HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Regenerative Medicine, HC 275

Wednesday 19 October 2016

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Watch the meeting

Members present: Dr Tania Mathias (Chair); Victoria Borwick; Jim Dowd; Chris Green; Derek Thomas

Questions 92 - 190

Witnesses

I: **Dr Ian Hudson**, Chief Executive, Medicines and Healthcare products Regulatory Agency, **Professor Paul Whiting**, Member, Medical Research Council Regenerative Medicine Research Committee, **Dr Sven Kili**, Head of Gene Therapy Development, GlaxoSmithKline, and **Michael Hunt**, Chief Financial Officer, ReNeuron Group.

II: **Ian Trenholm**, Chief Executive, NHS Blood and Transplant, **Ian McCubbin**, Medicines Manufacturing Industry Partnership and co-chair of the Advanced Therapy Manufacturing Taskforce, **Keith Thompson**, Chief Executive Officer, Cell and Gene Therapy Catapult, and **Dr Ruth McKernan**, Chief Executive, Innovate UK.

Written evidence from witnesses:

- Medicines and Healthcare products Regulatory Agency
- GlaxoSmithKline
- NHS Blood and Transplant
- Cell and Gene Therapy Catapult
- Innovate UK

Examination of witnesses

Dr Ian Hudson, Professor Paul Whiting, Dr Sven Kili and Michael Hunt.

Q92 **Chair:** I thank the speakers for being so prompt. Welcome to this afternoon's session, our second session on regenerative medicine. To begin with, may I ask you to introduce yourselves and give us your background in this area of science? The Committee will then ask you different questions, if that is okay.

Michael Hunt: Thank you. I am Michael Hunt, chief financial officer of ReNeuron. ReNeuron is a pure stem cell research and development business. We are quoted on AIM and we have been developing stem cell treatments for the last 15 or 16 years. I have been with the company pretty much since the get-go and led it as CEO for nine of those years. Our treatments are focused on stroke, limb ischaemia and blindness-causing diseases. We are in the clinic now in all three of those areas in the UK and in the US. I sit on quite a number of committees, with an industry focus in terms of the BIA. I am involved with the Cell and Gene Therapy Catapult on their advisory panel and I have given evidence before, to the House of Lords Committee on regenerative medicine. I was involved with the ARM group as well.

Dr Hudson: My name is Ian Hudson. I am chief executive of the MHRA. The MHRA is very much involved in regenerative medicine in a variety of different ways through two of the three centres within the agency. We have the National Institute for Biological Standards and Control, producing biological standards; it has an advanced therapies division and a stem cell bank. The other centre where there is a lot of involvement in regenerative medicine is the regulatory—

Q93 **Chair:** I am sorry; this is a funny room, so can we speak up a bit? Thank you.

Dr Hudson: Sure. The first centre within the agency where we are very much involved in regenerative medicine is the regulatory centre where we have responsibilities for medicines, devices and so on. We are involved in a number of different ways: first, through our support for innovation, our innovation office; all our outreach work with people working in this area; our one-stop shop in relation to advice; clinical trial approval in this area and support for those wanting to do clinical trials; market authorisation approval, working in the European context with our colleagues throughout Europe; and support for manufacturing, GMP, inspection, and so on. It is quite broad involvement in the area.

Q94 **Chair:** Forgive me, as we go along, if I ask you not to use an acronym. If you could say what it is, it would be helpful for all of us, but thank you. That was great.

Professor Whiting: My name is Paul Whiting. In my current role I am professor at the institute of neurology, University College London, and chief scientific officer of the Alzheimer's Research UK UCL Drug Discovery

Institute. In my previous role at Pfizer I led and co-led two cell therapies into the clinic, one a mesenchymal stem cell-type therapy for inflammatory diseases and the second a UK-based therapy based on human embryonic stem cells for the treatment of eye diseases. In addition, I am, as you can see, on the MRC regenerative medicine research committee and I am a member of the regenerative medicine platform, again for the MRC.

Dr Kili: Good afternoon. I am Sven Kili. I head the cell and gene therapy development group with GlaxoSmithKline. We sit as part of the rare disease group. My history is that I am an orthopaedic surgeon. I have been developing and working with cell and gene therapies for probably 15 years. I was instrumental in and led the first combined advanced therapy medicinal product that was approved in Europe for cartilage defects and subsequently moved over to GSK, where I head the group. We had the first rare disease gene therapy approved for children, which is life saving for a condition called ADA-SCID; it was approved earlier this year and is the first one in the world. We are currently developing a number of other cell and gene therapy approaches, both in the oncology space and in the rare disease space. I also chair the Bioindustry Association cell and gene therapy advisory group and sit on the advisory groups for the Alliance for Regenerative Medicine and the standards co-ordinating body.

Q95 **Chair:** Thank you. Could I ask the panel, starting with you, Michael Hunt, to set the scene for us? What do you think are the major therapeutic opportunities in regenerative medicine and the specific challenges in moving from the bench to the bedside, as it were?

Michael Hunt: To answer that question, I suppose it depends how you define regenerative medicine, because it is such a broad area. I will restrict it to the area where most of my experience has been gained, which is in the area of pure cell therapy, using cells themselves as therapeutics as opposed to, say, gene therapy or perhaps CAR T-cell therapies focused on cancer. Cell therapy in particular, which is where ReNeuron has spent all of its time since inception, tries to harness the power of stem cell science and biology to target intractable diseases.

I suppose the real notion of cell therapy is its ability, at least in theory, to offer a curative potential for intractable diseases, so we are looking at diseases that might be acute or chronic. We are focused on the chronic spectrum, including stroke or the consequences of stroke. You can take that further into perhaps islet cell transplantation for diabetes. Obviously the central nervous system is also a big area of interest for us, so we have had research programmes looking at Parkinson's and Huntington's as well. The potential applicability of pure cell therapy is broad, and that is why I think it attracts attention and has the profile and importance that it does—the potential to offer a completely new paradigm for treating diseases where conventional approaches either have not been tried or clearly do not work.

Q96 **Chair:** Okay. I note that very powerful word "curative." What are the

challenges specific to the field?

Michael Hunt: There are still many technical challenges associated with certain stem cell approaches. A lot of nuts have been cracked over the last couple of decades in terms of sharing the early proof of the principle of cell therapy at a pre-clinical level, testing cells in various animal models of diseases, for instance. There is a lot of published work there that has known a good deal of success, to be honest, including work that we have done. Trying to fit cell therapy into a regulatory system has thrown up many challenges over the years, and again, thanks to the work that the MHRA and others have done, the UK has largely cracked that problem as well, in terms of the regulatory pathway to get commercially sponsored cell therapy treatments through into the clinic. The biggest challenge that now remains, beyond garnering clinical data for proof of concept in man, is getting these treatments adopted in the UK through the NHS in routine practice and, of course, paid for—reimbursed. How are we going to pay for treatments, especially where there is the potential for very significant long-term healthcare savings, quite apart from patient benefits in the long term, that may come at a considerable up-front cost compared with more conventional treatments? That is the difficult equation that the field now needs to tackle and solve.

Q97 **Chair:** Excellent, thank you. That is very clear. Dr Hudson, would you add to that or disagree with any of that?

Dr Hudson: No. I would very much agree. There are very many opportunities available with regenerative medicine out there, whether it is in the tissue repair area, oncology, gene defects or rare diseases. As with any new area of science, there are challenges but there are also ways round them. Some of the areas of challenge are in relation to defining the mechanism of action, the potency of cell, the shelf life, the manufacturing, that side of things, and the clinical trials would be often in very small populations, but there are ways around all that. One key thing we have been very keen to do is work closely with those developing products in this area to support them coming into a regulated environment so that there is consistency, quality, safety and efficacy, and products can be developed appropriately and ultimately get licensed. We have put a lot of effort into that support-type activity through things like our innovation office, our scientific advice service and—we may come to it—a one-stop shop on behalf of other regulators in terms of advice. We are trying to overcome some of these issues in relation to the challenges I think some people have faced.

Q98 **Chair:** It sounds as though, for you, the challenges were kind of expected.

Dr Hudson: As each new set of products comes along, they throw up new challenges, as science always does, but I do not think we have yet found anything that we cannot find a way to overcome by close collaboration between ourselves and the person developing the product.

There is usually a way. I think to date we have always found a way forward.

Q99 **Chair:** Thank you. Professor Whiting, would you agree or disagree with any of that?

Professor Whiting: I echo one of the previous points. I am not entirely sure that regenerative medicine is a very helpful term, because it means everything and nothing, and I think somehow we need to move away from that to a more prescriptive and descriptive definition of what regenerative medicine is.

Q100 **Chair:** Do you offer a better one?

Professor Whiting: We can think of it in a spectrum of cell therapies, perhaps acellular or biomaterials, and then a combination of the two. Perhaps that is a more—

Q101 **Chair:** Cell therapies and acellular ones.

Professor Whiting: Acellular therapies, that is correct, and then there are combinations of the two together. Perhaps that might be a more useful way of thinking about it, particularly in the context of pharma. Traditionally, pharma is very used to delivering small molecules as drugs, or antibodies and biotherapeutics as drugs, more recently, and of course there are other modalities. When one lumps them in the term regenerative medicine, it is potentially a disruptive set of technologies but it is not always clear how it fits in and alongside those two other very traditional modalities. It is very important that we have clarity over how we define it, because it is going to be important for the pharmaceutical industry to understand those modalities and how they fit within their portfolio, and how they position them towards the various disease areas they are invested in and in which they are interested. That is one point.

The second point is that in the UK we have an absolutely outstanding science base in this area, not just in the basic science but the translation of that basic science, in my view. Our two main international competitors, I would argue, are the US—not surprisingly—and Japan. For us to continue to be leaders in this field, we need to continue to maintain investment in the basic science and the translational science. Otherwise, our ability to stay in the vanguard of moving it into commercial products is going to severely wane, I believe.

Q102 **Chair:** Thank you. Dr Kili, would you agree with this way of talking about regenerative medicine, as you are with GlaxoSmithKline?

