HOUSE OF COMMONS

Health Committee

Oral evidence: Brexit – medicines, medical devices and substances of human origin, HC 392

Tuesday 12 December 2017

Ordered by the House of Commons to be published on 12 December 2017.

Watch the meeting

Members present: Dr Sarah Wollaston (Chair); Luciana Berger; Dr Lisa Cameron; Rosie Cooper; Dr Caroline Johnson; Andrew Selous; Maggie Throup; Dr Paul Williams.

Questions 114 -218

Witnesses

I: Dr Jayne Spink, Chief Executive, Genetic Alliance UK; Dr Beth Thompson MBE, Head of UK and EU Policy, The Wellcome Trust; and Aisling Burnand MBE, Chief Executive, Association of Medical Research Charities.

II: Steve Bates, Chief Executive, BioIndustry Association; Leslie Galloway, Chairman, Ethical Medicines Industry Group; and Suzanne Halliday, Head of Medical Devices, British Standards Institution.

Written evidence from witnesses:

- Dr Jayne Spink
- Dr Beth Thompson
- Aisling Burnand
- Steve Bates
- Leslie Galloway
- Suzanne Halliday

Examination of witnesses

Witnesses: Dr Jayne Spink, Dr Beth Thompson MBE and Aisling Burnand MBE.

Q114 **Chair:** Good afternoon and thank you very much for coming to the second session of our inquiry into the effect of Brexit on medicines, products and devices. Could we start by stressing that there is another inquiry going on by the BEIS Committee that will be predominantly looking at the impact on the life sciences industry itself? The main focus of this inquiry is going to be the impact for patients. So, keeping that in mind, could I ask you all to introduce yourselves to those following from outside the room, starting with you, Dr Spink?

Dr Spink: I am Jayne Spink, chief executive of Genetic Alliance UK. We are a membership organisation with over 200 members of the voluntary sector who support people affected by genetic conditions or fund research. We also lead the Rare Disease UK campaign and we are home to SWAN UK, which provides support to families who have a child or young person affected by a rare condition that is likely to be genetic in origin.

Dr Thompson: I am Beth Thompson, head of UK and EU policy at the Wellcome Trust. Wellcome, if you do not know us, are a medical research charity. We are a global foundation that is dedicated to improving health. We spend around £1 billion a year, and about 75% of that is within the UK. We support around 10,000 researchers here too. We fund across the pipeline, from basic research through to translation.

Aisling Burnand: I am Aisling Burnand. I am chief executive of the Association of Medical Research Charities, a membership organisation that comprises over 140 medical research charities based here in the UK. Wellcome is one of our members. Our members collectively invest about £1.6 billion in medical research. In the past year it funded 17,000 PhD students and had 170,000 patients in clinical trials here in the United Kingdom. The members fund research from basic research in the lab, in universities, through translational research, perhaps in a hospital setting, right through to research at the patient's side, which could be thinking about care pathways and how to improve care and other things that are close to the patient.

Chair: Thank you very much. Andrew is going to open the questioning today.

Q115 **Andrew Selous:** Thank you. If we are unable to secure continued access to European research funds and the collaboration that goes alongside that, what would that mean for patients in practical terms? We will just wait for the bell to finish. Did you hear the question? Shall I repeat it? Let us start with you, Dr Spink.

Dr Spink: I am sorry, but could you repeat it?

Andrew Selous: Yes, of course. Bells are an optional hazard of this place. If we cannot secure continued access to European research funding and the collaboration that goes alongside it, what would that mean in practical terms for patients here in the UK?

Dr Spink: In terms of rare disease research, it is completely impractical to imagine a scenario where a clinical trial for development of a rare disease medicine could be supported entirely within one state just because there are too few numbers of anyone with a particular condition to support a clinical trial. I was in fact trying to think whether there is any licensed product that has been developed solely within the UK and I could not think of one.

Orphan designation is a requirement for framework programme funding in select topics, and that has been so since 2009. Since that came into force, there has been over a 50% increase in the number of orphan medicinal product applications submitted, and the number of designations granted by the Commission in the period 2009 to 2015 was significantly higher in comparison to that previously.

There has been about €900 million of funding since FP7 into 160 projects that are researching orphan medicinal products in the context of rare diseases. The ability to participate as part of those funding collaborations and clinical trials collaborations is absolutely fundamental to patients in the UK and our ability to access those trials, and for the researchers and the expertise that we have here to collaborate as part of those European groups. If we did not have that, it seems very likely that access to trials, and then access to licensed medicines for patients in the UK, would be very much impeded.

Q116 **Andrew Selous:** Dr Thompson, again with a continued focus on what this would mean for patients specifically, what is your take on the question?

Dr Thompson: I would support what Jayne has said. It is interesting that when we look at the outputs of research collaborations and international collaborations we see that you get higher quality, as in papers that are more cited, when people have collaborated together internationally. There is a direct chain there from the quality of research and doing really strong research that leads through to the benefits to patients. We cannot underestimate the impact of the importance and significance of collaboration.

I would say that there is reason to be optimistic in terms of a future collaboration on R&D funding in particular. We have seen ambitious statements from both the UK Government and from the European Commission, because there is so much mutual benefit to patients but also to the wider research sector.

Q117 **Andrew Selous:** Can I interrupt? To what extent do you think Europe needs our world-leading expertise? That is a bit of a leading question to

you. How valuable is that to our European friends?

Dr Thompson: I think that the UK strength across many types of research is really valuable to Europe and we should make sure that we can continue collaborating so that we can deliver that strength together. If you look at genomics, for example, we have huge genomics capability in the UK in places such as the Wellcome Trust Sanger Institute and developing through the 100,000 Genomes Project. The strength that we see there would be hard to reproduce easily within the EU very quickly because it takes a significant amount of infrastructure. Those UK strengths contribute to those studies across the EU. Equally, we benefit from the data sharing and the trials, as Jayne has said, that take place across the whole of the EU 27 and the UK.

Q118 **Andrew Selous:** Thank you. Ms Burnand, is there anything you would like to add to that?

Aisling Burnand: We have talked already about the collaboration bit being vital and the importance of clinical trials for patients. Another area, if we are looking at the R&D environment, is around talent and ensuring that we can continue to collaborate and generate a strong talent base here in the United Kingdom, and for that talent base to be able to share its knowledge across Europe. It is also about benefiting from collaboration with the best breast cancer surgeon, for example. If they happen to be in a particular country, you want to be able to collaborate with them in order to get the best care. You also sometimes want your young people to go and train with the best person, and to come back to the UK to train up our best and brightest.

I would emphasise the talent bit as being really important as well as the collaboration that absolutely we want to see. The UK has been a great collaborator in European research. I am sure that will continue as best it can afterwards, but we need to understand how we will be able to engage. We also need to understand about the financial situation and where the money will come from post 2020, in order to continue to fund research.

Q119 **Andrew Selous:** That leads me on to my next question. Given the referendum result last year, what would be the ideal scenario for the UK in relation to the EU's research and development activities?

Aisling Burnand: From a patient perspective, patients want faster access to clinical trials and to medicines. Those are the sorts of things that a patient absolutely would want. Thinking about the post-Brexit era, how do we ensure that we maintain as close as possible regulatory alignment and collaboration with other European member states in order to deliver positive results both for UK and European patients? That is essentially what we would like to see.

Q120 **Andrew Selous:** Dr Thompson, you were expressing some optimism that there is no reason why that could not happen.

Dr Thompson: Under a wide range of Brexit scenarios, we could get to a positive agreement between the UK and EU 27 on research because of that mutual benefit that we have already talked about. If there was no deal, that would be extremely challenging for the reasons about funding, the movement of people and regulatory alignment, which would be really difficult both for patients and the research community. Under any other situation that is not no deal, if the political will is there, we should be able to reach a good agreement.

Wellcome and the Royal Society are working on a new project at the moment to bring together key stakeholders in the UK and in the EU 27 to discuss what we think the shape of a future partnership should look like, and we will be able to report on that in February 2018. We hope that will inform the negotiations towards a science and innovation agreement.

Q121 **Andrew Selous:** How would we need to adapt our legal framework for research and development after leaving the EU in order to make this happen? What would we need to do?

Aisling Burnand: That is such a massive question, practically speaking. Let me paint a picture. We have spent the last 40 years putting together, essentially, a patchwork of frameworks to support research, clinical trials and so on to benefit patients. That has taken a lot of time, painstakingly stitching together each particular piece in order to put a framework together. We have seen things like GDPR, which is coming into force in May; we have seen the clinical directive and all these things.

Q122 **Andrew Selous:** Sorry, but for the benefit of people listening who may not know, could you say what GDPR is, and, if we can, avoid acronyms as much as possible because not everyone knows what they are?

Aisling Burnand: They are the general data protection regulations. A whole series of regulations and directives have been put in place, which have served patients very well in ensuring that patient safety has remained paramount. We have been able to ensure, for example, that, should we need to remove a medicine quickly, we have been able to do that.

The point I am making by using this metaphor of a patchwork quilt is that, essentially, to try to move to creating a new one overnight is just not workable. With clarity on where we want to get to, with a clear transition period that allows us to think about how that plan would be put into place, and with an implementation plan, I believe that we can get to a better place, or at least the place where we are now.

There are risks in this area. If we suddenly find ourselves in a situation with no regulatory alignment around clinical trials, for example, we are going to see that there is likely to be a delay where the UK system has to run similar trials, which will delay access to patients for those drugs.

There is well-documented evidence here. Switzerland at the moment receives its products for patients about 157 days later and it does not

have alignment with the EMA, but with countries such as Australia and Canada, which do have a reciprocal agreement in place, they often receive access to products six to 12 months later because of that. So, there are risks in the system. What we are clear about, and one reason we wanted to give evidence, is that we believe there should be no impact on patients from day one and that UK patients should continue to receive, as they do now, access to innovative products and medicines, as indeed should other member states.

Q123 **Andrew Selous:** As a final question from me, do you think it should be possible to avoid those delays that you talked about in the case of Switzerland, Australia and Canada?

Aisling Burnand: At the moment, my personal view is that, with the closest possible alignment that we can have that really thinks about how we mitigate against doing that, you would expect that we could minimise that. When you look at the examples that I have given, they are both under different types of regimes and have not been able to achieve it. It should be our vision and ambition to be able to do that, but absolutely I think that it is a real challenge to be able to do that.

Q124 **Chair:** There is a clear ambition and intention on the part of stakeholders in the UK and in the EU to make this happen because it is in everyone's best interests. However, we also know that there is a message that there will be no sector-by-sector deals. So, should all this start to fall apart at some point in the process, what kind of contingency planning are you doing at the moment to cope with that in the future?

Dr Thompson: That may be a question for the later panel rather than us, because, as funders, it is the people whom we fund who are thinking about that more directly at the moment, but it is absolutely critical from our perspective that we get as much certainty as soon as possible to enable them to plan. We have seen from the deal on phase 1 that was published on Friday some very positive signals in terms of Horizon 2020 funding, for example, and future alignment. As you say, we have seen the intent from both sides but it is hard for people to plan.

Q125 **Chair:** How closely are you working with your partners in EU nations to make sure that they are also providing a very clear message to EU negotiators that we absolutely cannot have patients on both sides of the channel suffer as a result of this?

Dr Spink: There are in the case of rare diseases particular risks to the remainder of the EU 27. As I have already said, it is unrealistic to expect a rare disease clinical trial to take place in a single state, and we do have a great deal of leadership in the UK around rare disease research and clinical trials research. The UK has historically provided a lot of influence and thought leadership, particularly with innovative medicines and innovative approaches such as gene therapy, research using human embryos and advanced therapies. If we add into that the MHRA's lead on between 20% and 35% of the EMA's licensing and vigilance work—which

is higher in the case of advanced therapies—if we have a gap there in that provision of expertise, you could expect to see a knock-on effect for patients across Europe and also in standards and safety monitoring, and the impact that that might have on exports and imports of innovative products, many of which are manufactured here in the UK. So, I do think that there is a risk to patients across Europe, and the impact of any divergence will be felt by people with rare diseases first.

