cranmer:*** I am the accountable director for it in the organisation. The new policy will be signed off by our executive board, which is chaired by the principal of the university, on 12 November. There is a committee structure in the organisation that reports upwards. Our research committee, which is one of our senior committees, chaired by our deputy principal for research, will have regular oversight as well.

Q87 **Stephen Metcalfe:** Síle, do you want to make any comment about the changes Mr Cranmer says have been introduced?

***Dr Lane:*** They all seem to be sensible changes. Making it clear whose responsibility it is is probably usually the first step that an organisation has to take: naming somebody and saying, "This is your job from hereon in. How are you going to make it happen?" and having that percolate right down through standard operating procedures as far as putting it into researchers' job contracts and job descriptions, so that nobody can say, "We didn't know."

Q88 **Graham Stringer:** Professor Eddleston, I have very similar questions to

those put by Stephen. We wrote to you as a Committee. You did not respond. Is there any particular reason?

***Professor Eddleston:*** I thought we had responded. Apologies. As executive medical director with responsibility for R&I, I thought we had responded to say we were working to achieve compliance.

Q89 **Graham Stringer:** My notes say you haven't, and I look to the Chair to confirm that.

***Professor Eddleston:*** I will certainly check that. I was told that a letter had gone out. It should definitely have gone.

We take R&I extremely seriously in the organisation. At board level, I carry responsibility for research and innovation. At the time your letter came, we were in the process of restructuring R&I across the group because we had had a merger with University Hospital of South Manchester. We took that opportunity to look again at how we delivered the R&I function across the group and how we delivered our sponsoring function.

Each hospital now has a research manager embedded within it, and an associate medical director at each of the individual hospitals carries responsibility for R&I. They sit on the research governance committee. I do not chair the research governance committee. I sit on it, but there is a separate clinician who chairs that committee.

In terms of our processes, we have revisited roles and responsibilities. At the moment, we are looking, with the University of Manchester, to streamline our sponsoring functions. It is likely that Manchester University foundation trust will take on the sponsoring function of both the university and the trust.

We have made investment in our sponsoring personnel because, as I mentioned, that particular CTIP role is quite complex and a significant element of skill is required to deliver it. The team has been re-recruited and bolstered, because the historical team in one of our sites, University Hospital of South Manchester, moved on when the merger occurred.

We take this absolutely seriously. At board level, I carry responsibility. I am extremely sorry if that letter has not arrived. I will find out why. It was a holding letter that was written or drafted, and it specified that we were in the process of restructuring and would be looking to get our compliance up to 100% as quickly as possible.

Currently, if one looks at the studies that terminated early and removes them from the database, and the 10 that are being uplifted at the moment, we would be at about 84%. We identified two studies with MHRA that had finished when the last patient was recruited. Recognising that we had a year to upload, we anticipated that analysis would be quite straightforward, but in fact analysis has been extremely difficult because of the complexity of the testing we were doing. It has taken us a year to

get that analysis completed, so we are now in the process of finishing it. That particular scenario applies to two studies, and they should be uploaded as soon as the analysis is complete.

The other four studies require a lot more information because they date back to 2004. Some of the investigators have now retired, and we are having great difficulty acquiring information relating to them. We have asked MHRA for more information. They were studies from University Hospital of South Manchester. We are absolutely on course. I anticipate that before the end of November, assuming the European database accepts our submissions, we will be at 84%, and then we have a final few studies to upload when we have additional information.

Q90 **Graham Stringer:** You have answered a lot of my questions that I have not asked.

***Professor Eddleston:*** I thought I would give a full answer.

Q91 **Graham Stringer:** I will ask Dr Lane while I reorder my questions.

***Dr Lane:*** I want to clarify that. The results of studies that terminate early need to be reported. You cannot take them out of your numbers. It is just the ones that never started that we were speaking about earlier. If they terminate early, you still need to report them.

***Professor Pearse:*** They need to be reported, but reporting them is not straightforward because they do not fit in the database.

***Dr Lane:*** It is a tough one when a researcher moves, leaves or, God forbid, dies, isn't it? As you all know, it remains the sponsor organisation's responsibility to make sure that those trials still follow the rules.

Q92 **Chair:** We have heard that the European database is complex in terms of reporting in those circumstances. Is that something you have come across?

***Dr Lane:*** For trials that happened before 2014 or 2013, one can upload a PDF that contains the appropriate level of results you would be expected to put into the tabular system—the complicated system for older trials. If any of the researchers had published a paper based on those clinical trials, uploading that PDF would be a possible way to report them easily.

***Professor Eddleston:*** We have uploaded papers that pertain to the period prior to 2014. The 10 studies that terminated early due to recruitment numbers or other issues were all in 2010 or earlier, and six of those came from our University Hospital of South Manchester site. We are having enormous difficulties in even getting any of the data from the few patients who were actually entered into the study in the first place. It is very difficult to see how we can upload that on to the European database.

Q93 **Graham Stringer:** Is the main barrier being able to report to the

European database?

***Professor Eddleston:*** For those 10, yes.

Q94 **Graham Stringer:** The HRA wrote to you in the spring at about the same time as we did. Did you respond to that letter?

***Professor Eddleston:*** I thought we had responded to both, because I drafted the same letter.

Q95 **Chair:** Given your answer, we are double-checking because we do not want unfairly to malign you.

***Professor Eddleston:*** I can check as well. I thought we had written the same letter.

Q96 **Graham Stringer:** The structures that you have set up over the nine hospitals, some of them very large hospitals in their own right, sound very complicated indeed. Are you going to simplify those structures?

***Professor Eddleston:*** They are not particularly complicated in that it is important for each hospital in the group to have their own R&I committee. They have their own R&I committee. They now have their own clinical lead that pertains to that particular hospital, and they have their own manager. Then they feed into a central system that is held at group level and has a central group governance structure with one clinical lead. I oversee the entire portfolio.

Q97 **Graham Stringer:** Finally, for the record, when do you expect to be at 100% compliance?

***Professor Eddleston:*** Bearing in mind what Dr Lane said about the 10 studies that terminated prior to 2010, and the four studies from University Hospital of South Manchester that we are having difficulty with because they date back to 2004, I am optimistic that, if we can resolve this with the European database for those that terminated early and we can get some data from our investigators who have retired, we should be able to complete that before the end of the financial year, but we have been trying for the last nine months to locate information for those particular studies.

Q98 **Graham Stringer:** When North Manchester General Hospital gets into the structures, will it be absorbed more quickly than Wythenshawe was?

***Professor Eddleston:*** Yes. We have a clear understanding at the moment of the studies being undertaken through the clinical research network on the North Manchester site. We have already started that work.

Q99 **Chair:** That completes the questioning for this panel, but before we finish are there any points you want to make reflecting on the session we have had? Dr Lane, do you want to add anything? We have the regulators next, so this is your opportunity to give us any further information that we can put to them, or indeed anything else you feel is relevant that you

have not already said.

***Dr Lane:*** We have covered a lot of the issues that the regulators will probably be questioned about in the next session.

I want to remind everybody that right now the Department of Health and Social Care is building a new register for the UK, to be used after Brexit if the UK can no longer be a member of EMA and use the European register. I would like to recommend that the developers of that new database work as early as possible with the end users of the database to ensure that all the issues about usability, interface, the intricacies of trial design and issues that might pop up get resolved in the design as early as possible, or else we will be facing the same stumbling blocks.

Q100 **Chair:** It is critical for the Department to liaise with people working on the frontline who are trying to comply with the requirements to make sure there is an ease of registration that we do not have at the moment.

***Dr Lane:*** Yes, exactly, so we do not come up with the same situation, where it is very, very difficult for a lot of clinical triallists to interact with the database because of the design.

I want to go back to sanctions before we end and make a point that has not been made anywhere else, which is really important to us. We work with the public—patient groups—people who have been part of clinical trials and take and use medicines all the time. It flummoxes them that there are medicine regulators who are purportedly about safeguarding public health and safety but do not seem to be bothered about bringing in sanctions for those who break the rules on running clinical trials on the medicines people use all the time. It flummoxes people that no one takes responsibility.