Dr Kili: Yes. We need to think very hard about how we describe regenerative medicine. I do not disagree with Professor Whiting; it does create some disturbances and uncertainties, particularly in big companies. The other thing to bear in mind is that these are not small molecules, these are not large molecules and these are not vaccines. They are very different and, as such, we need to take a different

approach to developing them. We have had some extremely good work done, as others already have mentioned. The discovery and the translational capabilities within the UK are superb and world leading. We also have the MHRA, which is probably one of the best agencies helping to understand, and it is working collaboratively with companies to develop good ways of taking these therapies forward. There are lots of things in the typical way of developing a small molecule that do not apply to developing a cell therapy or a gene therapy, or even a tissue-engineered product. I will give you an example. If you have a technology, a cell or a gene therapy product that is autologous—using cells from the patients themselves—it is often very challenging to show how you might overdose that patient. How do you overdose someone with their own cells? It is things like that. The agency has been very forthright and proactive in working with companies to work through different ways of showing things. Also for cell and gene therapy we have the Catapult; the Cell and Gene Therapy Catapult has been really helpful for investigators, companies—small and large. It has helped them solve a number of problems in different products. That is a really great way.

One challenge I still see is that, as we get into clinical development, the infrastructure and the end-to-end work that is required to develop a product in a clinic is somewhat lacking in the UK. Very often, companies have to go outside the UK. The US is obviously one of the big places they go to and, more recently, Japan, as has already been mentioned. If we can optimise that and help to accelerate the work that is done in the clinic to show the benefit and then bring in mechanisms for rapid reimbursement so that patients are able to get hold of these therapies very rapidly—a cost-effective mechanism so that the companies benefit, with all the outlay of the very high manufacture, the very high development costs—that will really help to foster things.

Q103 **Chair:** That is similar to what Michael Hunt was saying. You say that there is a barrier to these medicines coming to market? Are you able to tell us why the US does the clinic work better? What is the difference?

Dr Kili: It is a multifactorial difference. There is no one specific reason. Very often we have large clinics with very well-staffed groups that are able to carry out the clinical studies. Very often, if you approach an NHS hospital, they are understaffed. The nursing staff who are working on support are so busy just taking care of patients that they do not often have the time to look after a study and things like that. We need a mechanism to make them better to be able to do clinical trial work.

Q104 **Chair:** Okay, thank you. Professor Whiting, on this barrier to getting product to market, would you add anything, in your experience, on the difference between the UK and perhaps the US on the clinic side of it?

Professor Whiting: No. That is very reasonable. I would also like to reiterate what was discussed about the MHRA. From personal experience, I can say that they are very open and supportive in terms of helping to understand the path towards patients. In the context of these very novel

types of medicine, novel modalities, where they have never been into people before, it is very helpful to have an open dialogue. Nobody knows the clear answer. You have to work it out. It is on a science-driven and risk-driven basis, and the partnership that you can have with the MHRA is enormously important in enabling you to get these medicines first of all into early-stage clinical trials and then, hopefully, accelerate them through.

Q105 **Chair:** Dr Hudson, what makes the MHRA work so well? Is it just, as we are hearing, about listening, being open and understanding? I love this kind of question, but how come you have got it so right?

Dr Hudson: I would like to thank my colleagues on the panel first for their kind comments. The philosophy we operate is that we want to see new products getting through for the benefit of public health, because if we do not have new products getting through we cannot see the improvement in health. We then put a lot of weight behind how we can support those developing the products optimally to get them to the market. For many years, we have had scientific advice, then we launched the innovation office and we have been trying to make it easier across a number of regulators, with a one-stop shop, to bring in advice from other regulators—HFEA, HTA, HRA, DEFRA, the Health and Safety Executive, that sort of thing—to try to facilitate that as much as possible. The products are difficult enough, so let's make the environment that we operate in as smooth as possible to transition through and generate the appropriate data to give us the assurance we need that the products are of appropriate standards of safety, quality and efficacy.

Victoria Borwick: Might I follow up on the question to Dr Kili? You were talking about the actual patients and clinical trials. How are the patients selected? Do you think enough people come forward? The point you have all talked about is getting it right at the frontline, for want of a better word. Could you elaborate a bit more on what the Chair was asking you? You said that nurses were busy and it does not always fit in with the timetable of what is going on. Are enough people being put forward? How are those people selected? That would just complete the question.

Chair: I will hand over to Chris because that covers his questions.

Victoria Borwick: It sort of does, but I was not quite sure.

Chair: Let us see what happens with Chris on the trials.

Victoria Borwick: Okay. I would be very happy if the panel added that to their answers. I do not quite understand how people get included.

Q106 **Chris Green:** Dr Hudson, how well do you think the existing clinical trials framework operates?

Dr Hudson: As you know, the history is that there was the introduction of the 2001 clinical trials directive, which came in, I think, in 2003, and while it achieved a lot in terms of a common approach across the

European Union, it was not without its faults, in that there were still some local/ national requirements and some duplication of assessment across the community. There was recognition that it could have been more risk based as well. A lot of work went on between then and now on what further things could be done, and bit by bit some of the national requirements have been eroded and we have been taking a more risk-based approach. The main thing is the new clinical trials regulation that has been negotiated across the European Union, which should be coming in in October 2018, and addresses many of the shortfalls of the clinical trials directive: it has a single application across the community; it has a portal; it takes a much more risk-based approach; there is publication of the results at the end of the study, and so on. It really addresses across the community the shortfalls, as a regulation, of the clinical trials directive. In fact, we have actually found a way round many but not all the shortcomings of the clinical trials directive and there is still further room for improvement, but the regulation should address many of them.

Q107 **Chris Green:** That is one of those aspects where it is sometimes good to have bad law that you can work around, and you have stability rather than constant change all the time. It is positive to hear of the new regulations, and I think most people regard them a substantial improvement, but in the process of those regulations being developed there are no doubt some outstanding concerns. Now that we are leaving the European Union, are there other opportunities that you might see to further improve those regulations?

Dr Hudson: The whole Brexit discussion is long and complicated, but in relation to Brexit the agency has put a taskforce in place to look at scenarios and options and, if it is a hard Brexit, what the options may be. Certainly there is an opportunity to reflect, in the whole regenerative medicines or advanced therapies area, what those opportunities might be. We should also remember that the UK is a relatively small market, and products are developed for European or global markets, so there is some limitation on asking for lots of different things; but, absolutely, I think we will be looking to see whether we are as risk based as we can be, and whether we are asking for all we need or whether there are further things we can do on classification of products, for example, or certification in terms of rolling reviews of products, that sort of thing. There may be some opportunities there. We are at an early stage of thinking about them, but there may be some opportunities. The MHRA's thoughts on this will feed into the Department of Health and broader Government in negotiations, but, depending on where it all gets to, there may be some opportunities in that area, yes.

Q108 **Chris Green:** As long as there is equivalence between what we do in the UK and what the EU does, as long as they recognise our standards, there should not be any problem working with the EU, and having that market of 500 million, because we are already so in sync at the moment.

Dr Hudson: There are several points on that. One is equivalent standards, yes. Then the question of who is deciding, and whether that decision is agreed by others or not, would come into that. If we deviate in terms of standards, it could be problematic, given that we are a relatively small market, but there may be ways that we can still help on the way to those standards, for example. The bigger picture, ultimately, is going to be the decision making—whose responsibility it is for what. I think your questions started off with clinical trials. Clinical trials remain a national authorisation. It is up to us, the UK, to decide on clinical trials in our own jurisdiction, but if companies want to do a multi-state clinical trial, indeed about half the clinical trials in advanced therapies that we see each year are multi-country, we will want a common approach to that. We will not want to do too many different things.

Q109 **Chris Green:** That is a very clear message to the Department for Exiting the European Union: we need that co-operation after Brexit happens. Are there any other comments from the panel?

Dr Kili: I agree completely. It is absolutely important for companies developing these therapies to be able to have harmonisation in terms of clinical trials, on authorisation and things like pharmacovigilance when we are looking after patient safety. For us to be harmonised with the rest of Europe will be a very useful thing and will make the UK much more appealing. We need also to think about whether there are mechanisms we can find to make the UK more appealing. Some of the things that have been talked about are being able to encourage companies to do phase 1—early phase—trials within the UK to try to keep them developing and doing a lot of the work in the UK.

Q110 **Chris Green:** Can you give an idea of the typical timeline for a clinical trial, how you think you could perhaps accelerate that process and whether the UK, perhaps doing its own thing, could give an opportunity? How long would it normally be, and do you have the sense of how long it could be if we improve the process?

Dr Kili: That is a bit of a tough question, because it depends on the therapy that you are looking at. If you are looking at pure cell therapy, where an outcome may be two or three months down the line, versus a gene therapy, where your outcome may be five or six years down the line, they are two very different potential timelines. If we can think of ways to improve the ability to stay in the UK from an early perspective, and show phase 1 safety within the UK environment, it would encourage researchers and companies to have a lot more faith in UK clinical research and translation from pre-clinical to clinical, and that would be useful.

Q111 **Chris Green:** On a distinct note, you made reference about NHS understaffing and pressures within the national health service. I think there ought to be far more collaboration between people developing new therapies, new drugs and our health service. I get the sense that on a national health service scale it is quite difficult. As a Greater Manchester

MP, I think there is a huge possibility within Greater Manchester for devolution to give opportunity. Do you think there is that possibility of greater collaboration between the private sector, the research sector and the national health service?

Dr Kili: Absolutely, yes. It is critical to be able to do it. The national health service is under a lot of stress at the moment and, if the private sector is able to help ease some of that burden, we should look at imaginative and unique ways of being able to do that. Developing much closer collaboration gives ownership to the NHS centres as well as to the developing companies. I am sure that will also help create better relationships and encourage people to stay for further stages of development within the UK.