Q126 **Chair:** If there was not access, say, to the EU clinical trials portal, you think they would be the first to be disadvantaged by it.

Dr Spink: Yes. The orphan drugs legislation has provided a great deal of incentive for the development of orphan medicines. We now have 164 marketing authorisations across 147 products since the introduction of the regulations, and, as of the end of last year, 1,805 orphan designations, which is absolutely fantastic and really shows the impact that the orphan drugs regulations have had on incentivising the development of such products. One asset of the European Union is that it has a population of 500 million, so you can use that critical mass to leverage those types of incentives and it is difficult to imagine how you would replicate that in a single state.

Aisling Burnand: To give the example of Duchenne muscular dystrophy from one of my members, at the moment there are some very promising products that are currently in front of the EU and awaiting authorisation. There is a real worry among that community that, essentially, there could be further delay if we suddenly find ourselves not part of the framework that is going to govern these medicines. For patients, that is devastating news because it adds extra months of time where they might have to apply to the UK separately for a new licence and go through the whole process, which of course is going to be costly and thus more costly for the NHS as well.

Dr Spink: A concern for rare disease patients is whether, if the environment in the UK does not enable that seamless transition to continue collaboration on drug development, there will be a knock-on impact in that the UK will not only not be the first choice of country in which to launch or apply for a licence, but, in fact, in the extreme, it may be a disincentive to launching in the UK at all.

Q127 **Dr Williams:** I think you have partly answered my question already. I want to know what the Government need to do to make sure that UK patients do not experience any of those delays. What I have heard is the words "closest possible alignment," but I have also heard that Australia, Switzerland and Canada have not been able to achieve that. Is there any country that has been able to achieve that close alignment, and is there anything else that you would like to add that we should be asking the Government to do in order to make sure that patients are not getting delayed access?

Dr Thompson: Can I pick up first on the clinical trials point, because there are two separate but related issues here? There is how we conduct clinical trials in the regulatory framework on that, and then perhaps I can pass over to Aisling or Jayne to cover the licensing point, to which they are closer.

As to clinical trials, the UK has had a leading role in shaping the EU legislation, the current directive and the new regulation that we expect to come into force later. That was a really pivotal role. The new regulation is a great improvement on the directive. We know in terms of the practicalities of running trials that there is a lot of bureaucracy, and that is right because it is there to protect patient safety.

Researchers do not want to see duplicative bureaucracy where they have to do the same but slightly different things twice, because it will make the UK a less competitive destination to run those trials in, which is a long way of coming back to your answer in terms of what needs to happen, which is that we do need alignment on the legislation. The clinical trials regulation will not be included in the withdrawal Bill because it takes effect later, so it is bound to put that off. There will need to be some legislative fix to manage clinical trials, but it is not as simple, if that is simple at all, as fixing the legislation itself. We also need to negotiate alignment because it is a partnership. We cannot just unilaterally say we will take part.

As part of the phase 2 negotiations, we would like to see the Government and the EU 27 agree how they are going to manage that process and how they will align, and that will include things such as access to the portal and how that data sharing will work.

Of course, the legislative framework is very complex. As Aisling said, it is a real patchwork. There are other things such as data protection law where we will also have to align, otherwise we will see fragmentation in other ways.

Aisling Burnand: I will give you some facts. Between 2004 and 2016 there were almost 5,000 UK EU trials involving patients actually happening. Currently, there are over 1,500 clinical trials taking place that have a UK sponsor and 50% of those are going to continue post 2019. There will need to be clarity on what happens to patients involved in those trials and what the legal status is of some of those things. Those are vitally important things and will be causing real anxiety among patients if they are not resolved in that sense.

Also, on Jayne's point and giving you another example, Cancer Research UK is involved in over 200 clinical trials; about a quarter of those are run with at least one other European country. There is a good example of a pan-European study in the area of pancreatic cancer. Pancreatic cancer, as you may know, is something that many people do not survive, and do not survive for very long, so improving survival rates is vitally important. Also, it is very difficult to recruit patients into clinical trials. But through

this trial, which has been spearheaded by the University of Liverpool working with EU experts, they were able to recruit about 732 patients into clinical trials for that and have seen an improvement in survival rates of about a third surviving for more than five years. The challenge sometimes is in rarer diseases.

We must remember with the genomic revolution that is coming that the ability to stratify patients into smaller cohorts means that we may find more needles in many haystacks and bring them together. That is going to be really important in trying to have a framework that is in place that allows us to run multination studies in rare diseases, the paediatric area and, possibly, as we go forward, into the diseases of the ageing.

Q128 **Dr Caroline Johnson:** I have a question about rare diseases and collaboration, because collaboration is more than just regulation; it is about interpersonal communication and relationships. You talked about doctors moving from one hospital and one country to another, and then working together on those same topics, which we know happens, but it happens outside the EU already. We are already doing studies in neonatology with Australia; we do studies with Canada, China and America. You have said already that they do not have regulatory alignment with us, so we are managing it already, are we not?

Aisling Burnand: I would say certainly we are, but we know what we are dealing with and we have taken a period of time to get to that regulatory alignment, so we know what the rules of engagement are.

Q129 **Dr Caroline Johnson:** I am sorry, but I am confused. You were saying there was no regulatory alignment between ourselves and the EU and Australia, for example, but now you are saying that we do have it.

Aisling Burnand: Maybe the better phrase would be regulatory understanding. We have a framework; we know what the rules of engagement are with Australia, for example. If we move to post Brexit, we want to know and understand what the framework would be in order for us to be able to collaborate and engage with other member states. At the moment that is not clear.

Hopefully, as we move forward, it will become clear, and there will be a pathway—a transition—to allow organisations to adapt and for companies also to think about ensuring that the right framework is in place legally to continue to conduct clinical trials. At the moment, UK organisations, both charities and commercial organisations, are sponsors of clinical trials. On day one of Brexit, if we have not sorted out what the legal framework is for that, the sponsor of that clinical trial will no longer be able to be a sponsor for it. So, who is sponsoring that clinical trial and what happens? Those are the sorts of detailed things that need to be sorted out.

As Beth says, we can end up thinking about how we collaborate more broadly, but the challenge at the moment is that we need a clear pathway to it and some time to unpick what has been 40 years of putting

a framework in place. I am not saying it is going to take us another 40 years, but we need to be clear about how we ensure that we understand what the framework is and what the legal certainty is to be able to ensure that patient safety is maintained.

Q130 **Dr Caroline Johnson:** From a legal point of view, though, we are bringing into UK law all that is in the EU law as part of the EU withdrawal Bill. Presumably, at least on day one, the legal regulatory aspects of the framework will be the same.

Aisling Burnand: For clinical trials not, but I will let Beth explain why.

Dr Thompson: Because the clinical trials regulation will take effect later, we will need to deal with that separately from the EU withdrawal Bill. The clinical trials directive is already active, so that will be covered under the withdrawal Bill. It deals with some of the legal problems, as you say, so people will be operating in the same legal framework, but, where at the moment there is co-ordination that really simplifies the process for researchers, we do not necessarily get that from copying and pasting the legislation. It is not quite as straightforward as just having the same law.

I think it is important to look at the wider set of regulations as well. If we look at the general data protection regulation and the data protection directive, as it is now, that governs not only data sharing between the UK and other member states as they are now, but it also sets the framework by which the UK shares data with Canada, Switzerland and other adequate countries. That is really important in the way we share patient data within clinical trials, for example, but also for other epidemiological studies. There is a risk that if we do not pick up those things now we will end up not being able to share data easily. There are mechanisms, but everything gets more complicated and difficult, and that is where patients start to lose out.

Dr Spink: On the point of rare diseases and collaboration across Europe, there is an important mechanism under the cross-border healthcare directive in terms of the incentives to set up European reference networks. There are 24 of those, in which the UK takes a role in 22, and a leadership role in a quarter of those. That is an important mechanism for ensuring collaboration and also clinical and research development in the UK.

If we look to the United States, they have a huge population and it is perfectly possible to conduct a clinical trial entirely within the United States for a rare disease. I cannot think of an example of a trial that has been undertaken jointly by the UK and US in terms of the regulation of that and the ability for UK participants—UK volunteers—to take part in that trial.

Having access to pan-European trials, particularly in the context of a rare disease, is critically important, because for many rare diseases there are no existing treatments, or existing treatments may be suboptimal. For a

large proportion of rare diseases, those conditions are degenerative, so your ability to access medicines early, even if that is through a clinical trial, is incredibly important to patients with rare diseases.

The least desirable scenario would be for trials to be ongoing in Europe to which UK patients have no access, and then to see products licensed in Europe to which UK patients have no access or delayed access, and not to support that clinical and research expertise that we already have, which we have built up over decades and which is so well integrated across Europe in terms of influence, partnerships, collaborations and data.

Q131 **Dr Caroline Johnson:** But since we are leading in so many of these trials, or so many of these missions, actually it is in Europe's interests as well as ours to ensure that that continues.

Dr Thompson: Hopefully.

Dr Caroline Johnson: It is very much, "Where there is a will there is a way," and it does not sound as if it is excessively complicated to sort out.

Q132 **Maggie Throup:** Given the NHS's existing track record of below-average uptake of new medicines when you compare the UK with countries such as France, Belgium and Germany within the EU, and, outside the EU, Australia, Canada and the States, do you think most patients will wait longer than they do now for new treatments after we exit the EU, or, because we are already behind the game, will it not make any difference?

Dr Spink: I think it will extend waiting times, but the UK is not at the top of the league, as you have pointed out, in terms of providing access through the NHS to new and innovative products. There are instances where patients have waited three to five years post licence to have reimbursed access through the NHS on a routine basis, and that is in the rare disease arena. I think there is something else beyond the incentive at a European level. There is something about how we evaluate and price medicines in the UK that does not work terribly well, particularly in the context of health technology evaluations and assessments for rare disease medicines; but perhaps that is something else that needs fixing that is not directly impeded or favoured by Brexit.

Q133 **Maggie Throup:** Perhaps we will come on to the Accelerated Access Review and all that side of things as well.

Dr Thompson: It is further from the space that we work in at Wellcome, but we are very pleased to see that the Accelerated Access Review is being implemented. It is definitely a step in the right direction and we welcome it for that reason. This is one of those things where, following Brexit, there is going to have to be more focus and attention to make up for those things that are completely within UK control at the moment such that we really enhance and shape those as much as we can. We are seeing some of that come through the life sciences industrial strategy and other discussions. There is also a new paper from NHS England and the

National Institute for Health Research on research and uptake. The more that kind of thing happens, the better from our perspective because it can only make things better for patients.

Aisling Burnand: I was part of the life science industry strategy board and obviously trying to ensure that patient views and charities were considered as part of that. I do not underestimate the challenge that we have in the UK. Clearly, some of the things we have talked about would see a delay to medicine, further exacerbating a problem that is already difficult. There is a question around what that does in terms of costs, what the impact is of some of the additional costs and whether anybody has thought about that. From a patient perspective, that is something about which I would be worried. We are already seeing an NHS that is under pressure, so anything that might add further cost that could be mitigated would seem to be unwise at this particular moment in time.