Q101 **Chair:** Do you think there is a quid pro quo, in that the regulators need to get their act together to sort out an easy registration system? We have heard some very legitimate concerns about the problems of registration that inevitably make it more difficult and time-consuming to comply. It is ridiculous to hear that some processes take four or five hours. Do you agree that there is a quid pro quo that along with sanctions there needs to be ease of reporting?

***Dr Lane:*** It has to go alongside removing the barriers and making things easier and raising awareness. There are probably three planks: sanctions—we know that with these letters professional embarrassment works; removing barriers and making it easier; and raising awareness.

***Professor Pearse:*** You might also celebrate good practice. That is well known as a good thing to do.

**Chair:** Incidentally, I absolutely applaud those organisations, including some of those before us, who responded to our prompting in getting their act together, because that is exactly what we were trying to achieve. Among many organisations, there has been a seriousness of intent that

we very much recognise and appreciate, so thank you for that.

Q102 **Stephen Metcalfe:** I have a very brief point that I missed when talking to Mr Cranmer. You explained how you had missed our letter. I think the HRA wrote to you at the same time. As we are speaking to them next, did you reply to their letter?

***Mark Cranmer:*** We did reply.

**Stephen Metcalfe:** You replied to their letter. Thank you.

Q103 **Chair:** According to our records, Manchester University responded, but there was nothing from the trust, or group of trusts.

***Professor Eddleston:*** I can go back and check.

Q104 **Chair:** Perhaps you could find us the letter that was sent. It appears not to have arrived, but if you could tell us, that would be appreciated.

***Professor Eddleston:*** I will. I will come back to you.

**Chair:** Thank you all very much indeed. I found it a really useful session. Thank you.

## Examination of witnesses

Witnesses: Dr O'Kane, Dr Godlee, Juliet Tizzard and Professor Stephenson.

Q105 **Chair:** Let us start with some quick introductions.

***Dr Godlee:*** I am Fiona Godlee, editor-in-chief of *The British Medical Journal*.

***Dr O'Kane:*** I am Martin O'Kane. I manage the clinical trials unit in the licensing division of the MHRA.

***Juliet Tizzard:*** My name is Juliet Tizzard. I am director of policy at the Health Research Authority.

***Professor Stephenson:*** I am Terence Stephenson. I am a practising doctor and researcher, and I have been chair of the Health Research Authority since 1 September.

Q106 **Chair:** Thank you very much indeed. I appreciate all of you coming here this morning.

Dr Martin O'Kane, we have received lots of feedback from universities and NHS trusts, including this morning, which referred to the difficulties and delays in dealing with the MHRA. We understand that there was an administrative backlog of data that had not been dealt with, or uploaded, by the MHRA.

Can you confirm that you have now got your act together and cleared the backlog, and are robust enough to deal with any further surges so that there are no more delays in future? Bluntly, it is not you who takes the

flak; it is the universities and trusts, and it is not fair to them that you have a system that is not functioning effectively.

***Dr O'Kane:*** I can confirm that we have got our act together. We had a backlog from late 2016 until the end of 2018.

Q107 **Chair:** Why was that? That seems like a failure to address it.

***Dr O'Kane:*** We have a dedicated position in MHRA to deal with the European database. Unfortunately, there was staff turnover at that time and difficulties in recruiting for that position.

Q108 **Chair:** Over two years?

***Dr O'Kane:*** We have a support team of three. One left, and one went on maternity leave, so we had a gap that was difficult to fill over that time. We managed to secure resource from another part of the agency and address the problem, and we have put in place, moving forward, a number of things to try to stop this happening in future. For example, we have cross-trained other members of the support team. We have increased logins to the EudraCT system, and we have a better way of monitoring and tracking progress to ensure that the system is up to date. Maintaining the accuracy of the EudraCT database is an EU-wide issue.

Q109 **Chair:** Is part of it that your organisation was not taking it seriously enough?

***Dr O'Kane:*** No, I do not think that is accurate at all. We have a dedicated position to deal with the European database. We are taking the lead in Europe in ensuring that the database is accurate. Other member states ask us how we manage to tackle keeping it up to date.

Q110 **Chair:** You think genuinely that it is now robust enough to cope with further surges in demand, and there will not be a repeat of what has happened over a two-year period.

***Dr O'Kane:*** Yes. We have put in place a number of things to keep it up to date. As I said, we have cross-trained more members of the team to ensure that it will work. Our current performance is, essentially, updated every week. As far as we are concerned, the information in the database is accurate as of today. There may be some technical issues with EudraCT, and we are dealing with them with the EMA, but in terms of the accuracy of the data up there, we are confident that, moving forward, we have the processes in place to achieve that.

Q111 **Chair:** In the event of a no-deal Brexit, which now appears to have receded in terms of risk, would the MHRA expect a significant increase in workload with respect to handling requests on data within the EU clinical trials register? Have you done work on that to prepare for it?

***Dr O'Kane:*** Yes, we have been preparing for every Brexit scenario since the referendum, and we have been working with our colleagues in HRA and the devolved Administrations across the UK. Clinical trials are managed on a national basis, so a multi-member state clinical trial is

managed in the UK by MHRA. In a no-deal Brexit scenario, the guidance that we publish on our website encourages sponsors to use publicly available registers to register their study and report results.

Q112 **Chair:** Dr Lane mentioned that the Department is working on a new database to replace the European one. Presumably, you are working closely with them.

***Dr O'Kane:*** That database is being developed by HRA as part of the integrated research application system.

Q113 **Chair:** It is being done by HRA, not the Department. Is that right?

***Dr O'Kane:*** It is being built by HRA with partnerships, including MHRA and across the Health Research Authority.

Q114 **Chair:** Are you all collaborating and making sure that you get user experience built into the design of the new system?

***Juliet Tizzard:*** Yes. We have a long-established committee called the IRAS partners, which are the organisations, such as the MHRA, other regulators and the NIHR clinical research network, working together on the new version of IRAS. We have some funding from Government to do that, and we have started that process.

Q115 **Chair:** What is the timescale for completing it?

***Juliet Tizzard:*** I do not know the answer to that.

Q116 **Chair:** Perhaps you would come back to us to confirm it.

***Juliet Tizzard:*** Yes.

Q117 **Martin Whitfield:** To put it on the record, you are the authority that is responsible for authorising and regulating all the clinical trials in the UK.

***Dr O'Kane:*** All the interventional and clinical trials of medicinal products.

Q118 **Martin Whitfield:** Behind all of those are individual patients. We have been looking at drug trials predominantly. Would you like to comment on clinical trials for medical devices and about reporting those?

***Dr O'Kane:*** Medical devices do not sit within my particular remit in the clinical trials unit, but I am aware that a new medical device regulation is coming that will match some of the transparency requirements for medicinal products. Obviously, MHRA will take a role in ensuring that those are complied with, moving forward, but it is not within my remit.

Q119 **Chair:** Is it right to assume that, in the event of Brexit, we will effectively sign up to those new rules?

***Dr O'Kane:*** I cannot answer that for medical devices, but I can find the answer for you.

Q120 **Martin Whitfield:** If you could reply in writing, that would be very helpful. Presumably, MHRA operates a risk register and has done so for a

while. I was wondering how long the backlog sat as a red risk on that register.

***Dr O'Kane:*** The backlog was identified and tackled. Staffing is a risk on the risk register, and there was difficulty in replacing that resource. It was not that we had not looked at it. We had started the recruitment process, but it was very difficult to backfill that post, particularly with other priorities at the time. During that time we had a support team, but the priority had to be focusing on assessment of clinical trial applications and patient safety activities.

Q121 **Martin Whitfield:** The actual registration was not the element that was the red risk; it was replacing staff—I think you said one left and one was on maternity leave—and the efficacy of the actual trials.

***Dr O'Kane:*** The risk was replacing staff for that function, not the function itself.

Q122 **Martin Whitfield:** To go back to a previous answer, was the backlog identified as a risk? Was that a consequence of circumstances that were happening?