Michael Hunt: There is a very important rider to that comment, which I also agree with: the earlier you can get these treatments into the NHS system—let's say, at clinical trial level; early-stage studies, as Sven says, are fine—the earlier you are getting the NHS familiar with these types of treatments, how they are dealt with, how they are processed at pharmacy and how they are then delivered to patients, the better, because that is what the NHS is going to have to square up to as these treatments get closer to market anyway, and the earlier we can promote that innovation in the NHS at a clinical trial level, the easier it is going to be further down the line when these treatments start to get approved, all being well, and adopted in the NHS for patient benefit. It is vital. The NHS is a resource that we have that is not replicated anywhere else in the world, so why don't we use it for that purpose?

Chris Green: Do you think there needs to be within the national health service, perhaps within Greater Manchester, but also within politics, a change of mindset? At the moment there is very much a kind of "Private sector bad, NHS good."

Q112 **Chair:** I am going to override you, Chris, because this might help with the answer: do you find that the science parks attached to teaching hospitals are already making that difference?

Michael Hunt: I think that is right. In our experience, we have aligned ourselves with a number of clinical centres up and down the UK, specific to the trials that we are undertaking in the UK, and there are some very good centres. Not every hospital is going to be innovation focused, either because of resources or because of the demeanour of the key principal investigators and their various priorities, but there are a number of centres that I could see, or we could see, being centres of excellence for promoting these types of treatments in certain disease areas, perhaps.

Q113 **Chair:** What are the top three?

Michael Hunt: I probably ought not to say—

Chair: The joint top three.

Michael Hunt: In our particular case, where we have been conducting trials in stroke, for instance, Glasgow is an absolutely excellent centre. Glasgow Southern General is the actual hospital where we have conducted two studies so far. One is completed and the other is ongoing. There are a number of other centres—Newcastle and Southampton. How can you tell? Because recruitment rates are great; they manage to get patients into these studies, which picks up on the earlier point that was made.

Q114 **Chris Green:** That is what I was going to follow up on. If you can get that in Greater Manchester, it is large enough to be meaningful, in terms of population, but small enough that people have a sense of connection. If that occurred, once you saw the development and the innovation locally, hopefully people would identify with it more and it would be easier perhaps to get the volunteers you need.

Professor Whiting: Can I build on that? I was at an analogous discussion earlier this week, on developing UK industrial strategy as regards the drug discovery sector as opposed to the regenerative medicine sector. One of the points that came out clearly was that the national health service is potentially a unique selling point—USP—for the UK in terms of leveraging investment and fast-tracking medicine through to patients. That cuts across the two sectors that we are in danger of dividing. In fact, they should not be divided, I would argue. We need to be thinking more holistically and in a more joined-up way around regenerative medicine and about other therapies as well, because some of the challenges and issues are very similar.

Q115 **Chair:** Which other therapies?

Professor Whiting: Small molecules.

Q116 **Chair:** The vaccines.

Professor Whiting: They are all medicines for people at the end of the day.

Q117 **Chair:** More the biological ones.

Professor Whiting: Yes, and antibodies and things. I think a joined-up strategy at the top level would be most helpful, rather than trying to slice and dice too much. The other point that came across very clearly, and may resonate with the discussion here, is that it is not so easy to interact with the NHS very often. It is not obvious where the portal is, the entry point, for some things you want to do, and people are enormously conscious of the perceived or otherwise "stress" that the NHS is under. That is, if we are not careful, going to build a reluctance to interact with the NHS.

Q118 **Chair:** And a Catch-22.

Professor Whiting: Exactly, and we will lose that USP potentially, because it will become a self-fulfilling prophecy if we are not careful.

Q119 **Victoria Borwick:** I want to go back. The question was strategic, but my original question, to follow up on what the Chair asked, was back on the ward, which is what you talked about. If there is something on the ward that could be improved, we really want to know for the benefit of our report, such as if somebody is not on a trial and could be recommended. You hinted, in response to the Chair's question, that things could be improved, and I am very keen that we not only do the strategic points, but find out if there are other points we should be feeding in. I would welcome your comments.

Dr Kili: It is a slightly difficult question to answer in such a broad scale, because it would depend on the specific trial and on the indication that is being looked at.

Q120 **Victoria Borwick:** But that is also valuable information to put in, the fact that not every trial is the same, isn't it?

Dr Kili: Absolutely. I can speak from my experience of looking at therapies and trying to recruit patients in an environment that is looking more at younger patients who have cartilage injuries, and developing a cell therapy for cartilage repair. We found that a relatively small number of patients would be referred to the centres that had the capability and were set up to run the clinical trial. You would have certain centres of excellence, as Michael has already alluded to, that you would tend to run these trials through, and that is very often due to some of the complexities of setting up, running and keeping a trial going in terms of data collection, just having people to do that. It is also around the logistics of developing and shipping cells in and out of a centre. There is a requirement to be licensed for that. It is not something that every hospital can do at the moment, so you are limited to a number of centres where you can study those patients, and getting patients from outside that catchment area can often be challenging. Then, and this is something that was hinted at by other members of the panel, if we can look at the NHS as a holistic group and refer patients and even get out there that there is a trial going on looking at this, that or whatever indication and encourage clinicians to refer their patients, if appropriate, into that trial, all of a sudden we go from a catchment area of Manchester to a catchment area of the United Kingdom and things change very rapidly from that.

Q121 **Chair:** This is a bit baffling, though, because it is not new for the NHS to have patients informed about trials and to have clinicians aware of trials, wherever they are in the country, and it is not new to have websites where patients can put in their clinical information and work out where the most appropriate trial is. This is not specific to this field, is it?

Dr Kili: No, it is not.

Victoria Borwick: Is it just because we are regionalised—NHS England, London, and—

Chair: No, it works for other medicines.

Victoria Borwick: I agree, but I just thought—

Dr Kili: Very often in the cell and gene therapy space it is about the capabilities of the clinician and the willingness to share patients and get involved.

Victoria Borwick: That is good for our recommendations, thank you.

Q122 **Chair:** You are saying willingness to get involved is a problem.

Dr Kili: It has been the case with certain therapy areas, in my experience, that clinicians are loath to send their patients because it is almost a case of giving up the patient.

Chair: Even though, as we have been told, the opportunity is curative.

Q123 **Derek Thomas:** Can I bring our attention to animal testing? MPs receive a lot of emails each week about local and national concerns, and animal testing is usually in there somewhere. To what extent is animal testing in regenerative medicine unavoidable, and how is the need for testing human cells in an animal model best handled? Dr Kili, you might want to address that one.

Dr Kili: It is a bit of a difficult one. A lot of the regulations to which we have to work require a degree of testing in animals, and I think our capabilities to test in silico at this stage are probably not as good as they could be to completely replace animals, but there is always concern that many of the animal models that we use, even though they may be humanised, may only give us certain amounts of information. Some of the discussions earlier with Dr Hudson were about having a risk-based approach. There are certain things that we still need to do in animals, but we should be, and I think most companies are, looking to minimise that amount of work in collaboration with the regulatory agencies.

Q124 **Derek Thomas:** Is there anything you want to say about that, Mr Hunt?

Michael Hunt: The issue with animal models is their predictability. You could say that for any type of therapeutic, I guess, but it certainly applies to cell therapies. At the moment, to get to your first question, it is unavoidable. In the case of cell therapy approaches we have adopted, we have done all our work in small animal models, by which I mean rodents, so there is a limit to the amount of animal work that one can or has to do to get a product through to the clinic.

I agree with Sven's point: there is only so much that an animal model is going to tell you, and in the past there has been a predisposition that, unless you have tested your therapeutic candidate ad nauseam in just about any animal model you can think of, you cannot get into man, whereas I think there is another approach that would both mitigate the use of animals in testing and still mitigate the risks in taking a new intervention into man. You do it on a very cautious phase-1 basis, which is precisely what we did with our first stroke programme, a very cautious

DSMB—Data and Safety Monitoring Board—governed phase-1 study, where one patient essentially was treated at a time. Then there was a stop-off and a holding period, and then the DSMB met and made sure everything was okay to proceed to the next patient. That type of risk-based approach would mitigate the use of animal testing, which, at the end of the day, is not particularly predictive of outcome anyway, clinically.

Dr Hudson: Could I add a comment? We are very keen to see a reduction in the number of animals used. In some circumstances, it is not possible yet to avoid using animals. We have been very committed to, first, giving advice to companies that, if there are alternatives, they use the alternatives, and indeed to develop alternatives ourselves. NIBSC has been involved in the three Rs, trying to find alternative ways of doing things to avoid animal studies, but it does not—

Q125 **Chair:** What are the three Rs?

Dr Hudson: Reduce, replace and the third R I cannot quite—

Professor Whiting: Refine.

Dr Hudson: That's it. Thank you. If we are to move away from animals, which we all think is absolutely the right way to go, we have to have appropriately valid alternatives, which have to be developed properly, and we have to have confidence that we know what they are telling us. We are certainly a long way from the tick-box "Must do animal work," and indeed if we think an animal study is not going to tell us anything useful, we advise companies not to do it; we do that through our scientific advice meetings on occasions. We are working on a journey in this direction, but we cannot replace the use of animals completely.

Professor Whiting: Can I add one example? There is new technology, induced pluripotent stem cell technology, for which the Nobel prize was awarded a couple of years ago. One can imagine how that could be used for autologous therapies, that is, taking a fibroblast from me, turning it into a kidney and then putting it back into me. If one thinks about that at a whole population level, it is simply not going to be possible either from the scale or from the financial perspective actually to do an animal safety study on every single person, looking to the future. It is simply not going to be possible to do that, I would argue. Therefore, we need to develop smart technology, smart approaches, to be able to define at cellular level the safety of that autologous transplantation or self-therapy. That again speaks back to the critical importance of our basic and translational science in the UK for developing enabling technologies so that when these therapies reach a point whereby they are put in—you want to test them in people and you want to do that at scale and bring them to the patient—we are able to do that and we have the technologies in place.

Q126 **Chair:** I am a bit confused. If we are talking about autologous medicine, what is the point of the animal experiment, scientifically?

Professor Whiting: That is exactly my point; arguably you will not learn a great deal from that.

Q127 **Chair:** Okay, so why are there animal experiments? Are you just saying that is a hangover from the 20th century?