That said, we can recognise through the life science industry strategy that there are some fundamentally good things about the United Kingdom. There is real opportunity in a post-Brexit era to build on some of those things. We are particularly good at clinical trials. In terms of where we are in the world, we are world leading in phase 1 clinical trials. There are some things that we can build on, but we need to ensure that there is the opportunity for new things to be adopted fast within the NHS so that patients have access to them. That is absolutely what they tell us they want. They want faster access to new medicines and treatments. Sometimes faster access can keep them more productive and contributing more broadly, minimising the impact on their social care budget, if we see that, but we do not necessarily take a joined-up view, as I am sure the Health Committee will know, across the space. We have to recognise there is a challenge and that all our problems are not going to be solved on day one.

Q134 **Maggie Throup:** Dr Spink, you want to come back in.

Dr Spink: I want to add something on the life sciences industry strategy and the proposal for a single, value-led, NICE-managed process. The position from Genetic Alliance UK is that this is not necessarily the answer, unless there is a reconsideration of the approach and process to HTA. That is something that has been highlighted by the all-party parliamentary group on rare genetic and undiagnosed conditions. Also, there is a concern that, with the AAR, there is a requirement around cost neutrality, which means that there is unlikely to be a positive impact in the context of rare disease medicines. I just wanted to add that into the mix.

Q135 **Andrew Selous:** I would like to go back to Canada for a second in respect of United States licensed drugs. We are obviously focusing on Europe because of Brexit, but America has a huge drugs industry and its own licensing regime. Have you looked at how Canada accesses drugs approved in the United States, how quickly that happens, how the UK could be helped by access to US-approved drugs, and what are our links

there?

Aisling Burnand: I am afraid I do not know enough about that. I would have thought that the people coming next from the pharmaceutical industry and others would be able to give you something. That data absolutely exists and I am sure they would be able to provide it, but I do not have access to how Canada does it versus anywhere else, for example. There is something here, though, about the size of market that is important for us at least to acknowledge. With the European Union, effectively, it represents 25% of the global pharmaceutical market, so it is a sizeable market, whereas the UK represents 3% of the market. I do not know how much Canada represents in comparison.

These things are important because it is about the attractiveness of the country to launch a product in the country. At the moment, the UK has probably been seen as not necessarily an interesting place to launch a new product, but, because of the science and because of the clinical trial environment, it has been a positive environment in which to conduct the research and thus sometimes to think about a launch market. We cannot jeopardise the clinical trial environment. We have to ensure that, otherwise we lose the piece that anchors the larger organisations and the emerging biotech organisations to the UK, and, with it, patients will lose access to the newer products that are used in clinical trials. Subsequently, that would be a very bad day for UK patients.

Q136 **Luciana Berger:** If the Government are unable to secure a close relationship with the EMA and therefore diverge from EU regulations, what impact do you think this is going to have for UK patients?

Dr Spink: In terms of rare diseases, the impact would be first felt there and it would be very severe in that, if there is not alignment, regardless of how favourable the general environment is for trials, the likelihood of a company seeking to trial a rare disease medicine through to licence in the UK would be vanishingly small, mostly because we just would not have the population to support recruitment into a study. That is perhaps the fundamental reason why misalignment or drift between the European regulations and the UK would be so disadvantageous to rare disease patients in the UK.

Dr Thompson: I would reiterate the point that there is this combination. We have some great characteristics within the UK at the moment in terms of the strength of our research base, the industry that is located here and the medical research charity sector. There is a lot of potential in that and we do well on some of it at the moment, as Aisling has said, but there is a challenge. Because we are only 3% of the share of the global pharmaceutical market and because we only have a small population compared with the EU bloc as a whole and the US, when you combine those factors, we have to work even harder to be really competitive as a destination for trials and launch of products.

It is really important to consider that in the round because the whole system works together and the different parts feed off each other, and we need to keep that whole system working well and tweak it, where we can, to make things better. Absolutely, if we cannot align, we will have to find something as close as possible, otherwise it is the patients who will miss out.

Aisling Burnand: The worst possible thing is that we have a hard Brexit and we do not get the alignment that we need. That would be very worrying for patients. We are clear that there must be no adverse impact on patients because of Brexit. In fact, we need to be thinking about how we can ensure that we can improve things for patients as we go forward. For me, it would be unthinkable that we were not able to do that. There are practical issues on day one, which I think the industry will be able to talk about, but simply the movement of medicines and their components in and out of this country would be an immediate worry on day one. We have sometimes seen the impact of that with a couple of weeks of the channel tunnel being blocked through a strike, when we have suddenly realised that, from a resilience perspective, we have some challenges in being able to deliver certain important life-saving medicines. If you are on dialysis or if you have had a transplant, there are certain products that you need in order to thrive. There are some really serious concerns if we do not think through what happens on day one of Brexit.

I believe optimistically that where there is a will, as you have just said, there is absolutely a way—we can find a way—but we need to understand where we are going, how long we have for the transition and we need a clear implementation plan to make that happen. That will reassure patients and give them a degree of comfort that there is hope, which, in the end, is absolutely what patients want. They want hope—hope to be part of clinical trials, hope to be able to improve on medication and lead a productive life.

Q137 **Luciana Berger:** We are going to address the questions of possible border disruptions in our next panel section, but can I ask the panel whether you think there are any opportunities for the UK if we were to diverge from the EU in a way that could in any way add value to both patients and the economy? You might think that there is not, but we have to ask the question.

Dr Thompson: We have to be very careful about having our cake and eating it. Regulatory alignment is crucial, as we have already discussed, and therefore the opportunities in those specific areas are limited because we need to prioritise ongoing harmonisation and alignment. Where there may be opportunities, though, are outside those specific areas of legislation where there are things that the UK can do even better. Some of those we have touched on in the discussion on the life sciences industrial strategy, but there may be specific regulatory opportunities.

If we look at something such as mitochondria donation—where the UK has a world-leading regulatory framework—that is something that is currently in UK competence and would go on being in UK competence in the future. We have to make sure that we make the most of those. I am thinking of things such as machine learning or genome editing, where the UK could be at the cutting edge of these technologies in the science, but there would also be a regulatory framework that respects the ethical and social issues that underpin them. We have a great track record in that and it is something on which we absolutely need to build.

Q138 **Dr Cameron:** Given the issues that you have been raising and that we have been leading on for such a long time in many of these areas, it seems to me that many of the top people will be here in the UK doing this work. What are the risks, in terms of the brain drain from the UK, that we could lose the excellent scientists that we currently have?

Aisling Burnand: Maybe I will kick off because I have some information from the British Heart Foundation, who polled some of their researchers fairly recently in June. There is anxiety, as has been well reported among researchers in the scientific community. The key findings probably help illustrate the point. Almost half of those BHF-funded researchers are more likely to take up a post outside the UK than before the vote to leave the EU. This figure rose to about 80% among non-UK EU nationals. Of those who said they are more likely to take up a research post elsewhere, almost 80% said they are uncertain about the availability of funding, and they were at that time—it has changed—uncertain about, obviously, EU nationals. That has since been cleared up. Almost half said that they feel there are more opportunities for collaboration now elsewhere. Also, there had been a perceived reduction in the proportion of applicants from the EU to research posts; 70% of those advertised posts in the past year had seen a reduction of applications.

We have to accept that it is already having an impact. This means that in the post-Brexit era we need to be able to communicate, as the life science industrial strategy sets out a little bit, about what is the future, the hope, how we are going to ensure that we have an immigration system that is welcoming of people in research and science at all levels, from your leading eminent scientist right down to the researchers just starting out in their career, and everything in between. That is really important.

The other thing that is important and that we need to look to is how we tell our story, and how we tell it globally, about what is great about the United Kingdom and the excellent things that we have here in the United Kingdom where we have been world leading. To coin the phrase of the Mayor at the moment, we need to communicate that we are absolutely open for business, that we do want to be a good science and research citizen globally and to continue to play the role that we have. However, I have to say that we have our work cut out. What we really need from the

UK Government is to put some attention behind the narrative and what we are saying globally post Brexit.

Dr Spink: I do not think that research should be viewed by anybody as an add-on to the clinical aspects of care, because research excellence and clinical excellence go hand in hand. The more innovative and research-ready you have your clinical base, the higher the standards, the better the outcomes and the better the quality of life, ultimately, for patients. If we saw a brain drain in research, there would be some very noticeable impacts in clinical excellence also.

Q139 **Dr Cameron:** So that is a concern.

Dr Thompson: I would echo the message that we are starting to see an impact now. At the Wellcome Trust Sanger Institute we have seen around a 50% reduction in the number of non-UK EU applicants applying for PhD places. Talking anecdotally to the people who run our centres who have had people lined up to come to the UK, they are now struggling to attract and bring them in, and some of them have had really great positions in the UK that people would have jumped at. They have been turned down, so it is real and it is an impact.

It is great to see that we have some more certainty on citizens' rights for those currently in the UK as part of the phase 1 discussions, but, as Aisling said, we do absolutely need a simple and swift migration system following Brexit. For us, we think the current migration system of tier 2 visas, which is where most of them would be applying for skilled workforce visas, will not work if we just open that up to EEA nationals as well, because the Home Office simply does not have the capacity to cope with that. We need something that is easier and lighter touch, otherwise we will lose that easy flow.

Q140 **Dr Williams:** Just to understand that, what is the impact for patients of these non-UK EU nationals not taking up these PhDs? Won't people say that that creates more opportunity for UK professionals to fill those places and therefore provide services to patients?

Dr Thompson: It is critical that we train our students in the UK so that they are in the best position to take up places that they can, but we know that science thrives on the flow of ideas and the flow of people, and that movement of people. It is such a critical component of science that we cannot merely say, "We will stay as the UK." We have great talent here and we should celebrate that, but by moving people around they learn different things and bring in different ideas. That knowledge exchange is really important.

Aisling Burnand: A really good example of that is the Francis Crick Institute, which Wellcome and Cancer Research UK funded along with others. I always want to emphasise that the fact that charities fund some of these things is a real jewel in the UK crown—that so much money raised by the public then funds research in this country. What is

interesting is that it is all about interdisciplinary research and bringing in other aspects, but it is absolutely about the diverse intellectual talent base—different ideas and different people. The institute at the moment has people working from 70 different countries and 40% from EU countries outside the UK. If you have not been, it is a really vibrant place and very much looking at basic research and into early-stage clinical research. It is an excellent facility and very much part of the sort of thing that the UK can and does do brilliantly, which we would not want to see undermined.

Q141 **Chair:** It works both ways. We have heard evidence that 72% of UK-based researchers have spent time at non-UK institutions between 1996 and 2012. What percentage of that is within Europe? Is that the majority of them within Europe or is it just that you do not have any information about that?

Dr Thompson: I do not have that figure off the top of my head, but we have some more data on that that we could provide.

Q142 **Chair:** But it is significant that we can continue to benefit both ways.

Dr Thompson: Absolutely.

Aisling Burnand: It is this win-win, having people flow both ways and learn. As I said, if somebody goes off to a different country, they are learning from that person—perhaps the leading person—and then they can come back and set up a new team, and, essentially, spread their new knowledge and hopefully improve our knowledge in a particular area where it may have been lacking to date.

Chair: Continuing on the theme of international influence, Maggie.

Q143 **Maggie Throup:** In response to Luciana, you touched on the fact that the UK is a leader within life sciences and such aspects of the regulatory framework. Could you expand on the role that the UK has played in influencing EU and global standards? How has this benefited patients?

Aisling Burnand: The UK has a long track record in showing real leadership in a whole range of European regulations. I go back several decades to when there was a lot of work led by the UK on the patents directive at that particular time, not necessarily an immediate segue through to patients, but the UK recognised that that was really important and laid the pathway there. More recently, we have been seeing a lot of work around data protection, and perhaps Beth can tell you a little more about that as she has been significantly involved in that area.