***Dr O'Kane:*** The backlog was a consequence of the low resource.

Q123 **Chair:** In other words, it was not identified as something the organisation was that concerned about. It was not a risk on the register, and it does not sound as if you were taking it that seriously.

***Dr O'Kane:*** As I said, we have a role and the resource fills the role, so the function is there. If the resource is not there, the risk is obviously associated with uploading the data to the database.

Q124 **Chair:** Do you know how long the backlog was during the two-year period? The two years were from 2016 to 2018, but my understanding is that the backlog continued beyond 2018. It sounds more like three years to me.

***Dr O'Kane:*** The backlog was being addressed all through that time.

Q125 **Chair:** You were addressing it, but not solving it; it was continuing, yet it was not marked in your organisation as a red risk. It does not sound as if the organisation was taking it very seriously.

***Dr O'Kane:*** I do not think that is a fair assessment.

Q126 **Chair:** You were not doing anything about it; you were failing to get it sorted for three years.

***Dr O'Kane:*** The point is that we were attempting to resource that, and it was being dealt with.

Q127 **Chair:** The problem is that there are all those universities and hospital trusts out there getting flak for failing to respond, and they are not getting responses from the regulator. When they report stuff to you, it takes ages to get it on to the register. That is a failure, is it not, over

quite a sustained period of time?

***Dr O'Kane:*** That is not quite accurate. The backlog we had was looking mainly at trial statuses, complete or ongoing, in the database. Although that backlog was very unfortunate and we do not want it to happen again, it did not prevent sponsors from uploading their results.

Q128 **Chair:** I understand that.

***Dr O'Kane:*** The sponsors' obligation to upload their results to the EudraCT database is not prohibited.

Q129 **Chair:** How long was the backlog? How long were people waiting for the things that were in the backlog?

***Dr O'Kane:*** What you are talking about is when your letter reached sponsors and they realised that some of the information in the EudraCT database was not correct. From the Sense about Science submission, it is clear that sponsors have a frustration that they cannot go in and change that information themselves. European member states have the same frustration. We cannot go in and change that information. The information is received by competent authorities via a very specific file type called an XML. That data belongs to the sponsor; they send it to the member state and we upload what they send us.

Q130 **Chair:** We have a clear impression that the database is not really fit for purpose, but, one last time, do you know how long the backlog was in dealing with those inquiries?

***Dr O'Kane:*** For inquiries themselves, if it is a status update, we can solve it, and have solved it, in 48 hours.

Q131 **Chair:** You have accepted that there was a backlog over a two to three-year period. The question is quite simple: how long was the backlog?

***Dr O'Kane:*** The backlog was about two and a half years' worth of information.

Q132 **Chair:** People were waiting for two and a half years to get something done.

***Dr O'Kane:*** No. People were not waiting for two and a half years to get something done.

Q133 **Chair:** Let me try again. How long were people waiting for issues to be sorted during the period when there was a backlog?

***Dr O'Kane:*** If a sponsor or researcher contacted us to say the information sitting in the EudraCT database was not correct and it was a status update, 48 hours. If it is a problem with XML, they often go to the EMA service desk, which again takes quite a long time. Then they come to MHRA. More often than not, MHRA would have to ask for an updated

XML file. This adds time, so it could take two to three weeks to update that information.

Q134 **Chair:** The longest people were waiting during that two to three years was two to three weeks for the MHRA to respond. Is that right?

***Dr O'Kane:*** I have heard reports of a month, but I do not accept that that was waiting for MHRA to respond; I think that was the totality of time dealing with the EMA service desk, the MHRA service desk, uploading an XML file and getting it rectified.

Q135 **Darren Jones:** If you don't know, sometimes it is better to say you don't know. Are you able to write to us to tell us?

***Dr O'Kane:*** Absolutely. If something needed updating in the database, it would be 48 hours to do a status update.

Q136 **Darren Jones:** Do you understand why, in the context of a two to three-year backlog, telling us that it is actually a two to three-week backlog does not make sense?

**Chair:** It does not really stack up with the evidence we have had that people were very frustrated with the MHRA for not responding and not dealing with their requests. You are now telling us that it was taking only three or four weeks.

***Dr O'Kane:*** We have a dedicated clinical trial helpline. Overall, we receive about 3,500 emails and 5,000 phone calls to that per year. The average timeline for response is four days.

**Chair:** Perhaps you could write to us to clarify the details of what the backlog amounted to, because I have to say I am completely confused at the moment.

Q137 **Bill Grant:** It is not very helpful when the Chair says he is confused. I have a similar theme about the database, which seems to be the nub of many things. The question is for Martin and Juliet.

When things are perceived to be wrong with a facility—for example, a database—those who are tasked with putting it right need to receive information from those who are concerned. What information have the HRA and the MHRA received from researchers and research sponsors to push their concerns, not about trying to register but when they are frustrated and angry about delays? How have they got in touch with you to resolve the issues? I assume they have probably been doing so—you touched on communications—in fairly large volumes.

***Dr O'Kane:*** As I mentioned, we have a dedicated email address and helpline so they can contact us via that. We are more than happy to engage with sponsors and researchers to try to solve any problems and facilitate their obligations.

Q138 **Chair:** Do you think the helpline works well?

***Dr O'Kane:*** Yes, I think it is very successful. We receive 3,500 emails and 5,000 phone calls with a turnover of about four days and a target of 14 days. The helpline is very successful. We have good feedback from users of that facility.

Q139 **Bill Grant:** The time window for those 3,500 emails is over what period of time?

***Dr O'Kane:*** That is per year; it is in general.

Q140 **Bill Grant:** I am just clarifying it. I thought you said three or four days. It is 3,500 contacts over a period of a year.

***Dr O'Kane:*** They are contacts for everything to do with clinical trials of medicines, not just transparency aspects.

Q141 **Bill Grant:** Who has the gift or the power to resolve the issue? Is it the MHRA, the HRA or a combination? Who should have resolved the unresolved? Maybe that is the question.

***Dr O'Kane:*** There is joint responsibility in terms of the EudraCT database; it is probably joint responsibility between MHRA and the European Medicines Agency who administer and run EudraCT.

Q142 **Bill Grant:** My perception—forgive the terminology—is that it is a sort of ping-pong. Who can we nail down? Who is responsible for sorting it? People are telling you about the problems; that is clear. You have large volumes of emails. When they come in, who is responsible for putting right those concerns? Maybe it is not a name but an organisation.

***Dr O'Kane:*** If it is a technical issue with sponsors using EudraCT, that is for EMA; if it is an issue where MHRA has not uploaded information provided to us by a sponsor, it lies with us, and this is the work we have been doing and are up to date with.

Q143 **Bill Grant:** Excuse this statement, but there seems to be a missing link. You mentioned a helpline. It strikes me that it is not working. I may be wrong in that assertion. Are you confident that the helpline is known to researchers and sponsors? I am not suggesting that we increase the volume of emails or communications, but it strikes me that there is a breakdown somewhere. Have you any thoughts on what that breakdown is, or am I wrong in my assertion?

***Dr O'Kane:*** I do not think sponsors are shy in contacting us. Our helpline address and details about what to do if your information on the register is not correct are on our website, so we signpost researchers to come to us with any problem, and we are happy to escalate it. Sometimes it takes some time to resolve it, depending on the nature of the problem. If it is a technical issue with EudraCT, some interaction with the EMA is required. I do not think sponsors do not know where the helpline is or where to find help.

Q144 **Bill Grant:** Juliet, would you like to comment on that?

***Juliet Tizzard:*** Our role at the Health Research Authority is to review all the health and social care research studies taking place in the UK. We obviously liaise with the MHRA over clinical trials of medicines. As Martin describes, the MHRA is the competent authority under the clinical trials directive, which is the current legislation covering clinical trials of medicines. Our role is much wider than that.