Professor Whiting: No. At the moment, we can and will learn from specific animal experiments on a case-by-case basis, as Ian has just indicated.

Q128 **Chair:** Could you give an example?

Professor Whiting: An example is understanding, when we deliver cells to an animal, where those cells end up and where they go. We can trace the cells and understand where they end up in the body; we can determine whether or not there is any tumorigenicity or teratoma—a risk in terms of safety.

Q129 **Derek Thomas:** We have talked about how regulation has changed and will change at the end of 2018, or at least improve. Does the regulation framework at the moment allow smaller datasets to be used in clinical trials?

Dr Hudson: Yes, indeed. There is no one size fits all; the clinical package will be very much tailored to the circumstances. We have orphan legislation. At the moment, we are under European legislation, but there is licensing under exceptional circumstances, for example, that will allow much reduced data packages and there is conditional authorisation that allows for reduced data packages. There are opportunities, but the approach that is taken is very much what is appropriate for that product in the circumstances, taking into account what else is available, and so on.

Q130 **Derek Thomas:** Would you argue, particularly in 2018, that regulation strikes about the right balance to allow freedom to develop clinical trials and to get things into use?

Dr Hudson: In the clinical trial environment, yes, the clinical trial regulation has addressed a lot of the shortcomings. We are also looking at, again in a European context, a number of other initiatives, such as adaptive licensing pathways—the PRIME initiative that the European Medicines Agency is taking a lead on—that are tools, flexibilities, that allow products to come through. Yes, I think the framework is there, but it will need to continue to evolve as we learn more on new products. The current framework will allow products to be developed, yes.

Dr Kili: I agree exactly with what has been said. We have experienced the first gene therapy product that GlaxoSmithKline developed. Eighteen patients were treated and went into the main file. That requires a long-term follow-up and a registry to follow those patients over a long period of time, because you are changing their genetic make-up. The agency took a very pragmatic risk-based approach on reviewing the data,

and it allowed the therapy to get out to patients as quickly as possible so that it could actually make a difference for the patients it was developed for.

Q131 **Chair:** That is in this country.

Dr Kili: It is throughout Europe. It has a centralised authorisation so it is throughout Europe, but it is licensed.

Q132 **Chair:** Were there some UK people in that trial?

Dr Kili: Yes, absolutely. In all the indications, actually, a number of UK patients were involved.

Q133 **Victoria Borwick:** Going back to stem cell therapies, if I may, some of which you touched on earlier, do you classify them as a medicinal product and therefore subject to the ATMP regulations, or would they continue as they are? Who would like to take that on? I presume Michael.

Michael Hunt: Our products are certainly ATMPs and fall under those regulations for sure.

Q134 **Chair:** We are talking about advanced therapy medicinal products.

Victoria Borwick: I should have said that in full. Thank you, madam Chair, you are quite right.

Dr Hudson: The advanced therapies regulation defined what advanced therapies were in terms of cell therapy, gene therapy and tissue-engineered products, but of course the interpretation of that is a complicated matter, and some of those have to be case-by-case discussions, and again we have an open door to discuss that. Basically, if the cells are taken and there is a significant, substantial manipulation of the cells, the manufacturing process, and so on, that makes it a medicine. Simply taking cells and using them for the same purpose would not. It really depends on what happens in the whole process, and some of those have to be quite complicated case-by-case discussions.

Q135 **Victoria Borwick:** How much intervention, change or manipulation would have to happen?

Dr Hudson: They end up being case-by-case discussions on the manufacturing steps, and so on, that are involved in the process. We are very happy to have discussions on that. Clearly things like blood transfusions are not medicines, but if you start manipulating cells, putting them in different places, and so on, it becomes a medicine.

Michael Hunt: As an example, for one of our cell lines we genetically modify it to be able to expand it at scale, because we adopt an allogeneic approach to treating the very large patient populations that we target in stroke, for instance. That is clearly a manipulation that would bring that particular product within the ATMP regulations.

Q136 **Victoria Borwick:** That rather takes me on to my next question. What

needs to happen to mass produce some of these techniques? Professor Whiting, if I may summarise—probably badly—you explained how they were discussed on a case-by-case basis, and my question was really about when you take autologous cells from a patient and put them back. How do you make that at scale, or is it not possible? Does it always have to be for the particular patient?

Professor Whiting: For autologous transplantation, the scale you need to make it is dependent on the scientific basis for how many cells you need to deliver to have a therapeutic benefit. It is an open-ended answer. For other therapies—some of the mesenchymal stem cell-type therapies—we are talking about hundreds of millions of cells per patient. If one thinks about, for instance, a human embryonic stem cell-derived cell replacement therapy for the eye, that could be about 100,000 cells per patient, whereas for a liver transplantation, it would be hundreds of millions of cells per patient, probably. Therefore, there is no one size fits all and you have to develop your strategy and your manufacturing strategy to meet the needs of the patient basically, and the population that you are going to be treating.

Q137 **Victoria Borwick:** Making the decision about what is possible for mass production is obviously quite complex.

Professor Whiting: It is a critical issue and it needs to be built in at a very early stage of the development of your therapeutic, so that you can plan ahead to enable you to treat patients when you get to that point in the process. On the other hand, there is always the risk of investing too early and at too big a stage, and then finding that two steps further on from where you are, the whole treatment and the whole rationale implode and thereby you have invested money when you should not have. There is always a risk/benefit measurement in how you go about developing these types of therapies.

Q138 **Victoria Borwick:** Could you touch on the safety concerns about the stem cell therapies and the knowledge gaps—I do not know whether that comes under the strategic work you are doing—and then the regulatory challenges?

Dr Hudson: On the safety issues that we see with cells, first, in the introduction of cells you have to make sure that there is no contamination or no infection transmitted and then you want to make sure that the cell goes where it should, performs as it should, that it does not turn into a tumour or something like that, and does not migrate somewhere else. Those are some of the issues with cell therapies that we need to be careful about, and monitor very carefully for and be assured of as part of the review process.

Michael Hunt: Having been involved in this field as long as I have, the previous dogma, when it came to pure cell therapy, was risk of tumour formation and rejection if it was an allogeneic approach, and I think this is largely an empirical exercise. In order to get into man, one has to do

exhaustive pre-clinical testing to demonstrate that the therapy is safe, at least at a pre-clinical level: tumorigenicity studies, biodistribution studies, and so on. Once you are in the clinic, it is a question of long-term follow-up of patients and a cautious approach to treating the patients in the first place. As far as I can see, the safety of cells per se, certainly within the context of well-regulated environments, is much less of an issue, or perceived issue, than perhaps it was, say, a decade ago when none of these treatments had been tested in man. That particular issue, from my perspective, seems rather diminished compared with the concern there was perhaps a decade ago.

Q139 **Chris Green:** Is there an opportunity when thinking about the industrial strategy that is being developed that it is not just about heavy industry, and that there is a place for industrial strategy in this area? Are there any indications at the moment about what Government can or will be doing in terms of industrial strategy for the regenerative area?

Michael Hunt: That is probably going to be touched on by others who are due to give evidence, but one obvious area is manufacturing capacity for these advanced products. The Cell and Gene Therapy Catapult have done a lot of work around that and indeed are building their own capacity in Stevenage to address it, at least in part. It could be anything that addresses the issue of how you can secure manufacturing of these advanced therapies in the UK, and then put the relevant supply infrastructure around those manufacturing sites to deliver therapies in clinical centres, sometimes at very short notice—some of these treatments have very short shelf lives and so on and so forth—and how you make all that work. There is an opportunity in the UK. It is a bit spotty at the moment in terms of where those manufacturing sites are. A lot of them still reside in academia. There are very few large-scale purely commercially-ready sites, but hopefully that will come. That is certainly one area where an industrial strategy can play a part. It is getting the boring bit right, if you like: how you actually make and ship these products before they even get to the patient.

Dr Kili: I echo that; it is critical. We also need to think about the people who are going to work in these centres. There is a big training and resource issue that needs to come along with the investment to be able to manufacture these at large scale, exactly as Michael mentioned—the manufacturing, the logistics and getting them out there. Who is going to staff that? We need it to tie those two together as we think about that.

Q140 **Chris Green:** On a slightly different note, under the regulation of advanced therapy and medicinal products there are exemptions for stem cell therapies to be administered within a hospital setting as long as it has good manufacturing practices. Is the EU model that we have for dealing with such hospital exemptions fit for purpose? I do not know who would like to start.

Dr Hudson: Let me start. There are basically two mechanisms for giving unlicensed products to patients in this area. One is the hospital

exemption; the other is the so-called specials regime. There is a little bit of difference between the two. The main difference has been that the specials have a clear end date. When a licensed product is available, the provision of unlicensed material ceases. In general in the UK, where we have been approached—we have 20-odd, or so—I think we have only granted one hospital, but, increasingly, we use the specials regime, as it serves the same purpose and has a clear end date, if there is a licensed product that is available. People have interpreted the hospital exemption a little differently in different member states, and in the past people have asked for it to be harmonised, but in general it is a member state competence in terms of unlicensed use of medicines, and for us using the specials seems to work very well for the purpose.

Dr Kili: I completely agree. The big challenge is how it is interpreted in every country. Exactly as we have heard, in the UK, it seems to have been, as we would argue, in a very pragmatic way. It was designed very much for a clinician, based on a specific patient for a specific need for a cell therapy to be manufactured, and it was talked about as being on a non-routine basis, so there have been a lot of discussions with different countries as to what constitutes non-routine. There are certain other countries, and Germany is a very good example, where companies are actually able to sell products that everyone else seems to think should be covered by the advanced therapy medicinal product, but they are selling them under the hospital exemptions. The challenge with that is you do not get cross-European harmonisation on labelling and review, or a safety and efficacy perspective, or a pharmacovigilance capacity. The requirements for all of those are very much up to the local competent authority and the company potentially. From a company perspective, it does not always create a level playing field, because companies that have gone through all the requirements to have a licence and a marketing authorisation under the European ATMP regulations will have had to spend substantially more money and have substantially more infrastructure in place, versus a small company that is able to sell a product at a much lower price in a specific country. Potentially, it starts looking a little unfair.