Dr Thompson: In almost every important piece of legislation that you look at across our sector you see the work of the UK. That is a combination of the UK Government, who do really well at the moment in terms of influencing legislation within Brussels, but also organisations such as the charities—Wellcome, Cancer Research UK and many others—who play a key civil society role in influencing that legislation and

bringing often a non-industry or patient voice into those discussions. That was true for the clinical trials regulation and the animals directive, both of which are not necessarily directly relevant to patients but feed the lifecycle of research that leads to patients in the end.

As to the data protection regulation, it is a very broad piece of legislation; it affects the use of personal data across all sectors. A critical part of that impacts the way we can use health data in research, and Wellcome, working very closely with the UK Government but also a coalition of patient groups from across the EU, stepped in when it looked as if the European Parliament amendments would derail the use of those data in research. We really should not underestimate the strength of the UK in doing that, and there are a number of different actors who are doing so.

Our very strong regulators—the Medicines and Healthcare products Regulatory Agency—are world leading, and that helps to bring that credibility, for example, in the clinical trials space and in the licensing space. It cannot be underestimated.

Dr Spink: If there is a dilution of UK influence on standards—and standards are very clearly linked to safety and public trust—if we end up with a disharmonised or divergent set of standards, that would very much undermine the public's trust and the patients' trust in quality and safety. I think that is a slightly different consideration.

Q144 **Maggie Throup:** That leads me on to my next question very nicely. Depending on the outcome of the negotiations, what should the Government seek to do to create a suitable regulatory environment within the UK, probably to make sure that we are still shaping the environment rather than just taking from the environment?

Dr Thompson: There is a very interesting interplay between voluntary standards, which may be global and are there to shape the way people trade and to make trade easier, and legislation, both at the UK and EU level. Our regulators in the UK have to keep playing a crucial role across that spectrum of activities. Clearly, direct influence on EU legislation will be harder, and we see that EU legislation is often a gold standard or tends to shape wider international norms for regulation.

However, we must make sure that our regulators are well enough resourced so that they can continue to play in that space and be influential. When working on things like the International Council for Harmonisation of clinical trial guidelines, we have to make sure that the MHRA has a key place at that table and can continue its involvement in discussions, because the UK has a very pragmatic, proportionate approach to regulation, and patients everywhere, not just in the UK, would suffer if they lose that important role.

Aisling Burnand: I go back to the point that patients want faster access to new products, and, looking at this globally, we want to see all our regulators working together to create a greater harmonised framework.

Whether that is between the FDA and the EMA, and with the MHRA, the goal is to try to get in there to reduce some of the bureaucracy that exists within the system so that we can get things faster. This alignment globally and how much more we can do to improve and get things to patients faster is a really important thing to be thinking about.

Chair: There is one final quick question from Caroline.

Q145 **Dr Caroline Johnson:** You mentioned the Horizon 2020 programme as a form of group within Europe that allows for research, but that gives us a good framework, does it not, for how we would continue to work with the EU outside the EU, because there are already countries such as Norway, Iceland and Israel that work with Horizon 2020 and are part of it, and therefore it is an example of how we could work?

Dr Thompson: Pascal Lamy was commissioned to write a report for the European Commission on the programme that comes after Horizon 2020, framework programme 9, and in there he included incredibly warm words about the importance of the UK continuing to participate in that, because it raises standards overall and because the UK could make a great contribution. You are absolutely right; I would agree that it provides a great basis. We would have to work out legally how that works exactly, and that would need to be covered in the negotiations because it is not immediately obvious. Because of the UK's size, our research strength and the amount of money we receive through Horizon 2020 at the moment, the parallels with Norway and Switzerland are probably not perfect, and we may need to think about what influence the UK would have in shaping that programme if we are putting that much money in and how much we were getting out, but it provides a really good model to work from.

Dr Spink: Horizon 2020 has invested €200 million in rare disease research in orphan medicinal product development, so it has been a crucial source of funding for rare disease research.

Q146 **Dr Caroline Johnson:** Also, certainly in the EU itself, into other countries around Europe and elsewhere.

Aisling Burnand: It is a really good programme. I have at least six members who participate in it and sometimes are co-ordinating and leading in that area. So, the ability for charities also to be involved in that is really important.

Chair: Thank you. Is there anything that you have not been asked today that you would really like to put on record before we finish? No. Thank you all very much for coming this afternoon.

Examination of witnesses

Witnesses: Steve Bates, Leslie Galloway and Suzanne Halliday.

Q147 **Chair:** Welcome to our second panel. In case you were not here for the whole of the first panel, I emphasise that there is a parallel inquiry going

on with the BEIS Committee looking at the impacts for industry. The key focus for this Committee is going to be on the impact for patients. With that in mind, could I ask each of you to introduce yourselves to those who are following from outside the room, starting with you, Suzanne Halliday?

Suzanne Halliday: I am Suzanne Halliday. I am the head of the medical devices notified body, BSI. We are a full-scope notified body and one of five UK notified bodies that are part of the 53 European notified bodies that regulate medical devices for the European Union. We have about 450 employees globally who regulate all types of medical devices. We are considered co-regulators with the MHRA.

Leslie Galloway: I am Leslie Galloway. I am chairman of the Ethical Medicines Industry Group, which is a trade association for small and medium-sized pharmaceutical companies. In terms of size, we represent around 50% of the volume of branded medicines in the UK.

Steve Bates: I am Steve Bates. I am the chief executive of the BioIndustry Association—the BIA. Here, I am working in partnership with the ABPI. The ABPI presented to the Business Committee and I am doing the Health Committee, so hopefully it reflects the joint working that you guys have as well. Today, I am going to talk about a new report, which we are going to publish today, that we have done with the Office of Health Economics on the patient and public health implications from Brexit. Hopefully, that is some new data that I will be able to bring to the Committee on the implications of exiting the EU and the single market.

Q148 **Chair:** Thank you. To start, we are interested in this Committee in the implications of no deal and what kind of contingency planning you are making for that; and, luckily, there has been encouraging news over the last week. Even so, we know that nothing is agreed until everything is agreed. So, perhaps starting with you, Suzanne, would you be able to tell us what the implications would be for patients and what planning you are making towards it?

Suzanne Halliday: The implications of no deal would be very detrimental to patients. The role of the notified body is that the manufacturers declare compliance with European legislation. A certificate issued by a notified body means that we agree that they have demonstrated compliance—that we have seen evidence that they meet the requirements. We are currently issuing certificates for a period of five years, which then extends beyond 2019. We do not understand if we will continue to be a notified body working for the European Union after 2019. We do not understand if the certificates will be accepted by other member states within the European Union. We do not understand if we will have any legal standing and then be allowed even to continue to visit the manufacturers, so there is incredible uncertainty for us. It could mean no access to any medical devices as of March 2019.

So, we have contingency plans. We have opened a second office in the Netherlands and we have started the designation process for all medical devices to work under the competent authority called the IGJ, which is the MHRA's equivalent in the Netherlands.

Q149 **Chair:** Does that mean that you are losing staff as well as it having an impact on your current ability to perform in this country?

Suzanne Halliday: Manufacturers have the opportunity to choose one notified body. Once one of the 53 makes a decision that there is evidence that a device meets the requirements, then it goes to the entire European market. So, a German notified body could make a decision and it get to the UK market. Equally, there are other notified bodies in many of the member states, and, once the decision is made, it goes everywhere.

To come back to your question, we are losing business because of the uncertainty. Some manufacturers are choosing not to work with UK notified bodies, and it is also true that we are struggling sometimes to attract staff because there is more certainty if you get a job within an EU notified body.

Q150 **Chair:** Is the uncertainty the key issue for you at the moment?

Suzanne Halliday: The uncertainty is a big issue for us.

Leslie Galloway: If we consider the current environment in the UK before we even get to Brexit, it is very challenging indeed. The UK is the third in the world for global launch of new medicines, so it is a significant position for it, but in terms of uptake of medicines it is way behind. If we look at the global share of market for EU countries, Germany is at 5.5%, France, a country equivalent in size to the UK, is at 4.5%, but the UK is right at the bottom of the top five at 2.2%, so less than half. That is a very big issue for the people who make the decision about launching in the UK. Those people are usually based in the US, Japan or mainland Europe.

Then when we get to a hard Brexit, if that is what happens, the UK is likely to be relegated in the global launch sequence for new medicines, which means that medicines will be launched in the UK possibly up to two years after the rest of the EU, which would have significant implications for patients and for clinical trials. Why on earth would you set up your clinical trial in the UK, for example, if your main comparator is not available here?

The other issues are that the single market is very important for us and access to people. The industry is a global industry, and it moves its people around the globe to learn about different markets and to learn about the UK. Those are very serious issues for us.

Steve Bates: We were very pleased to see that there was some movement last week. The key priority for us is safeguarding patient and public health in the EU and the UK. That is the first priority as soon as

negotiations go into phase 2. Let me explain from a patient perspective why that is important.

We should have an understanding of the nature of what is happening on a monthly basis. Forty-five million medicine packs are exported from the UK to the EU every month and 37 million packs come the other way. That gives you a sense of the scale of the trade. There is complexity to this in terms of customs, trade and regulation. I know we are looking at regulation today, but there is a degree of complexity with all those elements.

On the regulation piece, devices are done slightly differently from more complex medicines. Some medicines have to go through a centralised procedure, which means that it is done in one go for the whole of Europe. About 20% of those are done by the UK regulator, and trying to reorganise that in the few hundred days we have until the hard Brexit date will be very challenging for an agency that is moving from London to Amsterdam. The European Medicines Agency has its challenges and it will be very difficult for companies to engage with an agency that is in the process of moving and probably not keeping all the staff it has at the moment.

The new work that we have done with the Office of Health Economics shows that there will be delays, as Leslie articulated. There is some data on that. We looked at that and thought that there could be two to three months of delay for those submitted; new medicines would come later. But we think that, if you look at markets that are not within the largest global regulatory environment—not the FDA, not America and not the EMA— we see that there is a difference of about 45% of medicines that were not launched in Switzerland, Canada or Australia.

My worry in the long term is that the UK becomes a market where not only is there no access to new medicines but also generic medicines going through. That would not be a day-one issue, but it would be a problem and may have cost implications for the NHS.

Q151 **Maggie Throup:** In your view, how has access to the EU funding for R&D benefited our UK patients?

Steve Bates: Perhaps I can talk to that. As a trade association of innovative companies that is used to getting money from the private sector as well as the public sector, I think the UK has done very well as a base for private sector investment, venture capital money and public markets money; and that is where the bulk of the investment into UK companies comes. Having said that, we are lucky to build off the discussion we heard in the previous panel about the excellent science base here, and it is fundamentally important, I think particularly for the science base, to be able to have that brain circulation, the circulation of ideas, the excellence that you see in UK universities. We are lucky, in a sense, to be able to build from that.

Leslie Galloway: I do not really have anything to add to that.

Q152 **Maggie Throup:** This is probably back to you, Mr Bates. What would be the ideal scenario in the longer term for the UK in relation to the EU's R&D activities?

Steve Bates: I think it depends on the deal. We see precedents in Switzerland, Norway and others, if there is the opportunity for a close working relationship, for the opportunity to participate. It would be fantastic if there was the opportunity for UK scientists to lead on some of those collaborations. That would be useful. I have to pay tribute to some of the work that is done by Innovate UK. Some of the systems run by the UK Government innovation agency are perhaps less bureaucratic and simpler for small and medium-sized enterprises to participate in, rather than complex European instruments, which have proved less popular with some of the BIA members than Innovate opportunities.

If you look at the £120 million that has gone into clinical research and £90 million into biosciences in higher education institutes, that type of stuff is very important. If we are going to continue to be as vibrant in the science base that we build from an industry, we need to make sure that that funding continues. The UK has done very well out of these schemes, and it has not largely gone to companies but into the science base.

Q153 **Maggie Throup:** You mentioned Innovate UK. What other steps should the Government take to support R&D in the UK once we come out of the EU?