Q145 **Bill Grant:** I am sorry for labouring the point. There is clearly an issue with researchers and their sponsors. The database does not seem to fit their needs or, maybe, better still, where there are concerns, they ask for responses, they ask for changes and that is not happening. There seem to be two opposing views on that. You are defending very well the system, yet on the other hand we feel that the system is not responsive. It is important that it is responsive.

***Dr O'Kane:*** I accept that. We stand ready to engage with sponsors. I am happy to escalate any problems that sponsors may have. It is demonstrable from the previous panel that 100% compliance is possible. Although we have heard that there are some issues and some historical issues, that will not stop us working together to ensure that compliance is met.

Q146 **Bill Grant:** What has stopped you up to now?

***Dr O'Kane:*** I do not think anything has stopped us up to now. The point is that, when a sponsor contacts us, we can change the information on the database if that is within our gift to do. We cannot change the information that the sponsor provided to us. They cannot do it themselves, so that is a problem with EudraCT itself. We have to receive a certain file type from the sponsor and upload that. That might take some time, particularly if it is a historical trial and someone has noticed as a result of the letter from the Committee that the information they registered in EudraCT is not correct.

Systems get upgraded, so, if it was a pre-2010 trial, there may be a technical issue with the file type they re-sent us to upload to EudraCT. They may have to redo the whole file again and re-send the updated version for us to upload. That is a frustration that I completely understand that sponsors have.

Q147 **Bill Grant:** You will be pleased that this is the final one from me. While you are confident in your helpline, I am less confident in your helpline. Would you be minded to make some improvements in how you communicate with those who are frustrated with the database? Are you minded to communicate with them better? Do you see that as a way forward?

***Dr O'Kane:*** Absolutely. That is something I can take forward.

Q148 **Chair:** There is a view that has been expressed to us that the HRA has taken this agenda very seriously—we will come on to more discussion about sanctions later—but the MHRA has dragged its feet a bit and is not

engaging quite as much in the seriousness of the issue. Do you reject that completely, or do you think you need to step up to the plate and recognise the absolute importance of complete, 100% compliance?

***Dr O'Kane:*** We recognise that. If there is an impression that we have not engaged with stakeholders on this, I think that is unfortunate. We have worked very hard to try to address any problems that stakeholders come to us with about registering their trials or uploading results.

Q149 **Chair:** We have heard about how not fit for purpose the current EMA database is. Does it require legislation to get that sorted or is it an administrative failure by the EMA to have a properly functioning, easily usable database for researchers to register with and to report their results on?

***Dr O'Kane:*** Some of this stems from the fact that—

Q150 **Chair:** You said it was a Europe-wide problem as well.

***Dr O'Kane:*** Yes. Across Europe, if there is a multi-member state trial, each of those member states needs to maintain the database. There is a huge duplication of effort and stretching of resources across member states. Part of the problem stems from the fact that there is no clear legislation for this in Europe. The clinical trials directive is silent on transparency as such. Moving forward, the clinical trials regulation, which has as part of that legislation a new IT portal where sponsors and researchers interact directly, will help solve that problem for both sponsors and researchers.

Q151 **Chair:** We have to wait for that for there to be any improvement.

***Dr O'Kane:*** It is a question for the European Medicines Agency, but there are improvements that could be made. There are frustrations in member states and from sponsors and researchers. I do not believe that legislation is required.

Q152 **Chair:** Could you write to us? We invited the EMA to attend here today. They said they could not attend. We would like to take up with them the things they could sort out here and now. Could you write to us with the things they need to sort out?

***Dr O'Kane:*** I would be happy to.

Q153 **Chair:** And anyone else. This is a general invitation that, if there are things that the EMA needs to sort out now without having to wait for the new regulation, we would like to hear from you.

Q154 **Graham Stringer:** Can I follow up Bill's question? You said you had 3,500 inquiries a year. Do you measure whether the people who have contacted you are happy with your response in that area?

***Dr O'Kane:*** We have a feedback link at the end of the email response. The satisfaction level has been very high.

Q155 **Graham Stringer:** Can you quantify it?

***Dr O'Kane:*** I cannot, but I can give you the results for the latest, if need be. It is a mark out of 10 and it is usually about seven or eight.

Q156 **Graham Stringer:** We have heard that there are a number of researchers and relevant organisations. I am not aware of their responsibilities in this field. What have the MHRA and the HRA done to communicate to those researchers what their responsibilities are and how they can improve?

***Dr O'Kane:*** In July this year, we were a co-signatory to a letter from the European Medicines Agency, the European Commission and the heads of medicines agencies that was sent to all sponsors and highlighted on our social media channels. It reminded sponsors of their obligations to report. It also provided some guidance and multimedia tutorials to try to facilitate that.

Q157 **Graham Stringer:** What was the response?

***Dr O'Kane:*** In collaboration with the letter from the Committee and work from HRA, we have seen an increase in contact with MHRA, saying that they are trying to upload those results. We have seen the data from AllTrials showing that demonstrably there has been an increase in reporting in the EudraCT database.

Q158 **Graham Stringer:** And the HRA? What action have you taken?

***Juliet Tizzard:*** As I described earlier, we have a broad remit across all health and social care research in the UK, and we publish guidance on how to fulfil the expectations set out in the UK policy framework for health and social care research. We have guidance on our website around transparency requirements and expectations. There are various things built into the approvals process when researchers come to us for permission to start a new study.

I will talk in a moment about the consultation we ran over the summer. One of the things we asked during the consultation was, what are the things that people would find most useful from the HRA to improve their performance around transparency? We listed a number that we thought were likely to be important to researchers and sponsors. One of those was greater clarity around what the requirements are, particularly for different types of studies and different aspects of transparency. That came out as the thing that people felt was most important to address, so that will be central to the strategy when we finalise it.

Q159 **Graham Stringer:** We understand that there has been a pilot study system for the joint authorisation of clinical trials. Can you tell us more about that and what lessons, if any, have been learned from the pilot?

***Juliet Tizzard:*** Martin might want to comment as well, because the MHRA and the HRA have been working together on that pilot. It is not

specifically about transparency; it is about preparing for the clinical trials regulation when it comes into force at some point in the future.

Q160 **Chair:** Do we know a date? Is it that you can't remember offhand when it is or has it not been set yet?

***Dr O'Kane:*** There is no public date for the EMA. The last we had publicly was during 2020. The application of the legislation is tied into the functioning of the IT system that underpins it.

Q161 **Chair:** If that gets delayed, the legislation gets delayed.

***Dr O'Kane:*** That is the problem we have seen; it has been delayed multiple times.

***Juliet Tizzard:*** The pilot you are describing is called the combined ways of working pilot. It invites sponsors to take part in a pilot to look at how we can streamline the process for approving clinical trials applications in the UK. There are the two aspects of the UK decision: the decision by the MHRA and the decision by the HRA, which is around research ethics approval. It is about them being more combined and happening at the same time so that applicants can benefit from a situation in the future where they have one decision with one communication at the end of the decision. At the moment, they run separately.

The pilot invited sponsors to take part. We have processed 80 applications to the pilot at the moment. It is done on a voluntary basis, and we are testing and refining processes as we go through it. It is done manually at the moment. The next phase will move to making it an electronic process. The pilot is going very well. As I said, it is about preparing for the regulation when it comes in.

Q162 **Graham Stringer:** Is it too soon to draw any conclusions?

***Dr O'Kane:*** We had a feedback workshop with the sponsors in the pilot in July this year. They felt that the overall timeline for approvals was shortened, so the increase in efficiency between the two organisations was welcomed. They found value added in having a single submission route, a single set of questions, if any, and a single UK decision on a trial. The MHRA and the HRA were not asking separate or potentially conflicting questions of sponsors. That will be the way forward in future. Importantly, the sponsors that are part of the pilot will form part of the group to inform the new IT system moving forward in terms of usability and their expectations of a new system.

Q163 **Graham Stringer:** It has been suggested to us that the HRA should host a single online resource in the UK for the approval, registration and publication of clinical trial information. Do you think there are merits in a system like that? Are there any obvious disadvantages to doing that?