Q141 **Chris Green:** This is not one of those areas that we always hear about with Britain gold-plating EU regulation or making it tougher, is it? Would you say this is one of those areas or not?

Dr Hudson: I would say that some other countries have gold-plated it actually. We have applied a very pragmatic, straightforward approach. We can object if we want to, but we absolutely have not, and some countries—I think Germany—apply a much stricter review for hospital exemption. We apply a much more proportionate, risk-based approach in our review.

Q142 **Chris Green:** Are there any regulatory barriers slowing the development of ATPMs—any regulatory barriers that we would like to overcome?

Michael Hunt: As I said right at the start, the areas of concern, or barriers, for want of another word, are really when you get closer to market. Companies like us spend a lot of time thinking or worrying about the ability of payers to pay for these treatments: how are they going to be paid for, are the existing mechanisms appropriate, in terms of NICE evaluation, HTAs, and so on, and, if they are not, what can be done about it? That is something that the ARM group put a lot of time and thought into and a mock appraisal was done of a CAR T-cell therapy for ALL, or cancer, to see whether the NICE evaluation system might work in terms of evaluating proportionately the benefits versus the cost of treatments of this nature, where perhaps there is a significant up-front cost but very substantial long-term benefits.

The general conclusion was that the NICE evaluation criteria in the UK could be applied, but there are some tweaks; the report said that tweaks might be necessary in terms of how you judge or deal with the uncertainty associated with lack of long-term data for some of these treatments. You are looking for long-term benefits but the datasets may not actually exist when treatments come to be evaluated, so how do you deal with that and how can you get those treatments reimbursed in the absence of those data? Thinking about payment for outcomes further down the line is an obvious model, but these are things that really matter to companies like us, because our investors want to see some kind of outcome and, frankly, as a UK player—this is somewhat parochial perhaps—we would like to have our treatments ultimately approved on our home turf. It matters.

Q143 **Chris Green:** We want the development and we want the research, but we also have to have the early adoption as well.

Michael Hunt: Yes, absolutely. We have a fantastic research base, as Paul said earlier. We have dealt with the regulatory hurdles that previously existed; those are, in our view, largely gone or eminently manageable. The big issue we are coming up to now is getting these treatments manufactured at scale, supplied and then adopted and paid for. That is where the focus is going to have to be, and those particular issues have not been solved yet.

Chair: This feeds into your question, Derek.

Q144 **Derek Thomas:** Yes. I do not know what the answer will be, and I am hoping you will know. How well does the current reimbursement system work for regenerative medicine? I guess if you want to invest money, you want a return—we all know how it works—but does investing in regenerative medicine provide enough certainty to the pharmaceutical industry?

Michael Hunt: Again, it is difficult to add much more to what I have said. In principle, it could. The way that regenerative medicine treatments might be evaluated under current systems could be problematic, because perhaps not enough emphasis might be placed on

long-term benefits, in the absence of having the long-term clinical data to support the fact that those benefits may arise in the future. An obvious example, thinking about it mathematically, is that, if one is evaluating treatments like this, in the models you are going to discount those future benefits, but you are not, obviously, discounting what might be an up-front cost of that treatment when it is administered. Already you are skewing the kind of cost-benefit ratio at a mathematical level against recommending the reimbursement of that treatment. There has to be close collaboration between NICE, the NHS, the industry and other players wishing to promote adoption of these treatments to see how that can be addressed. I am not sure I really have a definitive answer to your question.

Q145 **Derek Thomas:** It is a massive subject. Do you think there will be some research and development of medicine that will only ever be delivered or researched through public money, that there will be some areas that private money will never touch?

Michael Hunt: Conceivably. We have always tried to think of our treatments as no different from conventional treatments; they just happen to be living cells. We have tried to adopt a paradigm that makes them as straightforward as possible, and that is largely because, obviously, we are a commercial player and we do not particularly want to promote our products as being utterly unique or difficult to work with. You have to try to make them as boring as you can. To that extent, we would like to see them being reimbursed and adopted in the same way as other more conventional treatments. As to whether there are going to be more esoteric treatments that can only be treated in a slightly different way—I am sure there will be—I am not perhaps qualified to comment.

Professor Whiting: If we think about the stage of development of these therapies, we are at a very early stage. We do not really have any exemplars, so we have nothing to go by. If you reel back to 20 years ago, when the first antibody treatments were being developed, hardly any companies were developing them. Pharma was not interested at all because we only do small molecules, but then, as success begat success, suddenly interest grew in biotherapeutics—large molecules—and now for many companies most of their medicines are antibody-type modalities. One could conceive of a time, if this sector is successful and we bring patient benefit, and economic benefit through that to the country, when these will be adopted and they will be reimbursed. Clearly, other medicines have shown that it is possible; disruptive technologies will move through to become conventional technologies if they bring societal, economic and personal benefit.

Derek Thomas: I imagine this is a subject we can keeping revisiting over and over, because it will always be changing and developing, but thank you very much. That is helpful.

Chair: Thank you. You have been very clear and helpful in your answers and I thank you for your time. This is just the second of our sessions, so I

hope that, if the Committee contacts you later with other queries, you will be as generous as you have been this afternoon with your answers. Thank you very much.

Examination of witnesses

Ian Trenholm, Ian McCubbin, Keith Thompson and Dr Ruth McKernan.

Q146 **Chair:** Welcome to the Science and Technology Committee. Could our speakers introduce themselves briefly, and their background in the field, to set the scene for us?

Ian Trenholm: Good afternoon. My name is Ian Trenholm. I am the chief executive of NHS Blood and Transplant, which has three operating groups. We offer the blood service for England and the organ and transplantation service for the United Kingdom, and we have a diagnostics and therapeutic services group, which has a range of activities: collecting and processing stem cells from baby cords; collecting and processing human tissues—skin, bones, and that sort of thing; collecting and managing the processing of stem cells, both from patients and from donors; and helping to deliver the stem cell transplantation service for England. It is arguably the only live regenerative medicine service in routine use in a health system. We also work with a number of companies on developing cellular therapies, working from research through to manufacturing, helping them start to manufacture some of those therapies, getting them into a shape where they could be potentially a manufacturable product. Underpinning all that is a research and development group. Although it is focused largely on blood products, we do a lot of work on improving the manufacturing efficiency of clinical grade cellular products. We have contributed to the regenerative medicine expert group and we are an active participant in the ministerial advanced cell therapy taskforce. We are also members of the European Blood Alliance and the Alliance of Blood Operators, which means that we have active operational relationships with most of the major blood services globally, and gives us a reach, we think, of around 1 billion people.

Q147 **Chair:** Thank you.

Ian McCubbin: I am Ian McCubbin. Thank you very much for the opportunity to be here. I work for GlaxoSmithKline but am here in a different role today, which is as the chair of the Medicines Manufacturing Industry Partnership. By way of explanation, it was set up about two years ago in 2014 in response to a Government-industry initiative to create a way for the industry to speak to the Government with one voice about the future strategy for medicines manufacturing in the UK. That was important because the gross value add of the sector to the UK economy had been in steady decline since 2009, and it was our job to try to reverse that decline, even though the gross value add per employee in manufacturing is still the highest value add sector in the UK; we estimate

around £300,000 per employee in manufacturing, so it is very significant to the economy.

Because we had successfully created the group, and largely thanks to George Freeman's energy and enthusiasm when he was Life Sciences Minister, we set up the Advanced Therapy Manufacturing Taskforce, which, interestingly, all four of us are part of. We set that up at the beginning of 2016. The goal was by the end of this year to create an action plan to anchor advanced therapy commercial-scale manufacturing in the UK. We are due to publish our action plan in November. We have been working very closely with a number of regulatory groups, the MHRA, Innovate UK, the trade bodies, ABPI and BIA, and a number of small and medium enterprises. It is our hope that we will be able to publish that and create a platform, and maybe—Chris, to your question earlier—a manufacturing strategy on industrial scale for these products.

Q148 **Chair:** Thank you.

Keith Thompson: Hello and thank you for allowing me to talk to you. I am Keith Thompson, the CEO of the Cell and Gene Therapy Catapult, which started up over the past three or four years or so and has grown to over 120 experts dedicated to cell and gene therapy with the role of bridging the gap between science and industry. Quite simply, our job is to try to help accelerate the development of health and wealth for the UK around cell and gene therapies. I am sure we will come back to address how. Prior to that, I ran the Scottish blood transfusion service, so, rather like Ian, I had a range of activities, and was very pleased when we treated some patients with pancreatic islet cells for diabetes and saw remarkable clinical results, and treated patients with limbal stem cells and regrew the front of their eyes. That enthused me to try to make a difference in the sector. Prior to the blood transfusion service, I ran several biotechnology companies, all in monoclonal antibodies, and it broke my heart, being the inventors of this technology in the UK and its now being a $50 billion industry, that very little of the manufacturing stuck in the UK. I see manufacturing as a way of anchoring some of the wealth part of that equation.

Q149 **Chair:** Thank you. That is very clear.

Dr McKernan: Hello. I am Ruth McKernan, chief executive of Innovate UK. As you know, we fund, support and oversee the Catapult centres and also support company growth in all technology and innovation areas. Of particular relevance for this Committee, in my 27 years in the pharmaceutical industry, I headed a stem cell research group in Boston. Also, along with colleagues who are here or were in the previous group, I wrote the business plan for Pfizer regenerative medicine and set up that whole sector of Pfizer. This is an area of my particular scientific expertise.

Q150 **Chair:** Could I start with you, Dr McKernan? What do you feel is the opportunity for commercialisation of regenerative medicine—we are using that term, although I appreciate that earlier we were saying cellular and

acellular—in the UK, and for us to keep ahead of other countries?

Dr McKernan: The opportunity is huge. If we talk about cell therapy rather than specifically regenerative therapies, what we know is that the continued investment in the UK of research and translation in stem cell science, regenerative medicine, means we are one of the leading countries in the world and I would—

Q151 **Chair:** By translation, you mean what we are calling from the bench to the bedside, but maybe not beyond.