Steve Bates: We are very lucky to have a globally attractive ecosystem. You heard some of it from the last panel. It is a combination of everything at scale. The UK does very hard science well and then has the people who can translate that from science into real things that make a difference to patients. That is a combination of things, and I think we have reached the position where we are the third global cluster. The things you need for that are great science, great people and the right money in the private sector to back that.

The risks, as you heard, are around whether people will want to continue to come to work here, and—I would say—come and go, and go and come. It is brain circulation rather than brain drain. We do it well, and we have people from America, but having a vibrancy and the attractiveness of that is vitally important.

The pound's devaluation works quite well if you spend in pounds and earn in dollars, but less good if you are doing it the other way round, so it is horses for courses on that one.

I think some of the ideas seen in the budget around improving the flow of patient capital to high-risk reward businesses, such as bioscience, are very encouraging, and that is an area where we could work hard, and, in a sense, it is not relevant to Brexit.

Q154 **Maggie Throup:** From the businesses that you represent, does Horizon 2020 have an impact or is that at a much earlier stage?

Steve Bates: It tends to be more impactful for the science base than for the biotech companies. Some companies do have it. NovaBiotics in Aberdeen has done very well from some collaborations there, but I would not say it is the opportunity of preference for all companies in my sector.

Q155 **Andrew Selous:** This is a question I asked the earlier panel. I am interested in the parallel between Canada and the United States, and the impact of the United States' regulatory regime on medicines into the UK. Are there delays in getting medicines from the United States to Canada? You could see that as a possible parallel situation of the UK outside the EU. Is there anything that we can learn from that?

Leslie Galloway: I am happy to comment on that. It is back to the issue of regulatory alignment. The FDA and Canada, I believe, are not aligned from a regulatory perspective. If you look at the three advanced markets where new medicines launch globally, it is the US, the EU and Japan, and Canada does not feature.

Q156 **Andrew Selous:** My question is whether there is a long delay in the Canadians getting recently licensed US medicines.

Leslie Galloway: I do not know the specific answer, but I suspect it will be similar to what would happen to the UK once we had left the EU if it was a hard Brexit.

Steve Bates: The simple answer on medicines is, yes, there is a delay between regulatory submission for the US market and regulatory submission for the Canadian market. In our analysis, there were one or two, I think, probably domestic Canadian companies that have launched things in Canada first before they have gone to the US, but, by and large, it is the other way round—US first and Canada some time later. There are some complexities to the Canadian market and their healthcare system, which are probably too complex for this discussion, which may make it not exactly the right parallel for the UK post Brexit.

Q157 **Andrew Selous:** We have not talked about Japan either, but what is behind my question is whether there is anything we can learn from elsewhere in the world where that knowledge transfer happens pretty fast or instantaneously to give a neighbouring country more or less instant access to newly regulated drugs—perhaps Japan. Suzanne, can you add anything on that?

Suzanne Halliday: I can comment from a devices point of view. In addition to conducting work for the European Union, we conduct work for the Government of Canada, the Government of Australia and the Government of Japan and, through an international medical devices regulatory forum, we conduct a single audit programme. In devices legislation there are two aspects. There is a documentation review: what materials something is made of, how it is packaged, what information is

supplied with it and whether it can be sterilised. There is a lot of documentation to read. Then there is an on-site audit: what equipment is being used to manufacture something, how the equipment is maintained and how the people are trained to use it. So, there are two parts.

We currently conduct this second part for the Government of Canada and the Government of Australia through a mutual recognition agreement that allowed BSI to do both aspects. The IMDRF is a programme where we conduct one audit and it counts as the quality system audit for Australia, Brazil, Canada, Japan and the United States in one go. We speak very positively about that. The MHRA also spoke very positively about that. In the European Union, of the 28 member states, only the UK and Ireland ever spoke positively about considering joining that programme, and so, when the European Union had to make a decision on whether they would join the single audit programme, Europe voted no, which is not what the UK's position would have been in that particular programme.

Andrew Selous: That is helpful. Thank you so much.

Steve Bates: There is an element in trade that I could talk to in pharmaceuticals. If you look at the WTO agreements on pharmaceuticals, signatories include the EU, Canada, the US, Japan, Norway, Switzerland and China, and that was established in the early 1990s. That provides for finished pharmaceuticals to be subject to a 0% duty. So, there is benefit for some of these things at a global level. That means that signatories unilaterally set their tariffs at 0% on a zero-for-zero basis.

Andrew Selous: We are going to come on to the WTO later, but thank you.

Q158 **Dr Cameron:** It is my understanding in terms of research and development that the UK has received more IMI funding than any other country and 13% of Horizon 2020 funds awarded for R&D projects, but non-EU countries, such as Australia, although it can participate, has had a fraction of that funding awarded to it or made available. What levels of funding are we speaking about that the UK has enjoyed up until now, and what would happen if it only became a fraction of the actual funding in line with non-EU countries?

Steve Bates: My understanding of this, if I may, is that UK academic institutes have received around 30% of IMI funding and SMEs around 21% of the funding, so it would be significant, particularly for the science base, if this was not to continue.

I repeat the point that, if we are going to have a vibrant life sciences sector, we must not think of this as being a wholly state-funded enterprise. This is about attracting investment from the private sector into high-risk, high-reward businesses as well as asking taxpayers to support the science base.

Chair: Paul has a series of questions on the impact on clinical trials.

Q159 **Dr Williams:** Regarding clinical trials, what would businesses need to assure themselves that the UK is a suitable, good market to conduct clinical trials in the future?

Leslie Galloway: The UK has been a very attractive place to set up clinical trials, but that is the situation now. There was a survey done by QuintilesIMS—now known as IQVIA—and 70% of global CEOs were very concerned about the future of the UK based on uptake of medicines. Around 50% see it as a worse place to set up a clinical trial. That is before we even get to Brexit. The uncertainty around Brexit is adding a great deal of issue, shall we say, to where people will set up their clinical trials.

I come back to the point I made earlier on. If new medicines are going to be delayed in terms of launch for up to two years after Brexit, the standard of care will change and your comparator is unlikely to be available in the UK, so why on earth would you set up a clinical trial here?

Q160 **Dr Williams:** What do businesses need? That is the deficit. What do they need in the future for the UK to continue to be an attractive market in which to operate clinical trials?

Leslie Galloway: We need access to the EU regulatory framework. We need medicines to continue to be launched in the UK in the normal way so that we have the same medicines here as we do across the channel. That is the most important issue of all. Ideally, as well, we would have access to the single market, because of the tariff issue, and people. You cannot get away from people.

Steve Bates: We have a particular timing issue going on here because we have spent a decade getting a new clinical trial regulation together with significant UK influence at an EU level, which is due to come into application in the second half of 2019. There is some discussion both at European level, given the impact of Brexit, and potentially exactly when the Brexit date may or may not be, so it will not be covered by the withdrawal Bill. There is a degree of uncertainty as to this process that has taken ages; it will fall across the period when Brexit may or may not be delivered. Watching that is very important to us and there is a degree of uncertainty around that.

The key bits that we need access to and collaboration with in detail are the clinical trials database and the new, and as yet to be introduced, clinical trials portal. There are some technical IT data sharing issues that are at the hub of this. Why does that matter? Many clinical trials involve patients from multiple member states, and there are 1,500 of those running at the moment where the UK is the main sponsor. We have a very strong base of investigational medicinal products for use in clinical trials. This is not the stuff that is used for products that you would see in a pharmacy or a hospital, but these are batches that are used largely for clinical trials.

This is then linked into how you move those products across the borders, and they are not covered by the WTO rules because they are not pharmaceutical products; they are clinical trials products. You have to quality-release these into a market, so there is a whole host of linkages between single market issues and the ongoing activity of clinical trials in a European context. If we no longer have access to some of that, it is going to be far more difficult for some of these things that have been established on a pan-European base to continue to do that. My fear is not that this is activity that will move from London and arrive in Paris, but that it will move to China, where they have recently significantly changed their regulatory environment, or perhaps the US companies will just say they will do it in the US and not worry about Europe for a few years.

Q161 **Dr Williams:** So we need access to the database in the portal. Which organisation currently holds the database in the portal?

Steve Bates: The portal is being created as part of this new set of rules by the European Medicines Agency, and the clinical trials database, again, is under the EMA.

Q162 **Dr Williams:** It is our separation, us leaving the EMA, which is creating the problem.

Steve Bates: Correct.

Q163 **Dr Williams:** What we are looking for is a negotiated relationship—that we are still part of the EMA or that we are aligned to the EMA? What do businesses need?

Steve Bates: The BIA position has always been that we should be as closely aligned as possible. These are highly technical matters. I do not think people were thinking about this before they voted in the referendum, but it is related to a series of complex issues around what you do about data and then whether there is a desire on both sides for there to be continued close alignment. You can do that in a number of ways. Norway is aligned in a slightly different way from Turkey, and it is aligned in a different way from Lichtenstein. There are different legal models and it depends on the nature of the deal. I suppose it is that "plus, plus, plus, plus" bit, and what is in the plus.

Q164 **Dr Williams:** So Norway, Lichtenstein and Turkey are already aligned to the EMA.

Leslie Galloway: Not Turkey.

Steve Bates: It is in devices but not in medicines.

Q165 **Dr Williams:** Do companies conduct clinical trials in Norway? Is that alignment sufficient for businesses?

Steve Bates: The other reason why you do a clinical trial in a place is because there is a body of clinical knowledge and a capacity to be able to run a trial.

Q166 **Dr Williams:** We have that now.

Steve Bates: Some of this is about clinical leadership and some is about the ability to manufacture the product if it is a complex biologic, or cell or gene therapy. These are not necessarily easy things to do. You heard about rare disease trials in the previous panel, and I will not labour the point about patient pools, but with devices maybe there is a different perspective.

Suzanne Halliday: Shall I comment on devices?

Dr Williams: Yes, please.

Suzanne Halliday: I think the clinical trials regulation that you are speaking about is 536/2014. Devices are not subject to that particular piece of European legislation. The legislation that governs medical devices and in vitro diagnostics was published and entered into force in May 2017, so it would become part of the repeal Bill, but it is a very incomplete piece of legislation. There are 80 implementing and delegated Acts that need to be added to those pieces of legislation that entered into force. I am telling you that because it is a bit complicated exactly what we will follow or what the MHRA will get to influence in the future, and then what actually comes into UK law. It is those base pieces of legislation for medical devices and in vitro diagnostics that will govern clinical trials, and there is going to be a portal that is similar to the way that medicines work. It is called EUDAMED—the European Database on Medical Devices—and it is going to have a list of all devices, all manufacturers, all notified bodies, all the certificates that we have issued, all ongoing clinical trials, and then, post market, all the incidents and failed safety corrective actions. In medicines, you call those adverse events. Access to that database, again, is necessary.

Q167 **Dr Williams:** Who currently holds the database?

Suzanne Halliday: The European Commission in Brussels.

Leslie Galloway: Coming back to this question, the issue that underpins whether a medicine will be launched in the UK separately from the rest of the EU is a dossier. A company has to complete two dossiers. Even if they are very similar, the risk is that they will be asked very different questions by two different regulators. To complete a dossier in the first place requires a lot of highly specialised skills, and those skills are not easily replicable. You do not find these people every day and they have to have an intimate knowledge of the product. When you have two regulators asking different questions at the same time, a company would find that very difficult to deal with, especially if it is a smaller company.

Q168 **Dr Williams:** What I have heard is that to make the UK attractive for clinical trials we need close alignment to the current rules.

Leslie Galloway: Absolutely.

Q169 **Dr Williams:** Turning this around, are there any opportunities for the UK to become more competitive outside the EU?