***Juliet Tizzard:*** Thank you for the question. It is something we are thinking through and which formed part of one of the questions in the consultations that we ran on our draft strategy over the summer. As you

heard from some of the panellists in the first session, there is a strong desire for avoiding duplication and a preference for one single system.

Obviously, though, clinical trials take place across national borders. There are multinational trials going on. We want to try to simplify the process in the UK. That needs to apply not just to clinical trials of medicines but to all types of clinical trials and all types of research studies in health and social care. Thinking through the logistics and the resourcing of that is a question. It is definitely a live discussion to try to create a more co-ordinated and streamlined system in the UK, but one that is also visible and usable by patients and the public. That was something that came through very strongly in the engagement we did over the summer.

Patients and research participants are keen to get their hands on information about studies. They would not necessarily go to something like the European register or any of the other registers, because they are designed for sharing information for fellow researchers and healthcare professionals. That is their primary purpose. What they are hungry for, and something that we feel strongly about, is creating visibility for the public around the outcomes of research.

Q164 **Graham Stringer:** Are the organisations—the HRA and the MHRA—replicated in every other EU country?

***Dr O'Kane:*** More or less, yes. There is usually a competent authority and an ethics committee. HRA acts as a co-ordinating body for the ethics committees within the UK. Other member states do not have such a national co-ordinating body. The UK system is slightly more efficient than some others. The Netherlands' acts as both the ethics and the competent authority, but they are unique in that. All other member states have a competent authority and ethics.

Q165 **Chair:** There was also, along with our letter and the HRA letter, a letter from the European Medicines Agency, together with MHRA and other regulators around the Europe, in June this year. Do we know anything about the impact of that? Did it get noticed? Did it get acted on?

***Dr O'Kane:*** We did our best in the UK to highlight that through sending it to our sponsor list and through our social media channels. It is difficult to determine the impact of it along with the other initiatives that were happening with HRA and the Committee's letter other than the Sense about Science report that reporting rates have increased. It is difficult to know the direct effect of that letter.

Q166 **Chair:** We heard in the first panel about other registers around the world, including ClinicalTrials.gov in the States, and low reporting rates on that site. There was a plea for a sponsor to be able to register and report in one place and for it to be shared with all relevant registers. How much work is going on internationally and globally among regulators to get this sorted so that there are simple processes in place?

We will come to the issue of sanctions, but the sponsors in the first panel

made a legitimate point that, if there is to be a sanctions regime, it needs to be easy to register and to report, and at the moment clearly it is not. There is massive variability around the world. What work is being done by regulators internationally to sort that out?

***Juliet Tizzard:*** I will comment on the registration side of things. There is a question, which we have been discussing a lot this morning, around registration of clinical trials of medicines and using the European database. Setting that aside for one moment, registration is not difficult for other types of studies, but registration can happen in a number of different places. That is more the issue.

It is easy to register on ClinicalTrials.gov. It is easy to register on ISRCTN, which is a UK registry. It charges, which ClinicalTrials.gov does not, so that might explain why there is a preference for a number of UK sponsors to use ClinicalTrials.gov. One can register in more than one place, which makes following up on whether the study has gone on to report or not more difficult.

We have as a condition of a favourable ethics opinion that any clinical trial, not just of medicines but any type of clinical trial, should register on a WHO-recognised registry, of which there are many, before patient recruitment starts. The expectation is clear, and the opportunity to register is there; it is whether the registration actually occurs and that is what we want to address.

Q167 **Chair:** Then there is the reporting at the end of it, which is very variable. The question was how much work is being done internationally to simplify all of this, and to co-ordinate between registers to make it easy for researchers and sponsors to report, with the overall objective in mind that total transparency is very important for the furtherance of the pursuit of improved healthcare.

***Juliet Tizzard:*** Agreed. We are focusing on how we can simplify the system in the UK to start with and then moving on—

Q168 **Chair:** There isn't at the moment any discussion internationally about how we improve co-ordination between registers.

***Juliet Tizzard:*** Not from our point of view, but I cannot answer for MHRA.

***Dr O'Kane:*** It is the same circumstance. The WHO, which Juliet mentioned, is a primary registry. With the new clinical trials regulation, they are trying to mimic the fields from that primary registry, so it is easy to interlope data between the two. What state or stage those discussions are at, I am not sure.

Q169 **Martin Whitfield:** Thank you for your patience, Dr Godlee. I will gently move the light of investigation down the panel.

There seems to be a tension between UK universities and the trusts regarding academic publication, and this interferes with the reporting of

clinical trials. Several organisations have told us that they have concerns about publication and their obligation to upload results. Do you think that is an issue? Is it a problem? How do you view it?

***Dr Godlee:*** The anecdotal evidence suggests there is a problem. It is something we, the scientific community, need to address. Journals have done a good job in pushing for prospective prior registration and insisting on that before an article will be published. It is not by any means universal but that has made a difference. There has been clear support among the journals for the timely publication of results.

The ICMJE, the International Committee of Medical Journal Editors, which is a self-elected group of some of the major journals, of which *The BMJ* is a member, is very clear that the posting of summary results is not considered prior publication, and that is very clearly stated in several parts of the ICMJE guidelines. It is limited to a brief structured abstract or a table containing the basic information.

There is nervousness historically among journals—I would exclude *The BMJ* from that—about whether publication on a results database will damage the journal in some way or damage newsworthiness and the peer review process. The statement is there. It is very clearly stated. It replies to all registries that meet five clear criteria—I can give them to you; they are the ones that are shared with WHO and ClinicalTrials.gov, but there is still confusion.

We have just established a pre-print server, medRxiv, and that gives me and my colleagues insight into the broader clinical trials community. There is a huge amount of confusion around the world that we need to understand and address. People say, "We registered the trial and include the summary data here," thinking they have done the job. Other people have even more confusion about trial registration itself: "We have IRB approval, so we don't need to register the trial." We should not underestimate the extent to which people are confused and need education—that sounds very patronising—support and encouragement.

The journals have no statutory authority; they are not regulators and they all work independently. People want to get published, so we have some power to influence this and that was used with the registration move—the prospective registration saying that you cannot be peer reviewed in these journals if you do not register your trial at the outset. In this conversation, I wonder whether the ICMJE could do more not just to encourage, as we currently do, but to some extent say that you have to have put your information on the trial summary data on the database before we will consider the trial. I will take that back to my colleagues at the ICMJE.

Q170 **Martin Whitfield:** You mentioned before the concept of fear of prior publication and it not applying to part of it. Does that extend to the data that is currently on the EU clinical trials register? If the data is already there, is that deemed to have been prior published?

***Dr Godlee:*** No, that is not deemed prior publication.

Q171 **Martin Whitfield:** Again, that is part of the confusion that exists between researchers who rightly want to be published and the requirement for them to be open and transparent. You accept that the ICMJE can take a role in this. Do you think others need to take a role in removing the confusion?

***Dr Godlee:*** The journals have done a certain amount, and we could do more to make clear that fact. The issue is that the publishing world is a very broad and international effort; it is individual publishing houses and journals, each functioning in their own way. There is no regulator as such. There is a committee on publication ethics that encourages journals to comply with the ICMJE rules.

Q172 **Martin Whitfield:** Taking it slightly further forward, there was mention earlier today about concerns about breach of copyright. There seems to be much confusion. As a group of editors, do you have a view and are there any recommendations or guidelines out there?

***Dr Godlee:*** I was very surprised to hear that. As I understand it, it applies to the older trials, the ones completed before July 2013, where the option of uploading a PDF of the study in the journal publication is an option. *The BMJ* is open access, and open access journals would not have a problem with that anyway. I guess the answer is that people who have these older trials still have the option to upload in the normal way on to the form, but it seems to me odd that some journals would prevent you from doing that. Authors should push back on that. It does not seem at all right that journals should prevent people from doing that.

Q173 **Martin Whitfield:** As you say, the journals themselves are independent and, in essence, self-regulate wherever they are. Are stronger interventions needed from HRA and MHRA? Who should take responsibility to clear up the confusion? Who should take the lead?