Dr McKernan: It is from science to business and economic growth, I would say: the translation of science into a business proposition, companies, growth in the UK, employment, tax and jobs—all of those great things. The opportunity here is huge. We have invested a lot in this area. Regenerative medicine is one of the eight great technologies. Between us and the MRC, we have invested heavily in it. Innovate UK put in £54 million in grants, completely separate from the Catapult centre. We funded 126 advanced therapy projects, and 68 companies with additional matched funding from industry or the private sector investors. However, I would say we are still probably only two notches along what is an eight to 10-step journey to real value in the UK. We have already talked about some of the challenges, some of the hurdles to be overcome. However, I feel that our scientific knowledge base, the work that has been done to invest ahead of the need, such as for manufacturing, sets us up very well. The two countries that we have to compete with are particularly Japan and the United States, and we see more small and medium-sized businesses growing very quickly, such as, for example, Juno in the States, where we are building a manufacturing centre close to an airport so that they can supply globally.

Q152 **Chair:** Where is that in the States?

Dr McKernan: I will have to get back to you on that.

Q153 **Chair:** It does not matter, but I like the principle; I hear your principle.

Dr McKernan: There is an opportunity for us to think globally about how we get ahead in the different steps that are required to make us a global leading country for cell-based therapies.

Q154 **Chair:** Thank you. Do the others agree? Is there something further you would like to add?

Keith Thompson: Yes, I agree; the size of the prize is very large. Market estimates range from 20 billion to 80 billion, depending on who has done the sums, but nevertheless that is very large. The UK has about 16% of all clinical trials at the moment, and that is pretty good. It is probably the second place globally for investment. It is probably viewed as the right environment to work in, especially over the past several years when we have seen a lot of movement on regulatory, so that that pathway has become absolutely clear and firms recognise it is a good place. They like the support mechanisms such as those that are given by

Innovate UK, working with us and working with the research councils. All that is very positive. As things push forward, the UK as a base, in the right global environment to develop these things, is really attractive.

Frankly, the next step in the deconstruction of all the barriers is to get more rapid access to the NHS and to join up the reimbursement challenge. Compared with Japan as a for instance, Japan's regulatory regime changed; it is fairly complex, but they gave earlier conditional licensing plus reimbursement. They get early access to patients and they get paid for it. Although global pharmaceutical firms probably take a more global view, certainly SMEs are very attracted to that, and it is SMEs that come in, do the early work and put their roots down into complex supply chains that simply cannot be uprooted and moved elsewhere.

Q155 **Chair:** Can you say that again? They cannot be—

Keith Thompson: They cannot be uprooted and moved elsewhere, because most of the firms will get bought eventually, but their factories will stay.

Q156 **Chair:** Thank you. What would you see as the Catapult's role?

Keith Thompson: Our role has been simply to understand the barriers to the acceleration of the industry and then to work with both academics and industry to address them. I put the barriers into three broad buckets.

The first one is business-related barriers, understanding health economics, which a lot of firms have not done, frankly, and now they are starting to do so. It is no good saying, "My product is special; give me a special price." The price is only ever going to be the health benefit and therefore you have to be able to make that product within what the reimbursable price is.

The second barrier is understanding the autologous business model—the autologous cell. A cell is not simply something that you can manufacture and ship to pharmacy like conventional molecules where it is going to be prescribed. New pathways will have to be developed, and therefore the participation of the private sector supply chain to develop the pathways in and out so that these things can move seamlessly is not only essential for the NHS but it is replicable globally. The technical challenges—how you scale these up, how you quality control them and how you do all the tests to make sure they are safe—are all slowly being addressed.

Lastly, there are the clinical and regulatory barriers, and we have heard the marvellous story about how well the MHRA is doing, and I absolutely endorse that, but now it is about clinical and adoption. I would like to see broad adoption, yes, but there are some specialist centres to be put in, in addition to the excellent biomedical research centres, which will crack the nut of how you get these things in and out, how you thaw a cell at the point immediately before it is put into a patient and know that it is okay, because that is quite different from current medicines, and how you have

specialist staff on the ground who know how to deal with these things. That is not to say that those centres would be the be-all and end-all, but they would establish the paradigm for the rest of the NHS, so I would really like to see that happen.

Q157 **Chair:** You mean like leader specialist centres that could disseminate eventually.

Keith Thompson: Yes, absolutely. Breakthrough centres.

Q158 **Chair:** Ian, would you add to or disagree with any of that?

Ian McCubbin: I certainly would not disagree. The size of the commercial opportunity is large and it is completely predicated on the products being used in this country. Some might see that as a problem in how you pay for it, but it is more of an opportunity for the UK, both from a health perspective and from a manufacturing and economic perspective. I make the observation that the UK is large enough to be significant in a global sense but small enough and organised enough to be able to get the right people round the table quickly—be that industry, NHS, MHRA, Government and MRCs—because we do not have a lot of time. The nature of these products is such that they move very quickly, and within one or two years they will be much more common. As Keith and Ruth mentioned, once SMEs set down roots and start manufacturing products, they will not move very readily. That was the issue we had with the biologics. Once they set down roots outside the UK, they were almost impossible to get back, and we really ought not to repeat the same mistake.

Q159 **Chair:** Do you see that happening already?

Ian McCubbin: No, actually the opposite. At the moment, because of the work that Innovate has done, because of the Catapult and because of the SMEs and the good research base we have, SMEs are growing, but they will hit a tipping point quite quickly where they have to make their mind up. Do they invest in manufacturing capability here or go somewhere else? We have to make sure that, when they reach that tipping point, they do it here and that the mechanisms are in place for them to do that.

Q160 **Chair:** The access to the NHS is not enough or historically has not been enough to keep them here, in manufacturing.

Ian McCubbin: My reference was to the biologic products. They can be manufactured anywhere around the world.

Chair: Because that transfer is not difficult.

Ian McCubbin: Exactly. They were slightly different, but the conditions were not right to keep manufacturing here for biologics. We need to make sure the conditions are correct to keep regenerative medicine, cell and gene therapy manufacturing here.

Keith Thompson: Do you mind if I add one point? Ian is absolutely right, and the other thing that I truly believe the UK can still be is a destination for firms that want to develop products or go to the second stage in Europe. Often the supply chains are critical, so if they have a plant in Seattle in the US, say, or wherever it is, and are thinking of coming to Europe, the right conditions can make the UK the landing pad for those firms. That is the second string to that bow.

Ian Trenholm: To add to that, these therapies will require some new thinking. As other people have said, we would not expect pharmaceutical companies to deliver these therapies to the pharmacy of a hospital and expect the pharmacist to distribute them around the hospital. I would argue that the supply chain is probably more akin to stem cell transplantation. It is probably more bespoke in feel, and even the therapies that are in much broader use will have to be treated in a special way. You might be able to fly them in from the States, but you may have to do some kind of secondary processing very close to the bedside.

Q161 **Chair:** Is that very similar to the transplantation service at the moment?

Ian Trenholm: Yes. We would collect cells from a patient perhaps—

Q162 **Chair:** I mean when they bring in their specialist to the hospital rather than relying on the hospital pharmacy or whatever.

Ian Trenholm: We would not rely on the hospital pharmacy. As NHS BT, we would have a relationship with the haematologist perhaps; we would work closely with the haematologist. We would deliver perhaps a frozen product or a recently defrosted product and then the haematologist would deliver that directly into a patient. We are talking about, in some cases, a matter of hours, and in some cases minutes, before that product degrades. It is a different sort of timescale from a pharmaceutical product in a box, which would be delivered to the bedside on quite a different timeframe.

Q163 **Chair:** It is similar to the organ transplant service, with that timeframe and specialist staff.

Ian Trenholm: Yes, there would be specialist staff.

Q164 **Jim Dowd:** First, apologies for my late arrival. I was detained elsewhere. Mr McCubbin, you talked about commercial opportunities and Mr Hunt, in answer to Derek's questions in the last panel, looked at the commercial position. Do you think there is a sustainable business model to support regenerative medicine research that will attract sufficient investment? If you do, can it be improved, and, if not, what needs to be done?

Ian McCubbin: I am not quite with you. Would you mind running that one again?

Q165 **Jim Dowd:** As with all new technologies, there is a degree of risk involved. Obviously there is public support for this via the MRC, Innovate and so on, but is the business model sound enough to warrant the risk

that investors would need to take to support it?

Dr McKernan: I will start. We need to expect different business models for cell therapy, very different from what existing large pharmaceutical companies have done. My own experience is that the SMEs that are growing and leading in many areas of this field have the opportunity to grow very quickly. Most pharma companies do not have the right skills, expertise or even mindset to do it, so we need to expect a different business model.

I am always a glass-half-full person, so I am looking for the opportunity here, and you could imagine a future where we have the NHS, we know who the patients are and we have several specialist centres. You might need a few specialist centres for cell therapy for cancer, for CAR T, for example, across the UK; you might need one specialist centre for cell therapy in the eye—Moorfields would be the obvious one as they have all the experts; and you might need a couple of specialist centres in cardiology and maybe one or two in CNS disorders. That is the model that is evolving in the States and there is certainly a different business model here. If there are specialist centres, we have the opportunity to think more globally.

With the national health service we can put our patients into trials very quickly, providing we get the ethics and everything harmonised, but we could also put in patients from other parts of the world if they chose to come here, sign up and pay for the luxury. That would be a very different business model from the sort of model we currently have with the NHS, and would require a very creative approach and some different thinking. Such things could be done.

Keith Thompson: All that is spot on. I will take a slightly different tack about how one attracts and sustains investment and how the whole industry is propelled forward. Frankly, when I first came into the field in 2012 it was characterised as too risky for pharma investment. There were some modest investments. GSK, with their deal with the Italians, which actually resulted in the ADA-SCID—boy in a bubble—product coming through, for which they are to be congratulated, were an exception, but it was populated by SMEs and wary investors. Quite simply, it was viewed as too hard. Over the past four years, those pathways have started to clear so that the risk is starting to be around the product—"Does the product work?", not, "Can you get it through the labyrinth of regulations?" or, "Can you even make it?" That pathway has cleared.