Leslie Galloway: The UK has many strengths, and Steve has talked about the science base. We are global experts in real-world evidence. We had the opportunity with stem cell research. It is easier to get funding in the UK for stem cell research than it is in the US, but it is important to remember these are long-term opportunities that will take some time to develop. What we are likely to lose as a consequence is more immediate. The people who would start developing that regulation are very, shall we say, committed to the issues related to Brexit at the present moment.

Steve Bates: If you take the big picture, the randomised control trial was invented in the UK a generation ago and perhaps it is showing its age with regard to the new opportunities of data that is produced in new ways, whether that be genomic data, real-world data or data that is delivered through the NHS, whether it is people wearing wearables and all the rest of it. The UK is quite good at inventing a way of scientifically looking at these things, and, irrespective of Brexit, we should be doing this for innovative purposes. We can get on with that because we have a combination of leading NHS data. If you look at the Salford lung study and the type of real-world evidence that has been generated out of the NHS there, if you look at the developments of the Wellcome Genome Campus and the data we are getting in terms of the 100,000 Genomes Project, under the leadership of John Bell, there is the possibility to do this. It would be nice to be able to continue to lead that in a European or a global sense in a discussion around—

Q170 **Dr Williams:** We are doing all those things inside the EU.

Steve Bates: Correct.

Q171 **Dr Williams:** The premise of my question is, does leaving the EU give us an opportunity to do anything that we could not do within the EU? Okay.

Leslie Galloway: It does beg the question, why has it not been done and will it ever be done? There is a step change in this issue of leaving the EU that we are really going to have to rethink what we are currently doing. We have many strengths in the UK, but there are issues such as cell-based therapies: is the clinical trial model of research and regulatory assessment of those suitable for animal-based models in the future? There are big questions.

Dr Williams: Thank you.

Chair: I am conscious of time, so we have a very quick question and then we are coming on to Rosie.

Q172 **Dr Caroline Johnson:** Going back to the markets, you talked about the complexity of the Canadian market as a reason why products took a little delay between getting from America to Canada. To what extent is the NHS market a particularly attractive one because it covers the entire

country in one shot rather than having to negotiate with lots of different healthcare providers? You are negotiating, essentially with one provider, and with NICE providing guidance to doctors throughout the UK on how those products should be used.

Steve Bates: Unfortunately, the NHS is not, in market terms, a single market. It may be a single organisation, but I do not think that is true. If you look at it, NICE guidance is essentially England guidance. There is different guidance in Scotland. NHS Scotland operates differently, and NHS Northern Ireland and NHS Wales both operate separately. If you look at clinical commissioning groups, where the vast majority of the money goes, they operate sometimes with their own perspective. For medicines companies it is a complex market. Leslie has already made the point about it being a market that does not necessarily adopt products as fast as other markets.

Q173 **Dr Caroline Johnson:** Why do you think that is?

Leslie Galloway: If all medicines were free, there would still be physicians who would take several years because they are slow to change. I have been in the industry for over 40 years and that is a very clear issue. Cost is now a very significant issue. We have an NHS that has no money, and, although the industry, through the Pharmaceutical Price Regulation Scheme, will pay around £3 billion in rebates back to the Department of Health, that does not arrive at the NHS with the people who make the decisions about prescribing, so they see no difference in their budgets. We are hoping that the new PPRS, which is going to be renegotiated in 2018, will be an opportunity to address many of the issues. We have been talking about Brexit. We have little control over Brexit. We do have control here over most of the issues that affect the adoption of medicines in the UK and we can do something about that. My own organisation is proposing a new medicines fund separate from NHS budgets in the new PPRS, and that would begin to address the issue of cost to the NHS. I can give you a lot more detail on that—

Chair: We will probably return to that on a future occasion, I suspect.

Leslie Galloway: I look forward to it.

Chair: Thank you. We now move to Rosie and supply chains.

Q174 **Rosie Cooper:** We are now turning to supply chains. Initially, I would like to ask what risk you think Brexit poses towards the supply chain for medicines and other products or devices.

Suzanne Halliday: As a notified body, we are allowed to audit wherever things are actually manufactured, and so there is a lot of subcontracted manufacture. I think we deliver between 20,000 and 30,000 audit days somewhere in the world. I guess it would impact the supply chain if there were tariffs, borders or delays in things getting through customs to the legal manufacturer that needed to put all the bits and pieces together for a device.

Leslie Galloway: We are a bit like the car industry in that a product may be manufactured in Germany, for example, then moved to the UK for repackaging and then go back to mainland Europe for distribution. There are issues related to cold chain, and so on; so, I agree with what Suzanne has been saying.

Steve Bates: Most medicines of Europe are made in a European hub way and often cross borders several times before they reach patients. Active pharmaceutical ingredients are perhaps imported at one point or made in a European country. I have a couple of examples of people who make an API in the UK and move it to Germany for formulation; it comes back to the UK for final fill-finish and then goes to the Netherlands for the distribution. If you think about that, that is three border crossings, if you ended up with that being a challenge. We have lots of those, and there is also quite a big amount of product that starts in Ireland and moves through the UK before going to the other European markets.

Q175 **Rosie Cooper:** Do you think businesses are already addressing those problems now? Are they working through contingency plans?

Steve Bates: It is quite difficult and expensive to move a regulated manufacturing facility. So, yes, they certainly do have contingency plans. Perhaps the plan that is closest to activation at the moment is about quality release and batch release of product, because that seems to be the thing that the European Medicines Agency is demanding that people have on day one of a hard Brexit. That means the testing of your finished product has to be done in the single market, and people are making sure that they are able to do that. Many people have been doing that from the UK. They are looking at whether they need to be able to do that from another market for European release.

Leslie Galloway: Indeed, and there are a limited number of testing houses. If everyone has to do it, it is going to be a serious issue.

Coming back to the issue of a hard Brexit, on the basis of no information—and, no matter what is said in the media about having reached agreement or whatever, nothing is final until it is final—companies have to be responsible in terms of their companies and assume a hard Brexit will happen. As a consequence, marketing authorisations have been moved to mainland Europe, at a very significant cost, and they will not come back to the UK. They are making preparations that will protect their businesses and that makes sense, otherwise medicines would not be available to patients.

Suzanne Halliday: I could add that, yes, we have seen some manufacturers moving manufacturing to Ireland and Switzerland recently.

Q176 **Rosie Cooper:** If there were to be contingency arrangements that would affect those plans, how much notice do you think businesses need in order to do that, or do you think they are just assuming that this is where

we are going to end up and are making those arrangements now?

Leslie Galloway: Businesses can take a while to make a decision, and it can take up to a year to move a marketing authorisation, from a regulatory perspective. If you have every company doing that, there is going to be a logjam, so people are doing it sooner rather than later. It is very difficult to put a number on it, but you can imagine that people are protecting their businesses—and they are quite substantial businesses.

Q177 **Luciana Berger:** The Government have recognised that customs will be a cliff-edge issue. We would like to know what you think the problems will be of any border disruptions, and particularly what problems border disruptions would pose for the import and export of medicines.

Leslie Galloway: Initially, we would anticipate there would be long queues both ways in the event of a hard Brexit. Can I address this issue of the WTO tariffs that was mentioned earlier? Steve rightly said that there is broad agreement. It is a complex issue, but, broadly, there are no tariffs. That applies to a list of medicines and ingredients, and that list was last updated in 2011. So, there is a very significant issue there from over the last six years or so where that would need to change.

One concern that companies will have is how much stock is transported which way, how much you have on the market, because a medicine usually has a two-year shelf life. A wholesaler will not take it into stock unless it has a minimum of six months. Even if you reach the six months, you've got problems. This issue of holding more stock because of the shelf life and so on will be an issue. Transporting across, it is going to be making more sense for companies to manufacture in mainland Europe and export to a smaller country—essentially, the UK—than manufacture in the UK and export to the EU.

Q178 **Luciana Berger:** Does anyone else want to add to that question?

Steve Bates: Standard issues that you would see in other sectors—cell and gene therapy products—if they are in cold chain, are that they may not survive very long, and a delay could be critical as to whether the product arrives in a format that can be used by a patient. I would suggest no incremental administrative burden at the border; is it possible to have self-assessment for EU movements; no divergence from EU rules and regulations; no hard border in Ireland—there is lots of stuff that goes across that border; and no expectation of reliance on an authorised economic operator certification in order to maintain current speed of movement, because that would slow things down. It depends a bit on what model we get.

Leslie Galloway: A practical question will also be, where are all the lorries going to park when they come to Dover to be assessed, and will that be done on a seven-day basis? Will people be working? People will have to work seven days a week. There are significant practical issues there.

Q179 **Luciana Berger:** Steve Bates, you referred to time and temperature-sensitive medicines or medical products. In the case of those specific types, where they do not have a two-year shelf life, are there any specific arrangements that you think the Government should seek to implement in the event of a hard Brexit?

Steve Bates: This is really why we are looking to ensure that safeguarding these public health issues should be the first priority when negotiations have reached phase 2. I think there is an understanding at the Department of Health here about the importance of this. I think perhaps it is as important that it is on the agenda for the EU 27 health ministers, because one thing that is critical is that the UK is the site of manufacture for more of these ATMPs than other parts of Europe. We are overweight and that is not a capacity that is easily recreated in another country, so this will be an issue for people and patients in other European countries. I think it is possible to come to sensible arrangements on these things—where there is a will there is a way—but we need to get on and see what they are.

Q180 **Luciana Berger:** Did you want to add anything?

Suzanne Halliday: No.

Q181 **Andrew Selous:** Mr Galloway, you mentioned the issue of where all the lorries are going to park, but is that not a rather old-fashioned view of customs? In the new environment, is it not possible to do your customs checks perhaps at the sending or receiving distribution centre, to have trusted trader status, as was mentioned by certain Members of the Cabinet last week?

Leslie Galloway: I have been dealing with Government and the NHS for many years and it surprises me to what extent perhaps their IT systems are not up to date. I do not know is the answer to your question. At the end of the day, we do not really want to find out. We want to be prepared. I have heard about electronic tagging working between Norway and Sweden, and there is talk about it working between northern and southern Ireland, but have we tried that? Have we actually done it?

Q182 **Andrew Selous:** It is theoretically possible, is it not, and we have time, I guess, to set up systems like that between now and then?

Leslie Galloway: I do not know the answer to that. I am not a technician in that regard. That is why I am saying we really need to be certain that we know what we are doing.

Steve Bates: I look at the complexities that have been involved in the development of the falsified medicines work around ensuring security of supply. These are not things that are easily done in little over a year. There has been a long time for discussion of that. There is a common European pack. How that is perceived and distributed, if that is continued to be allowed as the legal packaging, depends on the regulations. There is a slight difference with medicines in that the packaging is also

regulated and a part of the ongoing pharmacovigilance and licensing process, so there is some complexity there as well.

Q183 **Andrew Selous:** Have there been any discussions between any of you and the UK Government on these new types of possible customs arrangements?

Leslie Galloway: We have not discussed the customs arrangements yet.

Steve Bates: Yes. We have engaged really through the last year around some of the ideas that have come up with regard to goods on the market and customs arrangements—simplicity and straightforwardness—and we have expressed the challenges that are particular to our sector to the Government. They certainly are at the innovative end of the spectrum for the Government. We like innovation, but getting them to work in a year seems to be a significant technical challenge.

Q184 **Maggie Throup:** What would the impact be if the UK diverges from the EU regulations covering manufacturing, batch testing, distribution and qualified persons?

Leslie Galloway: Steve has already touched on that. You will have QPs both sides and there is a limited supply of QPs, so the risk is of delay. As to batch testing, there is a limited number of companies that can do it on both sides of the channel, so there are significant concerns there. That is why people are looking at moving their manufacturing out of the UK in the event of a hard Brexit.