***Dr Godlee:*** It is a collective responsibility, and there is working together; the ICMJE and other bodies have worked closely with registries. There is a collective responsibility. We are apparently going to get on to sanctions, but where 100% compliance has been achieved, we can learn from that. The real power rests with the funders and regulators. We would all like to see them encouraged and enabled to exert that power. As has been said, improving the registries themselves, making it easier for people to do this, has to be the other side of the coin.

I can see the challenge. We are talking about an international effort. Any registry that the UK designs could learn a huge amount from the difficulties that the current registries have already faced.

Q174 **Martin Whitfield:** I think it is right, and I presume that as a panel we all agree, that there is huge value in peer-reviewed publication. To open it up to you, Professor Stephenson, what would your comment be about the responsibility for removing the obscurity and confusion and clarifying the

situation?

***Professor Stephenson:*** As a researcher, I think researchers want to get published because that is how they are judged and they want their work to get out there. Of greater concern is selective reporting where data that reflects well is published and other data is buried.

Going forward, blockchain technology might have something to offer, where you have a distributive ledger that cannot be edited in retrospect. More than just people registering prospectively, you are logging your data and your recruitment as you go through and you cannot then go back and doctor it. That is an option.

I agree with Fiona that all the organisations have a responsibility to improve clarity, and that is where we would start—making these things easier to do, making it the norm that changes people's behaviour and giving clarity about what is expected.

Q175 **Martin Whitfield:** The norm should be that there is absolutely no conflict in publication for peer review and the requirement for, and indeed the advantage of, registering the trials.

***Professor Stephenson:*** And making quite clear the view of the editors that logging summary data does not interfere with your ability to publish. There was a discussion in the earlier panel about the research excellence framework. Sponsors, funders, researchers and participants would all be concerned if they had run a big study that had been very successful and then they could not get it in the public domain because someone said, "Ah, well, you've put this little abstract on a little European website somewhere." People would be very anxious. Anything we can do to make that clearer would be of benefit.

Q176 **Martin Whitfield:** Do you want to add anything on prior publication, Juliet? I was thinking about how much discussion has gone on about this, before the Committee sent letters on it—or before it came up from the letters we sent.

***Juliet Tizzard:*** I do not have much to add to what Terence said. It has not been the focus of our strategy. We have been focusing on what role the HRA could play more directly in its relationship with sponsors. Having said that, we convene something called the transparency forum, which brings together a wide group of organisations, including publishers such as *The BMJ* and registries and funders. At the moment, we use that as an information exchange and a way of understanding what the relative efforts are across the research community to push forward the transparency agenda. It has come up a couple of times in that context. It is part of our own refresh of our guidance to the research community. That is something we need to emphasise.

Q177 **Martin Whitfield:** We are probably all in agreement that there is clearly confusion at the moment, but there is no vested interest in having that confusion continue. Indeed, prior publication date or whatever, we are all

seeking the same thing, and it is a matter of sitting down and resolving the problem and then needing that to be the common standard of practice. Would that be fair?

***Dr Godlee:*** It is fair. This may be slightly out of scope, but when you say no vested interest, we should all acknowledge that the European Medicines Agency is under huge pressure at the moment, with the court case—the legal action by two drug companies trying to pull back on public access to information. It would be great if this Committee could speak out firmly against such moves; maybe it already has. It would be an enormous shame if the progress made by the EMA is lost.

Q178 **Chair:** That is very helpful. Thank you for that. Does the HRA get to hear of cases where journal editors have blocked requests from organisations to publish data on the EU trials register?

***Juliet Tizzard:*** Not generally, no.

Q179 **Chair:** We have heard reports of that happening. It obviously does not happen at the *British Medical Journal*, but if you did get to hear about it, would you call it out? It is not an acceptable practice, is it?

***Dr Godlee:*** No, it is not acceptable.

Q180 **Chair:** You have a role in ensuring the ethics of the whole process and in promoting transparency. That needs to be challenged, does it not, if you hear about that happening?

***Juliet Tizzard:*** Yes, and correcting misunderstandings in the research community so that they understand that what we have just been discussing about reporting to registries does not constitute prior publication.

I presented to a university last week where they had a lingering concern about that, and I was able to clarify with them that it was not the case. What they have done instead is to speed up publication of their journal articles. They now seek to achieve that within 12 months, so that they are publishing in a journal and reporting to the European register at the same time. The side-effect of that is speedier publication, but I wanted to clarify with them that they understood what the correct position was.

Q181 **Stephen Metcalfe:** Following the Committee's report in February 2019, the HRA indicated that it was going to write to NHS trusts to ask about their compliance. Perhaps you could clarify this? Was it all NHS trusts or just non-compliant NHS trusts?

***Juliet Tizzard:*** We wrote to non-compliant NHS trusts, yes.

Q182 **Stephen Metcalfe:** What response did you get to that letter?

***Juliet Tizzard:*** We wrote to 55 English NHS trusts who sponsor clinical trials and had at least one trial with an overdue report, according to the EU trials tracker tool. We used that tool. We co-ordinated with our colleagues in Wales, Northern Ireland and Scotland to write to their

sponsors who also appeared on the same tool. We wrote to 71 in total between the four nations. We got good engagement from them, as you would expect from the NHS Health Research Authority. We did not get a response from all of them though, and we chased up some of them.

We wrote to them for two main reasons. The first was to alert them to the status of their studies on the EU trials tracker, and I know that others have been making similar efforts, as we talked about this morning. We also wanted to let them know that we were going to be doing a wider piece of work and developing a research transparency strategy, as the Committee recommended to us in the report last year. We wanted to let them know that was coming and to give them the opportunity to feed back any difficulties or, indeed, good practice that they had implemented locally. Many of the things that came up chimed with what was discussed this morning.

There were reports back about some of the frustrations with the current system; we do not need to go over that again. There were descriptions of changed processes on the ground that a number of trusts had implemented. A general positive response was that they were pleased that the HRA was taking a lead, and they wanted to take part in the consultation, which had not started at that point.

Q183 **Stephen Metcalfe:** To be specific, of the 71 you wrote to collectively across the country, did you receive 71 positive engaged responses?

***Juliet Tizzard:*** I could not say, hand on heart, what was in the content of all 71, but there was a positive response. I cannot comment on the ones who did not reply to us. About 20% did not reply.

Q184 **Stephen Metcalfe:** Of the 71, 20% did not reply, so about 14 trusts did not reply. What action are you taking to follow up those 14?

***Juliet Tizzard:*** We did a follow-up and increased the number of responses to 80%. We then moved to a broader engagement with the whole community, because we launched the consultation in June. What we would like to do now is go back and see what the reporting status of the remaining 20 is.

Q185 **Stephen Metcalfe:** Very good. Do you not find it surprising that 14 trusts you wrote to as HRA did not respond to your letter?

***Juliet Tizzard:*** We found it disappointing.

Q186 **Stephen Metcalfe:** Is that list readily available?

***Juliet Tizzard:*** No, it is not, but we can share it with you.

Q187 **Stephen Metcalfe:** That would be very useful. Thank you very much indeed.

In your response to our Committee's report, you said you would be contacting other sponsors in due course who were not complying with the requirements. Has that now taken place?

***Juliet Tizzard:*** Not yet. We wrote to the Chair in August. Our chief executive, Teresa Allen, wrote to the Chair in August and gave some feedback on the engagement with NHS sponsors and said we were moving on to others. We will report to you when we have done that.

Q188 **Stephen Metcalfe:** But you cannot tell us yet when that will be.

***Juliet Tizzard:*** No, I cannot. It will be in the next month, I would say.

**Stephen Metcalfe:** Thank you very much.

Q189 **Darren Jones:** I am going back to the hot topic of sanctions. We understand that the HRA is due to publish the research transparency strategy soon. When is that due and how is it going?

***Juliet Tizzard:*** Thank you; it is going well. I will give a bit of background and then move on to the contents, if that is okay. When we responded to the Committee in February, we said that we would move ahead with developing the research transparency strategy. As part of that work, we have brought into play a number of the other recommendations made by the Committee on making information public, lack of visible reporting, a system of sanctions, and so on.