The other thing that happened during that period is that after, in some instances, decades in the laboratory and early clinical studies, outstanding clinical results are coming through, and these are not just 5% better on a hypertensive drug; these are immune cells that have been programmed to hunt down cancer cells for leukaemia, where we are getting 70%, 80% or 90% effects. They are results in gene therapies where whole classes of patients, essentially, are being cured. We will have to see how durable they are. This, quite frankly, has attracted the

attention of investors and that, in turn, has put pressure on people like me, Ruth and Ian to sort out how you do this. The promise is starting to be lived up to; money follows results and we need to see the absolute demonstration. Not only are these things working in clinical trials; they are starting to be adopted by health systems. That is where the UK can really punch above its weight and not only demonstrate that these products are really delivering but that they attract the industry at the same time. Somebody is going to make these products in the long run, and I want a disproportionate amount of them to be made here.

Q166 **Jim Dowd:** Could I follow up what you said, Dr McKernan? You said that the big companies, the big pharmaceuticals, really do not have the understanding, the belief—call it what you like—or the knowledge of these innovative products? Is that because they are not doing any work in the area themselves, and it is all being done elsewhere? If so, are they acquiring that knowledge? If, as Mr Thompson says, this is going to happen somewhere, there is going to be a breakthrough and something is going to happen.

Dr McKernan: This is an area where major pharmaceutical companies are looking to do partnerships, acquisitions. It is easier to buy it than build it, because the science is very complex and the intellectual property around it is very complex. Most pharmaceutical companies have focused on small molecules and biologics, and in order to move into this area they are going to need to buy it, I think, or partner, certainly.

Ian McCubbin: I slightly disagree with Ruth on that.

Jim Dowd: It is always good when someone says that because normally everybody just agrees with everybody else.

Ian McCubbin: We work well as a team on this, but my company GlaxoSmithKline have committed to it, we have expertise in it and we have a product already approved, so perhaps it should be "most" big pharma companies might not have the expertise.

Dr McKernan: I agree that GSK may well be the exception. They are certainly the leader in the UK.

Ian McCubbin: Thank you, Ruth.

Q167 **Jim Dowd:** "It's not me; it's everybody else." You made the point that you have one product already. In all innovative and novel technologies, there is a major requirement to provide public confidence. Even though you have authorisation for the one product, do you feel there is a need for continuing monitoring beyond that to show and demonstrate, and to inculcate that sense of public confidence that this is not weird technology, that it will become mainstream over time?

Ian McCubbin: This is not my expertise, I am afraid, but I think we are at a very early stage in the science of these products and there are some unusual processes that we have to follow. Ian Hudson, who was sitting

here a few moments ago, would probably be better qualified than me to answer that question, but you are right to raise it.

Keith Thompson: There is in the legislation a requirement for long-term follow-up of patients—actively managing this stuff—which is there precisely to answer that question. My sense is that the public are very supportive, not just in the abstract but when they see the dramatic results that might come out. You might remember the little girl who was treated in Great Ormond Street recently with one of the gene-modified cells. It was an absolutely outstanding result. When you see these things happening, it mobilises opinion.

Dr McKernan: Can I add a bit to that? The UK is uniquely positioned to do long-term follow-up, because of the NHS, where everybody has their identifier and people can get tracked through the system and monitored for a long time. That is not necessarily true, or largely not true, in many other places. That is an opportunity for us.

Ian Trenholm: Finally, Chair, the role that NHS BT plays in all this is that we have a long history of seeking consent for donation, both of human tissue and human cells, and we are already supplying tissue to organisations to do research on. The NHS brand, if you will, is a very positive front end to the process as well.

Q168 **Derek Thomas:** I want to bring us on to something else in a moment, but, before that, I want to talk about funding again. If there is a lot of public funding that is helping SMEs to begin the study and research, and there is concern about them going abroad, which we talked about earlier, what safeguarding is there on that investment if companies can be bought up and then moved? I know you referred to the fact they might not leave because of the factory location.

Dr McKernan: Today, when we provide funding, we fund British companies. There is no safeguard that those companies cannot be bought by somebody elsewhere.

Q169 **Derek Thomas:** Is that because of European legislation or just that it has never been considered?

Dr McKernan: It is a free market. They can be acquired if they choose to be acquired.

Q170 **Derek Thomas:** This follows on from that question. As we develop regenerative medicine, who bears the risk? How is the risk allocated? Is it the pharmaceutical industry, the Cell and Gene Therapy Catapult or is it the NHS as we initiate the research?

Dr McKernan: Ian might want to say more, but my expectation is that it would be like any other therapeutic product where the risk is borne by the company that makes and sells it.

Ian McCubbin: Did you mean the financial risk?

Derek Thomas: Yes.

Dr McKernan: I am sorry, I thought you meant—

Derek Thomas: Yes, I was picking up on the money bit.

Ian McCubbin: I think it would be the company making the investment. We work closely with Keith in a different route and we would have a commercial arrangement with Keith, with the Cell and Gene Therapy Catapult, and, if something happened, it would be the company's responsibility financially.

Q171 **Derek Thomas:** Obviously, we want, and certainly the patient would want, everything to come to us in treatment as quickly as possible. If something is being developed, we want that treatment. What scope is there to speed up the approval regulation around these medical therapies? Could we do it quicker than we are doing now?

Ian McCubbin: I will start and somebody else may wish to contribute. They are already quick. Because the initial indications for these products are being used, by and large, in rare diseases, the trials themselves, the processes of approving, are very quick. We measure them in a rather short space of time compared with the traditional way of medicine licensing. That is why we think the window of opportunity for us to make the UK stand out globally is a short time period. Maybe if I could just pull it together, we think that the various pieces of the jigsaw are here. We have a really good regulator—we have heard that before—we have our Cell and Gene Catapult, 42 active SMEs and some large pharma. The issue will be if these medicines are not used in the NHS. Then the whole stack of cards will fall, because the outcome will not happen and, therefore, the process will probably fail. The process of speeding up is already there, I think.

Q172 **Derek Thomas:** What is your experience with the NHS and NICE? Do you generally feel that, more often than not, they engage and that they purchase the product?

Ian McCubbin: I do not think we have any of these products in use in the NHS. I do not know if anyone else could correct me on that.

Keith Thompson: There are eight licensed products currently—several recently and some older ones, like the cartilage products—and none of them is in use. They are simply not in use. There are reasons for some of the older—

Q173 **Chair:** Islet cells will be.

Keith Thompson: Islets are not a medicinal product. They are essentially treated as a tissue. I think there are about 50 transplants a year, and about half of them are in my old unit in Edinburgh.

Q174 **Chair:** Thank you for that clarification.

Dr McKernan: At Innovate UK, we try to anticipate what would be the next barrier to economic growth and then remove it. For example, once the science started to get very exciting, we needed a method of translation, so we have a Cell Therapy Catapult. Then when we saw that genetics was really helping to change the way that cells are used, cell therapy modified its scope to be cell and gene therapy. Then the industry could see that the next big challenge would be manufacturing, so we have invested £55 million in a manufacturing centre. The next hurdle is going to be if, for example, CAR T therapy really works and we want to treat 1,000 patients a week in the UK, how would we do that? What is the next hurdle to overcome to create the centres that will be able to run large-scale clinical trials with cells and then treat people at scale with cells? How would we do that? That, for me, is one of the big challenges that we have to solve next if we want this to be part of an industry in the UK.

Keith Thompson: Absolutely. We will wait to see what the accelerated access review comes out with, but that was a very positive experience of working with all the stakeholders, and they certainly listened to the unique bits around cell and gene therapies. There are a number of things to speed up the process. Many of these products, at least initially, are for relatively small sets of patients, so the budget impact probably is not going to be that big. We would like early engagement of NICE in the process, evaluation through commissioning or any other route that was appropriate so that as the MHRA is going through the final stages of approval, NICE or the health technology assessors are also going through that. Perhaps there could be early conditional licensing, if there are products that have very dramatic results, like some of the CAR Ts or gene therapies, so that they get earlier approval with conditions on the licence, as indeed most of them are these days, and can get into use and get real-world data about them working.

All these kinds of approaches mean that the UK is an attractive environment for developing these products. Having addressed, if you like, the back end of the problem, we should now address the front end. That does not mean that all the other problems, like attacking the cost of goods and scale, have gone away; they certainly have not. They all have to be addressed, but for the wave of therapies coming through now, we need at least to guide and help them into the system rather than provide another Grand National for them to run.

Q175 **Victoria Borwick:** I want to go back to the intellectual property, because we talked about upscaling, or whatever a better word is. Is intellectual property in patients any more complex in this sort of medicine, particularly when you go back to the cells that are yours that you are feeding back in again? Who has the intellectual property? There are a lot of questions. Who would like to take on how they see the intellectual property developing?

Dr McKernan: I can start. Intellectual property in this area is very different from a traditional pharmaceutical. If you have a small molecule, you know exactly what you have. If you are producing a cell, it has many components, and showing that it is consistent and it is yours is very difficult. I do not personally believe that intellectual property is the only element of value. There is a lot in know-how and a lot in being able to produce cells at scale. All that together—the process, the intellectual property around the process and every element of making the cell—is a contributor to making that industry sticky, and the reason why Keith is saying that if you get the production in the UK, it will stay in the UK. Transferring production of a cell type from one lab to another is in itself a challenge and somewhat of an art form, and can take a lot of time to get right. It is a bit like a mobile phone; there are lots of components, lots of elements of intellectual property in there, that together form the product. It is an IP thicket. I think that is the phrase.

Keith Thompson: Certainly the IP landscape is very complex. The only really unique thing in this field was the Brussels judgment from the European Court of Justice, subsequently amended a year or two later, which was specifically about embryonic stem cells. That has not held back that field. Only about 5% of trials actually involve embryonic stem cells, so we must not get too hung up on that. A piece of intellectual property in the form of a patent to do a specific gene modification or something like that is no different from any other piece of intellectual property. These things tend to be assembled and to be able to protect the product so that the hundreds of millions that are required to develop it can at least have some protection as they come out the other end. There are some products and treatments where, essentially, there is no intellectual property in the form of patents, although there is some know-how, and it is going to be a challenge to say, "How are we going to get the money into that product when people have been working on it for decades and it is all know-how?" We probably have to pay special attention to that. In terms of the trajectory and the velocity of the industry, that is in the minority.