Suzanne Halliday: From a device point of view, there is very little data that is publicly available yet for devices. The new legislation that has entered into force and is applied in 2020 or 2022 will make much more of this information publicly available, but it is believed that UK notified bodies handle between 50% and 70% of the certificates that cover devices for the entire European Union. Are you asking in terms of what we contribute to the system? I think there is a risk that the European Union will cut the UK notified bodies out entirely, but, as I said in my opening statement or at the beginning, we are making contingency plans, so they are going to get our expertise and our capacity because we are moving to the Netherlands.

Q185 **Maggie Throup:** I am quite interested, if the UK diverges from current EU regulations, what the impact will be on the patient.

Suzanne Halliday: Okay.

Steve Bates: Perhaps I can have a crack at that from a medicines perspective. I have some stats so that you get where the UK sits in the EU. In the UK, we have the second highest number of all good manufacturing practice—GMP—sites at 684. We have the second highest number of manufacturing sites in general at 444, and the third highest number of sites involved in batch certification at 231 sites. We have the most sites certified to import medicines from third countries at 357. We

are a significant part of that supply chain EU-wide. The impact for manufacturers will be increased cost of doing additional batch testing, if we end up with a hard Brexit.

Q186 **Maggie Throup:** We are more interested in the patients.

Steve Bates: In a sense, the UK patients only pay for prescription, but there could be a cost implication for the NHS, which would then have a knock-on effect because this stuff does not come for free; so, there could be a cost implication. Then there is delay, and for companies choosing whether to put their goods in the market in the future, once you are in a second-division market or regulatory environment, global companies will see this as a place where they may choose not to come or not to come as soon as they would otherwise.

Q187 **Maggie Throup:** There is talk about a transition period. How important is it that the UK remains aligned with the EU rules as they stand during that transition period?

Leslie Galloway: Very much so.

Q188 **Maggie Throup:** Is there any reason why after that transition period—because we have helped to create a lot of the regulations anyway—we would want to change from what is there already?

Leslie Galloway: I come back to our original point, which is that we do not want to diverge in any way either during the transition period or subsequently from the EMA in terms of regulation. We want to be part of that framework to continue to assure that the UK is part of the first wave of launch of new medicines.

Steve Bates: Another impact for patients could be around the implications for the reporting processes for adverse reactions. If something has gone wrong or people are seeing that there is an adverse reaction to a drug, at the moment there is an EU-wide system that reports into the EMA, in which the UK is a very significant player in terms of being both integrated and innovative. With the MHRA, you can do it on an app on a phone with the yellow card scheme. Doctors will all know how to engage with that process.

If we end up with the UK not being integrated into the EMA and the systems not working, there is a reasonable chance that two things will happen. The first is that there will be a delay in the information travelling between us, and this may mean that, if there are new rules about a drug coming out that will impact on a patient, that will be later and they will be at risk for longer. The second is that the quality of the decision making at a European level will not have the UK experts in it, and because, in a sense, pharmacovigilance decisions are not just necessarily black and white—you may get a piece of information and then you have to assess whether that is the right thing to do or not—you may end up with a less good scientific decision being taken in that pharmacovigilance process. That may mean that either you end up with the withdrawal of a drug

that, on balance, it would be better to continue with, or the continued use of something that, on balance, it would be better not to use for a longer period as there is a discussion or a divergence about how that is operated. I am sorry that is a bit long.

Q189 **Maggie Throup:** Surely from that answer we should be looking at much wider alignment to get the data from other countries as well.

Leslie Galloway: It comes back to the fact that the MHRA is a world-class regulator. Who will replace the work that the MHRA does? It is not easy to replace that level of expertise that has been built up over years. They really know what they are doing. For the EMA to compensate in some way is going to take a long time.

Q190 **Maggie Throup:** What can the Government do now to prevent the loss of expertise that potentially is there from losing qualified persons? We need to act now. We cannot wait until—

Leslie Galloway: We would not be moving them. We would have them both sides of the channel, so we would be duplicating the effort rather than moving them. It all comes back to access to the EU regulatory framework, working very closely with the EMA, and having one dossier for a medicine that is managed by the EMA so that we have access to the EU market in that respect or from a regulatory perspective.

Suzanne Halliday: You used the words "GMP." The equivalent in medical devices is a standard called 13485. You used the term "qualified person." The equivalent in medical devices is the person responsible for regulatory compliance. I think the sentiments are the same. If there is a divergence, then the UK would be a much smaller market than the 500 million people of the European Union, so I think things that Steve and Leslie have said would be true for devices as well, but it is all slightly different for devices than you have described for medicine.

Chair: Thank you. I know that Lisa wants to come in.

Q191 **Dr Cameron:** We have heard in evidence already that, if there was some diversion, then perhaps the training and qualification of qualified persons would need to be adapted, they would need some further training, or they may leave the UK. What are the implications if there are diversions for retaining qualified persons and how long would it take to train our own?

Leslie Galloway: There would be greater demand in the UK for a product coming in and there would be a greater demand for product going out across the channel. I cannot comment on the training issue and on the qualifications, but there would be a great demand for QPs.

Q192 **Dr Cameron:** But if there were regulatory diversions, it might mean that their training would not apply in the same way. That is my understanding. I do not know if anyone could comment on that.

Steve Bates: We have had QP and batch release established largely, though not exclusively, from the UK for the European market. Now, as companies think through the implications of Brexit, some are thinking that they have to move this to an EU country. Then they ask the person who is doing that job whether they would like to move to do that job in Sweden. Whether that is something they want to do might depend on their family circumstance, and these are often senior people, established in their careers. This is a fairly specialist role such that there are not hundreds and thousands of people doing it at university.

Q193 **Dr Cameron:** You are saying they are sought after.

Steve Bates: They are sought after. If we do have a hard Brexit, we should put patients first and think very carefully about whether the UK, as the smaller market, would accept product batch released from the European market to ensure supply for patients. I am sure that is really the direction the MHRA would go in if they had to, so we should reassure patients that the industry would move to try to make sure that stuff was available rather than worry that we did not have exactly the right person on exactly the right day for the UK market. It is still the same stuff, but it is a problem for people.

Q194 **Dr Cameron:** But the people are likely to move.

Steve Bates: The people move.

Chair: Thank you. Caroline has a quick question.

Q195 **Dr Caroline Johnson:** You talked about us being a smaller market in Europe, but you also mentioned earlier that we had wanted to join a group with Australia, Brazil and others. Surely that provides an even larger market than the EU, does it not?

Suzanne Halliday: Yes. Because the United States is part of that group, yes, it does. The IMDRF is a larger group than the European Union. If I could go back to a question that Maggie asked as well about incident reporting, it is not called pharmacovigilance for devices; it is vigilance. The MHRA spent a lot of time on the European legislation that entered into force in May. So, it is now the most up-to-date legislation for devices anywhere in the world and it takes into account the way you describe a failure. They are trying to use common terminology in Canada, Australia, Brazil—the IMDRF countries—and the European Union, so there is benefit in describing a problem in a similar way and labelling packaging in a similar way so that traceability is global. We could join those things even if we leave the European Union, but I still think that it would be important that we have access to the EUDAMED database for the European Union.

Q196 **Dr Caroline Johnson:** If we joined the IMDRF with regard to medical devices, would that mean that we were able to access those new medical devices at the same time as the Americans and Australians, and would that be quicker or slower than or the same as Europe?

Suzanne Halliday: The initiatives that the IMDRF are doing allow the on-site auditing to be recognised by all countries. Each of the countries still then reviews the dossier, as the medicines people describe it. We would describe it as technical documentation, but each country protects that and reviews that themselves.

Q197 **Dr Caroline Johnson:** The answer is that we will be as quick as the Americans if our people are as quick at reading the dossier.

Suzanne Halliday: What is the legislation going to be for the UK after 29 March 2019? Are we going to adopt European legislation and just rubber-stamp things if a notified body in Italy says they are fine? Do we just take it? That is kind of the way that it works at the moment. If the UK chooses to diverge from the European system, then it could mean that things were delayed getting to this market. Again, manufacturers have to choose for which markets they are going to try to meet the requirements. The big market might be the United States; a second big market is the European Union. If we leave—

Q198 **Dr Caroline Johnson:** But how does the IMDRF play into that?

Suzanne Halliday: It is a group that is trying to harmonise things across the world—

Q199 **Dr Caroline Johnson:** To create one large market.

Suzanne Halliday: Yes, to create one large market. We are not quite there. Each of the countries still protects a number of things because they are responsible for ensuring patient safety in their own countries. I do not know that any country has ever said that another country can just do it all, except for the less well-established countries such as Malaysia and Indonesia, where there is just some acceptance: "You have already gone to market in the US, so you can come to market here," or, "You have already gone to market in the EU, so you can come to market here, and thank you."

Steve Bates: Harmonised standards does not necessarily mean a single market. Even if there are elements of this that are reducing the regulatory burden, standardising or moving them together, the markets will still remain very different. The US market will still remain very attractive both because of price and size, and the UK outside the EU will be a market, in pharmaceutical terms, of less than 2%. I do not know what it is in devices, and it will be in pounds. Those factors will be the driving factors where global players place this, because they will then put it in sequence even in a standardised or harmonised set of standards within this. They are not the same thing—the regulation and the market.

Suzanne Halliday: For devices it would be less than 5%.

Q200 **Andrew Selous:** Mr Galloway, let us go back to something you said a little while ago. You said that some businesses were looking at moving manufacturing out of the UK, but in the last few weeks we have had, I

think, north of a billion pounds of new investment put here into research from global pharmaceutical companies. That would appear to be quite a vote of confidence in the UK pharmaceutical industry pre-Brexit.

Leslie Galloway: I cannot speak for that company.

Q201 **Andrew Selous:** I think it was a couple of companies, from memory.

Leslie Galloway: They are two very large companies, which are not members of my organisation—yet. They may have a global perspective of why they are coming to the UK. It may have been that that decision was made some time ago. I do not know.

Steve Bates: Maybe I can help, because some of them are members of the BIA. The UK is fantastic at science and at doing hard things well. We are the global leaders. If you want to do the types of things that global companies need to do, we are a fantastic place to do certain types of the D of R&D, if you want to look at it like that. If you look at scaling companies, the company that has the global capacity in lentiviral vector, which is at the heart of Novartis's next generation anticancer drugs, the CAR-T drugs, is Oxford BioMedica.

If you look at the development, or the translation, of the fantastic UK science that won the Nobel prize in microscopy this year, the translation of that and the use of the fragments by Astex Pharmaceuticals, another UK SME scaling company in Cambridge, is what enabled Novartis to make the drug Kisqali. The reason why the global players come here is that we have global capacity a bit like the people who do Formula 1 engines, which is hard to do, and they come here because that expertise is not available elsewhere in the world.

It is right that we can be very confident about the future of UK life science as long as we have the fantastic life science sector in terms of the science base. We have done well at attracting global investment. We did that prior to the Brexit referendum. We have continued to do that post the referendum, and this is producing high-quality jobs and growth for the UK economy. It is right that the Government have backed the life science sector and I am delighted that they have put it up in lights at the beginning, but I think it would be wrong to say that it is because of Brexit.

Q202 **Andrew Selous:** Looking at the World Trade Organisation, if the UK went on to WTO rules from 29 March 2019, what would this mean for UK trade in the life sciences?

Leslie Galloway: I come back to the issue of the regulatory framework. If we are outside the regulatory framework, then we will become second division and medicines will be launched in the UK up to two years after launch in other markets in mainland Europe. There is a cascade following that, because there are implications for clinical trials and patients not receiving new medicines that may be transformative across the channel but not here.

Q203 **Andrew Selous:** The impact on patients would be taking longer to get new medicines.

Leslie Galloway: Absolutely.

Q204 **Andrew Selous:** Possibly those medicines would be more expensive as well.