We recognised that, if we were going to make a strategy that was effective and long term and the most efficient way of doing things, we needed to work in partnership, not just with professional organisations but with patients too. We started off by forming an expert group, a relatively small group of around 12 people chaired by one of the members of the HRA board. We had wide representation on that group from the patient voice, research ethics, industry, academia, medical research charities and so on. We worked with the expert group to develop a draft strategy, which we put out to public consultation in the middle of June and ran for three months over the summer.

In the strategy, we set out a number of commitments and what we felt was the HRA's mission in achieving a much wider vision for the whole research community. We posed a number of specific questions around registration, sanctions and another important area, which was the currently low reporting rate to participants in studies. One of the four pillars of transparency that is set out in the Care Act 2014 is making sure that people who have participated in studies hear about the findings of the study. One thing we found in the consultation was dismay among patients and participants that they do not get that information.

We asked for a lot of feedback, and we had five open workshops throughout the UK. We worked with our partners in the devolved Administrations to do that, and we ran an online survey. We got very good engagement and lots of feedback. We have analysed the responses to the consultation, and we are working with the expert group to finalise a recommended strategy. The HRA board will make a final decision about that strategy on 10 December.

Q190 **Darren Jones:** In time for Christmas, along with lots of other issues taking place.

In terms of the consultation, could you elaborate on some of the questions where you had a lot of responses, so it was something of particular interest, and areas where you did not get many responses, because perhaps it did not chime with the people responding to the consultation?

***Juliet Tizzard:*** As I said, we ran five public workshops and an online survey, and those two together amounted to over 700 individuals and organisations that responded to us, which is by far the largest consultation response we have ever had as an organisation. There is strong interest in the issue in the research community and among patients and research participants. The level of engagement was very good. Part of the reason we were able to have quite wide reach and attract a large number of responses was that we worked in partnership with lots of other organisations. They recognised its importance too and wanted to promote the strategy and make it public.

Q191 **Darren Jones:** That included the MHRA.

***Juliet Tizzard:*** Yes, and associated medical research charities, some of the big charity funders. We worked closely with the NIHR as well.

We had good engagement. We also got strong backing for our taking the lead on this. Although people taking part in a consultation are self-selecting, there was a strong positive reaction to the consultation from respondents. We asked specific questions around registration and what would be the right way to fix registration for non-medical clinical trials—the devices and other types of interventions. We can talk through the responses to that.

We asked respondents to prioritise a number of activities that we had already identified as important and that we should get on with. There were some things where we said, "These are the things we are going to do. What would you say are the most important things to start with?" We asked about a number of things that we could do. We wanted views on those and that was where we asked about the three possible sanctions.

Q192 **Darren Jones:** Would you like to elaborate on the sanctions, please? What were people's views?

***Juliet Tizzard:*** Working with the expert group, we developed three possible sanctions. The first was making information public about gaps in reporting. We described it as a league table. There are lots of different ways you can do that, but it was about making it very visible when performance was inadequate.

The second one we asked about is something that is more able to be done by regulators. When people come to us for approval to start their study, the studies are reviewed by a research ethics committee. The

sanction we asked about was whether it would be appropriate to look at the applicant's track record in relation to transparency, whether around reporting, registration or publishing their results. The third sanction we asked about was whether we should ask Government for the power to fine in the case of non-compliance.

In relation to fines, overall, we asked on a five-point scale from not at all appropriate to highly appropriate; 39% of respondents to the online survey thought it would be either highly appropriate or appropriate to use fines. When we asked about league tables, 69% of respondents to the survey thought they were highly appropriate or appropriate. It was an even higher rate for past performance; 75% of respondents thought that would be appropriate or highly appropriate.

People feel that it is partly that research transparency is a hallmark of good practice in research, of ethical conduct, and it would be entirely appropriate for an ethics committee or the HRA, as the co-ordinating body, to look at past performance. The thing that researchers most want is approval for their next study. That is why there was a lot of support for that. There was slightly less support for making public and visible information about poor performance, but again there was majority support for that.

Q193 **Darren Jones:** That all sounds very good. In the pack for our session today, there was a note from your research and transparency strategy group in May that "discussing further sanctions was premature" and that it was better to look at "better systems, collaboration with funders and data sharing." It sounds as if you are properly considering sanctions. Is it just misinterpretation of that note that suggests that you are not?

***Juliet Tizzard:*** The expert group, the research transparency strategy group, met five times and we published the minutes from those meetings.

Q194 **Chair:** Being transparent.

***Juliet Tizzard:*** Of course. That was an extract from a minute of one of the meetings before we went to consultation. It is fair to say that there are differences of view in that group. The resolution from that discussion was that it would not be right to make a recommendation at that point, but to put three possible sanctions into the consultation, and that is what we went on to do.

Q195 **Darren Jones:** In terms of your legal powers to adopt these positions in the future, do you have the jurisdiction to think about sanctions or would you need new powers to do so?

***Juliet Tizzard:*** We took some legal advice early in the process to inform our thinking in this area. We know that the power to fine would require a change in legislation. The Committee acknowledged that.

The advice was that we have scope to take action within the current framework. Not all of it is legislation. There is legislation covering clinical trials of medicines, but the Care Act, which created the HRA and gives us our statutory duty to promote transparency, is quite a short piece of legislation. Because we administer a research approvals process and the research ethics committee process, we have some ability to set conditions there and to use that potentially to take action in future. That is subject to good public law practice, which is that you are clear about your forthcoming requirements and consult widely on them, which is obviously what we have been doing.

***Professor Stephenson:*** We cannot take action retrospectively.

***Juliet Tizzard:*** Yes, that is right.

***Professor Stephenson:*** The legal advice is that we cannot take action retrospectively. We have to start from now and consult publicly.

Q196 **Chair:** Let us say that you implemented a system, or we implemented overall a system, whereby past performance on transparency was taken into account. That is in some respects retrospective because you are looking at what they failed to do in the past. Are you saying there is a difficulty there in terms of the legal advice or are you saying you can do that? They can still correct it, I guess.

***Professor Stephenson:*** I think we would need to pursue it further. That has not been a condition in the past. If we were to set that out as a condition going forward, we would need to be clear that we were allowed to look at people's past performance.

***Juliet Tizzard:*** One thing I would like to add is that we have some existing reporting requirements. I think we discussed this at the Committee's inquiry last year. People who have had research approval and a study approved by an ethics committee are currently expected to report 12 months after the study is finished. That is not something we have had the resources to chase up, but it seems an obvious place to start. There is not a defined dataset for that at the moment. We want to develop that so that we can include things like a lay summary of the findings, whether or not they fed back to participants, and whether they have reported to the relevant registry. That seems like a good place to start.

Q197 **Darren Jones:** I am conscious that I have entirely focused on HRA. Is there anything that the others wish to add on the issue of sanctions and powers of sanctions that you have not already said?

***Dr O'Kane:*** From an MHRA perspective, our good clinical practice inspectors inspect compliance with reporting on inspection. If it is found that a sponsor is not compliant, they can issue a finding, but we do not have legislation as MHRA to take enforcement action currently. That will change under the new clinical trials regulations when it will be part of the legislation.

***Dr Godlee:*** I have nothing to add except the point about needing to make it much easier for academics and companies to register. We have heard about the difficulties. I will take back to my colleagues on the ICMJE whether we could make it not a sanction as such, but a requirement in submitting a clinical trial, that the summary data are already on the database. I cannot see a reason why we should not do that.

Q198 **Chair:** Sir Terence, I appreciate that a decision has not been taken yet. You are not in a position to pre-empt that decision in early December. Can you give us your reflections from your position at the HRA? I have been very struck by all the impediments that were described in the first panel. They were legitimate concerns about the way the system operates and the need for the regulators and the registers to get their act together.

Subject to that, do you have a view about the appropriateness of there being some consequences to your actions? Taking into account, for example, that there are several organisations that have not even responded to a letter from the HRA, let alone responding to us, and are still at 0% in terms of compliance, there need to be consequences, don't there?