Q176 **Victoria Borwick:** Does anybody else want to add anything about what guidelines we should have or what will help or not help in this area?

Ian McCubbin: No, nothing from me.

Ian Trenholm: No.

Q177 **Chris Green:** Capitalism and free markets are both good things—

Jim Dowd: Some say.

Chris Green: So we ought not always to be blaming the Government or the national health service for the non-adoption of new productions that come out.

Chair: Chris, what is your question?

Chris Green: There must be some responsibility on the businesses themselves coming up with the products. What more can the businesses do to get the products into the health service?

Ian McCubbin: Maybe I could start. I do not think there was any intent previously to blame anybody for anything. I was trying to say that this is a new challenge for us. We have an opportunity with these medicines to be curative and for them to be infrequent treatments. That is a very different paradigm from everything that the industry, the NHS and everybody else has done before. The solution lies collectively, somehow. It means that we will all have to change in some way. Keith referred to the accelerated access review.

Q178 **Chris Green:** In Japan.

Ian McCubbin: No, here in the UK there is an accelerated access review, of which we have not seen the outcome. Whatever comes out of that, there is a need for industry, the NHS and for all the people who play in this space to get together and say, "Do you know what? This is a new challenge for us, and we are all going to have to change a bit in order to make it work, but the prize is both the health treatment to patients and the economic benefit through the manufacturing and the industrialisation." That, I think, is a bigger challenge than we can solve, but there is something around collectively finding the way. There is a will in the industry to do that and to find a different way, and there is a will in all the other parties. We just have to get them to try to figure it out.

Q179 **Chris Green:** This area is a good example of globalisation of business and other examples where we might lose out if we do not take that approach.

Ian Trenholm: I very much echo Ian's point. I see the supply chain being a hybrid in a way that conventional pharmaceutical development is not. In conventional pharmaceutical development a drug is developed and then it is sold to the NHS; the NHS buys it, in very crude terms. With these sorts of therapies, organisations like my own will be involved perhaps in harvesting cells from a patient; they may go to either a small or large company for some kind of manipulation; we then may be part of a supply chain that delivers that back into the hospital; we then, collectively, provide clinical advice about how best to administer that therapy; we might then do follow-up work and look at long-term outcomes and so forth. Depending on the therapy, there is a range of different shapes of supply chain, but it is not that conventional "Create a therapy, throw it over the wall and then someone buys it," as the conventional pharmaceutical model would be. What goes alongside that is a need, collectively, to tell the story about these therapies to create confidence in the public about their efficacy.

Q180 **Chair:** Can I clarify, Ian McCubbin, did you say they are frequent or infrequent?

Ian McCubbin: They are infrequent.

Q181 **Chris Green:** Mr Thompson, you mentioned the early conditional licensing that goes on in Japan. Are there other things that Government can do, examples from around the world?

Keith Thompson: There is a scheme in the UK—I think it is called EAMS— but there is no reimbursement with it, so there are tweaks to be made to the system around that. Even if it is not full reimbursement, it would be very attractive to a lot of SMEs if they could get some revenue while they are trying to develop these products.

Q182 **Chris Green:** If I could perhaps narrow the ground between myself and Jim slightly—

Derek Thomas: He's gone.

Chris Green: The Conservative Government are now actively talking about the idea of an industrial strategy, and we have the National Institute for Health and Care Excellence, so that industrial strategy should to some extent inform NICE about treatments. Perhaps there ought to be an element where NICE should be considering future treatments as well as current treatments, and there could be more direction, involvement and connection between the drugs and the treatments that are made available.

Keith Thompson: Having run a piece of the NHS—I am sure Ian is just the same—I know how difficult it is to meet all the stakeholders needed in this. It is not an easy job in the NHS, and NICE does a pretty good job of trying to manage all these things. Specifically to your point, yes, it is an integrated system; you cannot do one thing alone and you have to look at the whole deal. It is not just about health. At least in the short run, it is an economic intervention. If you want the industries, it is an economic intervention, not necessarily a health intervention. There is a health benefit, and then it flips to a health benefit where you have already anchored the industry. Although industry is intensely competitive, and that is not going to change, there is certainly the opportunity for pre-competitive work among firms, where collectively they need to address a common problem, and indeed RUK often tries to facilitate that. We have also seen examples around the world where firms have worked with other health systems when there are mutual benefits.

I will give you an example: GE, the company, worked with the Mayo Clinic in the States to put together a joint venture to address the issue of how you get these things in and out of patients. Mayo had the patients and the data—years of it—so the company got access to that, and GE had the muscle, the IT and all that sort of stuff. That is a $50 million intervention, but it is a model of somebody trying to do something. I am not saying that it should be the one here, but it is an example of industry working with the health system, and if we can open up the door to address those specific problems here, it would be very beneficial.

Q183 **Chris Green:** Perhaps with devolution in Greater Manchester, if you can devolve some of these powers, some of these abilities to work between

the private sector and the health sector, there are opportunities as we go down the line with a more devolved health system.

Dr McKernan: I am not sure that a devolved health system is necessarily our friend because—

Q184 **Chair:** Because it is such a specialty.

Dr McKernan: In an ideal world, if you wanted to draw on all the patients in the UK who have a particular genetic problem and put them into one clinical trial, you would find that they were distributed and no one region or nation would have enough patients to do that. That is one of the challenges that the Precision Medicine Catapult, which is just starting up, is trying to address: how to help growing biotech companies access the right patients to get to the point of inflexion, to become much more valuable and to do that through the NHS.

Q185 **Chris Green:** Does there have to be a cultural change within the national health service, to have a more innovative culture?

Dr McKernan: I do not know what the answer to that is yet. I just recognise that it is not in every sense helpful to have lots of different decentralised organisations responsible for commissioning.

Q186 **Derek Thomas:** So far on the second panel, Brexit has escaped us, but it will not now. The Prime Minister reminded us today that MPs will have a chance to have a say on the Great Repeal Bill, which effectively transports EU legislation and regulation into UK law, at least as part of the negotiation process. By the end of 2019, we will be where we are now and we can carry on with the regulation we have today. We have referred to regulation that gets tied up in 2018. Are you aware of other legislation that has been developed in Europe that is coming upstream or that will come into being after 2019 that we in the UK should or would be wise to adopt?

Keith Thompson: Post-2019, I am not sure. Recently, there has been an ATMP GMP—what a mouthful—

Q187 **Chair:** Go on, just say it—party piece.

Keith Thompson: Advanced therapeutic medicinal product good manufacturing practice consultation—I will give up after that one. I think the outputs of that are working their way through the system. I do not think there will be any particularly large changes. I was advised by one of my colleagues earlier this morning—I might not have got this all right—that there has been some discussion of a common reimbursement health technology assessment mechanism, and that would be quite attractive. Whether that is a pipe dream or not, we have yet to see, but it is certainly being discussed. In the kind of Brexit debate about where we should be, there are two things, No. 1 being able to have mutual recognition around GMP, pharmacovigilance, so that there was seamlessness between the data, and between the rest of them. However, I would like to see a separate national pathway for advanced therapies

specifically developed in the UK so that people could get in early, quickly. That may not be capable of then flipping into the European landscape, but a lot of people want early clinical proof, and if we could provide that opportunity, it might be worth considering.

Q188 **Derek Thomas:** Does anyone else want to add to that?

Ian McCubbin: I was going to go back to the question Chris asked, so I will stay quiet in case there is something else.

Ian Trenholm: My only observation on Brexit is around research funding. Some of my researchers are certainly concerned that already they are being slightly sidelined in terms of European grants and leadership of groups that are going to extend beyond the Brexit point. Other countries are stepping up and leading those research groups. A lot of the research in this area is pan-European and in many cases global, so I think just keeping an eye on research grants that are no longer available is an important facet.

Chair: Thank you. We will be scrutinising again, so I am sure we will be using that point.

Q189 **Jim Dowd:** On that point—it is out there somewhere—are you sure this is not just apocryphal? Do you actually have examples of where this has happened? I know there is a fear of it.

Ian Trenholm: There is a fear of it and I have heard anecdotal evidence. My researchers have sat in meetings when people are looking for research—they are in a group of people, they are going to do some work: "Who is going to lead the group? Well, it can't be you because you are the British people." I have examples of that sort of thing. At this date, it is a relatively low level thing, but we are potentially two years out. Our expectation is that that will get worse. There is also the view that, as we get closer to the Brexit point, a British-led group is going to struggle to get European funding. The funding can be replaced from the UK, potentially, but we need to be clear about how that will happen, so there is not some kind of interregnum period.

Q190 **Jim Dowd:** The £350 million is going to the hospitals, I am afraid.

Ian McCubbin: Would you mind if I went back? Apologies. You mentioned the industrial strategy. Industry would really welcome that. There is an opportunity through that, because it could be a top-down but also very engaging process that helps us to address that particular issue. I should have said that at the time.

Chris Green: There is an absolutely huge opportunity and, whatever mechanisms are used, I think it needs to filter right across the state element of the health system to engage with the private sector and charitable sector to develop collaboration far better.

Chair: We really appreciate your input. We are getting the sense that

something is happening incredibly quickly—we are talking about a few years—but it is incredibly exciting at the same time. This is the second of our sessions and, as with the first panel, if we have further questions, I hope you will reply to our request. It has been very useful and, again, very clear. I appreciate your time today. Thank you for coming.

Victoria Borwick: Colleagues, I am sure you would like to join me in a vote of thanks to our Chair—

Chair: No. Order, order. Meeting over.

Victoria Borwick: She has guided us through this period and, please, may we record a vote of thanks to Tania for seeing us through this time. I know I speak on behalf of everybody.

Chair: It has been an absolute pleasure.