Leslie Galloway: It is difficult to say whether they would be more expensive, but the availability would be possibly a year or two years after launch in mainland EU.

Steve Bates: Can I get to the specifics of the WTO rules as we have done some work on it and it is reflected in the submissions that we have made to Government? Leslie rightly makes the point that finished products up to 2010 will probably be covered by zero for zero, and should be because of the nature of the things. Anything post 2010 or not listed could be subject to tariffs, and that would depend on individual tariff discussions either with the EU or with other third countries. We are only a signatory to the agreement via the EU, so we have to become a signatory in our own right on zero tariffs and that has to go through the WTO. We do not know if that is done. If we want to keep these tariffs at zero but cannot do it, we may end up with tariff suspensions on key products if these are not effective.

Chair: Thank you. We are going to come on to another aspect of regulatory alignment.

Q205 **Luciana Berger:** I think I know the answer to this question, but I am going to ask it anyway, and I have asked this of all the panellists. Do you believe there is any way that the UK could diverge from EU regulations after Brexit in a way that would either add value to our economy and/or enhance the quality of care for patients?

Steve Bates: Am I allowed to go beyond the narrow confines of therapeutics and touch on, perhaps, the benefits of good food and potentially genetically modified crops?

Luciana Berger: Sure.

Chair: It is not controversial at all.

Steve Bates: Potentially, if the UK was able to establish a scientifically-based approach to the introduction of some of the innovation that we can see in terms of new types of genetically modified food—we have seen golden rice being very effective at being able to work in drought areas of Africa, and there are new types of apples that are now better able to be preserved as a result of this type of thing—we could see the development of great science from Rothamsted and other institutes in the UK developing food sources that might have health benefits to patients that would be closer to this. Some of that has been stymied by the fact that the European Union has taken a non-scientific

approach to the GMO discussion, but obviously any discussion would be in a political context and that would depend on the political decisions that were taken in the UK Parliament.

Suzanne Halliday: I explained earlier that there is an opportunity possibly to join some of the initiatives of the IMDRF. I think that the UK is also a very strong leader in the development of standards, and standards impact on lighting, wiring, piping and plate glass windows. Standards development is a strength of the UK. If legislation is written very generally, and it is written very generally for devices because it has to cover everything from small syringes and plasters to heart valves and hip implants, it is the standards that provide the detail in what actually must be done to get a product to market, so we have some strength there.

Leslie Galloway: We have all the fundamentals. We have a population of 60 million and we have one healthcare provider in the UK, albeit in England there are 7,500 different NHS institutions alone. We have great science. We have great opportunity and we have a great regulator in the MHRA. NICE is a very great strength of the UK, and it is listened to outside the UK. The SMC is listened to outside the UK. There are many things going for us.

The issue always is how long it will take us to maximise those opportunities. If Brexit in just over a year's time is a cliff edge, there will be a chasm and we will have to recover from that; it will take time. It always takes time to develop. If you think of where we are today, NICE is at the forefront of health technology appraisals across the globe. That has taken 18 years. It depends how quickly we are able to maximise the opportunities. Yes, Brexit will make it a hurried necessity, shall we say, but we are not good at realising things very quickly.

Q206 **Luciana Berger:** What would the UK lose if it is unable to negotiate access to infrastructure developed as part of the new EU regulations for medical devices and in vitro diagnostics?

Suzanne Halliday: The European legislation, as I have said, is the most up to date anywhere in the world at the moment because it has just been written. It took eight years to write. It covers all the latest software, biological substances, interactions with pharmaceuticals and in vitro diagnostics; so, it would be a shame to lose such up-to-date legislation. The legislation will make things more transparent to patients. The legislation will make traceability greater. Those are good things for the UK and its patients, and the rest of the world's patients as well.

Q207 **Chair:** Did it really take eight years?

Suzanne Halliday: It took eight years, so they are not fast, but the MHRA made significant contributions to that, and we talked to them about our actual experience with things.

Q208 **Chair:** Are you concerned that, within the EU, processes will get even slower without the impetus of the UK?

Suzanne Halliday: Some of my colleagues on the panel have said that the MHRA is seen as a pragmatic and sensible regulator, and I think Europe will be sad to lose its voice.

Q209 **Chair:** Do you think it will find a way of continuing to have that voice there at the heart, or do you feel very pessimistic about that?

Suzanne Halliday: I have seen the UK already start to lose influence in the European Union. The MHRA is starting to step into roles in the IMDRF. Nothing has changed so far, and in Europe it is already, "You are from the UK. You are leaving. Why would we care what you think?" That is my actual experience now.

Q210 **Chair:** Is that the view of all members of the panel?

Leslie Galloway: Yes. Europe will be the poorer for losing the MHRA.

Steve Bates: I do not get that sense in my meetings. I get the sense that there is an understanding of the validity of having a science-based, sensible voice with capacity among those people who are on the team or around the table with experts from the UK, and there is a desire to see whether there is the possibility to put something together. They are not quite sure what or how, but I think that there is a pragmatic desire, certainly among some colleagues in the EU 27, and that is because the challenges that we are still going to face—the challenges of new forms of disease and of pharmacovigilance—are going to remain. In a sense, that is why Europe came together in this area, to battle the challenges discovered through the thalidomide scandal and the information flows of that being delayed, which caused problems continuing for a period of time that otherwise need not have. Some people have longer memories, understand the basis for this and have a desire to see that continue.

We also have a number of things that work through the Council of Europe and other formats. There are a number of layers of this that you can look at. We have grown together over a generation, over a lifetime, and I do not think everybody is of the view that it is, "Shut the door on your way out."

Leslie Galloway: There are big opportunities. The MHRA will have to forge a new world for itself, and that is an opportunity. To what extent it will be able to contribute to the EMA is another issue.

Q211 **Maggie Throup:** If you changed jobs for a moment and you were advising the Government, what advice would you give them as to what they could do to retain and expand the UK's influence in the life science sector? We have already acknowledged that we do have a lot of influence.

Steve Bates: I would look to putting safeguarding public health for the UK and the EU by making regulations on the supply of medicines top of the bill for phase 2 of the discussions. I think these are tractable problems with solutions that are based on public health outcomes for the

EU 27. So, I would get them top of the shop for 1 January onwards as soon as the deal is done.

I think, globally, we can continue to lead, and that is about investing in our science base, which the industrial strategy helps with, but, to be fair, has been supported by Governments of all colours and stripes over a generation. There is something here about long-term investment having made a real difference.

Support the UK being a great place to start and grow a business. We have to remain globally competitive. You see changes in the tax environment in America and regulatory environment in China. So, as I say, we have to stay up with the global leaders, but we can be confident that we can do this because we have done it very well, we are at the forefront of this and we should continue to do it.

Leslie Galloway: I would like the UK Government to give us some degree of certainty. I realise that absolute certainty is impossible. Uncertainty is a virus for business. People run away from it and they stop investing and move, and so on.

In terms of the implication for patients, we need to talk to the other EU 27—in fact the other 30, including the EEA—because the issues we will face are common to the issues faced by EU patients. Access to medicines across the EU is critical and everything else that goes with it, including clinical trials. That is the advice I would give to the Government.

Suzanne Halliday: From a devices point of view, there is a shortage in the number of people who are knowledgeable about the regulation of devices. If the MHRA invested in their team of people, I think they would be welcomed because there is a real shortage of people who understand what they are doing and they do have some of the best.

Q212 **Andrew Selous:** Mr Bates, you just mentioned the improvements to the regulatory regime in China. Is there anything the UK can learn or should be learning from that that would be helpful to us?

Steve Bates: The Chinese Government made this a significant priority in their last five-year plan. They have essentially retooled their regulatory route with support from the Gates Foundation in the US, and they have very rapidly adopted some of the best practice around breakthrough designation and other things in an endeavour to kick-start their industry. One of their big attractions is that they are going to be the biggest global market for this.

I think this is turning the heads of global companies and we should be conscious of it. If you have a very fast new regulator offering fantastic service, with a fantastically large market, at a time when we are removing ourselves from a significant global market, we just need to be on our mettle to make sure that we are making the most of the NHS assets, the NHS data, the genomics stuff, which we have, and be speedy

in understanding the rapidity with which other parts of the globe are moving on this.

Andrew Selous: That is very helpful; thank you.

Chair: Thank you. Finally, Paul.

Q213 **Dr Williams:** The final questions are on transition. I guess we are not really sure at the moment what we are going to transition to, but are companies planning for everything to change in March 2019, or are you planning for a transition, and what does a good transition look like for the life science sector?

Leslie Galloway: The ones I have talked to have to assume the worst at the end of March 2019. They cannot afford to take a gamble on that. As to what a transition would look like, going back to the points you were making, access to the EU regulatory framework and the single market and people, it will take another two years for companies to really get their heads around what life will look like after the end of March next year.

Q214 **Dr Williams:** In terms of the type of research and development they are doing, is two years about the right time if they are going to have to make that change?

Leslie Galloway: They will carry on with their research. I do not think that is going to affect that. The issue will be the priority of the UK as a market for launching new medicines. If they are doing research here, they will continue to do that, I would imagine.

Suzanne Halliday: The only things I would add are that in devices there is an entity called the EU authorised representative. At the moment, if the authorised representative is here in the UK for some US manufacturers or Japanese manufacturers, and that is a respected position for the whole of the European Union, I guess that would need to be discussed in a transition. There is a body in Brussels called the MDCG—the Medical Device Coordination Group. They are the ones who are driving the supplementary legislation that goes along with devices, and, as part of a transition, the MHRA would have to be allowed to participate in that group, lead that group, lead those sub-committees or whatever comes out of it.

Steve Bates: The EMA has been pretty fair to the industry and the industry has got the message that the EMA considers that the transition started when the UK Government signed article 50 and will finish in March 2019. The transition period that industry is operating in is now, and they are executing implementation plans against that as we speak.

Some in the industry are prepared to take some risk in the sense of the risk being that hard Brexit is not the outcome that we are heading towards and carry that risk at this point. You can buy certainty by investing against hard Brexit happening in March 2019, which probably

means significant disruption with some significant costs, or you can take some risk that perhaps something will come through. That is the corridor of uncertainty that companies are operating in at present.

Is sorting all this out in two years easy or doable for long development cycle businesses where it takes 15 to 20 years to take a drug from the idea to development? No. Are there certain elements that are speeding up? Yes. Is two years doable? Probably not, but at the moment we are being asked to do it by March 2019. Any form of transition or implementation that was added on to that or flexibility for things where there is complexity would be very helpful, and that is the way we have seen it done with other EU directives.

Q215 **Dr Williams:** What is the chance that, by the time companies get information about a transition deal, it is already too late because they have already planned for a worst-case scenario?

Steve Bates: This is why we wrote to the Government about this last summer and were pleased to see some action in terms of the Minister's letter to the *FT*. The transition has really been going since last summer through to now.

Leslie Galloway: For some companies it is too late.

Q216 **Dr Williams:** It is already too late, so, even if there were a good transition arrangement negotiated, they have already made plans to leave or—

Leslie Galloway: Absolutely. It is the message we have been delivering for some time.

Q217 **Chair:** If there are no more questions, are there any further points that any of you would like to make before we finish this afternoon?

Suzanne Halliday: There is just one other thing that I maybe did not explain clearly. There are European notified bodies currently in Turkey and they are working as part of the customs union. There are currently notified bodies in Switzerland under a mutual recognition agreement, and there are currently notified bodies in Norway. That is because they are part of the European economic area. Again, I do not know what the deal is going to be and how it might impact on the transition. There are opportunities for devices.

Q218 **Chair:** There are opportunities, but the uncertainty is—

Suzanne Halliday: The uncertainty is bad.

Chair: Thank you very much for that very clear point and to all of you for coming this afternoon.