***Professor Stephenson:*** Quite rightly, this Committee has focused forensically on things that have not gone well, but we should not lose sight. We should celebrate the success of UK health science. The year before last, there were 104 first-in-human studies in the UK, and there were 69 across the other 27 states of the EU. That is a thing to be very proud of. We now have 1 million patients of whom I am one—1 million people—recruited into trials in the UK, whereas 15 years ago, before the clinical research network, we were struggling to recruit people.

In terms of regulation, we want to be what would be called right-touch regulation, proportionate. I do not want to preclude 10 December, but most regulators would want these issues brought to attention, and we are grateful for that. Start with making it easy, educating people, and making our expectations clearer. The next stage would be telling people what we are going to put in the public domain, and then perhaps league tables, moving on to telling people that future approval would be contingent on past performance.

Q199 **Chair:** Are you suggesting that this is a two or three-year programme?

***Professor Stephenson:*** It is a regulatory ladder that any regulator would use. They would start with trying to change behaviour and sharing good practice.

Q200 **Chair:** You have had that duty in the HRA for some time. Behaviour has improved, but it has not changed enough. It sounds to me as if you are saying you are resistant to deciding in December that there should be some consequences for total flouting of the rules.

***Professor Stephenson:*** Not at all. I am saying that the consequences are on a ladder, and most people would not start with the heaviest approach first. They would try to start with the sanctions or measures that were most conducive. If they do not work, you move through that ladder.

Q201 **Chair:** Right. I understand that, in responding to an individual institution that has failed to report properly, you do not go straight to the hardest sanction. I totally understand that, but you are not ruling out the whole panoply of responses to be introduced as a result of your meeting on 10 December.

***Professor Stephenson:*** We are not ruling out anything. I think Juliet made it clear that financial penalties require legislation, which does not seem very likely in the present climate. That would be a reason. Why go for something that is undoable? Why not start with the low-hanging fruit, the things we can get on with quite quickly?

The only other thing I want to say goes back to Graham's original question. He made the very legitimate point that the most logical way of doing this would be a one-stop shop, where the body from whom you seek ethical approval and where you register the study at the beginning would be the body that would ultimately declare whether you had reported. That needs IT transformation.

The IT system we use currently was developed in 2004; it is 15 years old. That requires a lot of resources. We are working with MHRA. You asked a question, Norman, about when it would come into place. It can only come into place with resources, and anything this Committee can do to advocate on our behalf would be helpful. We have a bid in to the Department, but we need resources for a complex IT system that would deliver exactly what Graham was asking about, in a very one-stop-shop way. It requires resources.

Q202 **Martin Whitfield:** I want to pursue that point. We had our report in October 2018, which you responded to. I am looking for an update about the national audit programme and your discussions with the Department of Health and Social Care. How is it going?

***Juliet Tizzard:*** We included questions about how we would monitor performance in the consultation on development of the strategy. If we are to have clarity about performance, and if we are going to take action on the basis of poor performance, we need a really good monitoring system in place. The Committee recognised that a year ago.

When we first responded to the Committee, we provided a rough costing of what we thought a monitoring service would look like, and we shared that with the Department of Health and Social Care, and published it under freedom of information as well. That is the people side of things. As Terence described, there is a system side of things as well, and the two things interlink. We do not have that function in place at the

moment. We think it is crucial to be able to take forward the strategy, and we are in discussions with the Department now.

Q203 **Martin Whitfield:** Has the costed model changed since it has gone to the Department? Have you had any response about the resources side of it?

***Juliet Tizzard:*** Sorry, could you say that again?

Q204 **Martin Whitfield:** I was wondering whether or not there have been any changes to the costed model that you originally proposed, and that was published, as to where we are now.

***Juliet Tizzard:*** Yes, we are working on that at the moment. We do not have a finalised strategy yet, but we have a good idea of where it is going. We are looking again at that model in light of that. Originally, we had an allowance for monitoring registration. We have been consulting on ways that we can make registration happen automatically, much as it does for clinical trials of medicines at the moment, which would obviate the need for an after-the-event monitoring service for registration. It means that we could focus much more on reporting and feeding back to participants.

Sorry. That was a long-winded way of saying, yes, we are revising the model at the moment in light of the strategy.

Q205 **Martin Whitfield:** I suppose I would sarcastically say, "Take care of your risk register when you do that."

The final part I was going to ask about may be the final part for a lot of reasons. There was talk about a research summary tool being developed. How is that going?

***Juliet Tizzard:*** There are a couple of options. The research summary tool, for those who do not know, is a part of our website where we publish information about studies that have received ethics approval. It is quite old and not the most interactive tool. We could redevelop that, and we might think about doing so to provide a kind of registry service perhaps for the observational studies, the bulk of studies that we review—about 2,500 each year that are not clinical trials. We could fold it into a one-stop shop, as Terence described, and we are working on a model for that at the moment. Until we have some clarity about that, the research summary database will remain as it is, but it might be a good model for the observational studies in future.

Q206 **Martin Whitfield:** There are a lot of ifs and buts going around and "depending on other circumstances." Do you think that the one-stop shop is the answer, and that with the right sort of support, push and resources it would solve a lot of the historical problems that have come up? More importantly, would it be viable to go into the future as a way of ensuring that we are not back here in six years' time with a percentage of people unable to register their data?

***Juliet Tizzard:*** I think that is the direction we should move in.

Q207 **Chair:** We will finish with some joyous questions about Brexit. Will UK researchers and sponsors of trials be expected to register trials and data with the new EU clinical trials portal even if it comes online after the UK has finally exited the EU?

***Juliet Tizzard:*** Can I ask Martin to answer that question?

***Dr O'Kane:*** I will do my best. You are describing a situation after we exit and the new EU portal is online.

Q208 **Chair:** Yes, because of delays with the technology, as you suggested earlier might happen.

***Dr O'Kane:*** If UK researchers are running a multi-state trial, yes. Because of the other member states involved, the information about the study will need to go into the EU portal. We will also, at that time, have a UK hub, as being developed currently by HRA, so that sponsors can apply for clinical trial authorisation in the UK. Even after the new regulation in the EU, it is a centralised portal but it is not centralised authorisation. All the member states involved will still have to give national authorisation for that.

Q209 **Chair:** Are you happy with that answer, Juliet?

***Juliet Tizzard:*** I am happy with that answer.

Q210 **Chair:** Martin and Juliet, the Government's no-deal Brexit guidance on clinical trials reporting indicates that a UK-specific clinical trials hub will be in place next year. Is that hub the same as the MHRA/HRA pilot system discussed earlier?

***Juliet Tizzard:*** It is related. The pilot system is about testing the joint UK decision under the regulation. The portal is the wider thing that Martin described; it is a redevelopment of the current IRAS portal that will be ready for when the regulation comes into being.

***Dr O'Kane:*** It is a step-wise process. The first step is getting the integrated working together, and the next step will be allowing applicants to use a new UK hub to register their study.

Q211 **Chair:** Is the UK hub being designed to integrate with the new EU clinical trials portal regardless of whether we leave the EU with or without a deal? Is that part of the design?

***Dr O'Kane:*** We had to have discussions with HRA and manage the design of the new portal on a modular basis, building it potentially at risk but being able to pivot, dependent on the Brexit scenario. I cannot answer on whether it will be integrated with or without a deal. Certainly, if we have a deal and we have access to the EU portal, we will integrate with that in order to manage our national workload.

Q212 **Chair:** Currently, sponsors must go through the MHRA to make changes

to the data for studies on the EU clinical trials register. In the event of a no-deal Brexit, can you confirm who sponsors will need to contact, and have they been made aware of this?

***Dr O'Kane:*** You are describing a scenario where a sponsor has information on the current EudraCT database, and if we exit the EU and do not have access to that, how do they update that? The EMA will have to update that for them. If we do not have access to the EudraCT database, the sponsor will have to contact the EMA directly.

**Chair:** Thank you all very much indeed. We really appreciate your time; it has been very useful.