HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Regenerative Medicine, HC 275

Wednesday 7 December 2016

Ordered by the House of Commons to be published on 7 December 2016.

Watch the meeting

Members present: Stephen Metcalfe (Chair); Chris Green; Dr Tania Mathias; Carol Monaghan; Derek Thomas.

Questions 191 - 312

Witnesses

I: Dr Nick Crabb, Programme Director, Scientific Affairs, National Institute for Health and Care Excellence, Dr Jonathan Fielden, Director of Specialised Commissioning and Deputy National Medical Director, NHS England, and Dr James Palmer, Clinical Director of Specialised Commissioning, NHS England.

II: Dr Anthony Mathur, Professor of Cardiology, Queen Mary's School of Medicine and Dentistry, Professor Amit Nathwani, Professor of Haematology, Royal Free Hospital, and Professor Giovanna Lombardi, Professor of Human Transplant Immunology, King's College London.

III: Lord Prior of Brampton, Parliamentary Under-Secretary of State for Health, Department of Health.

Written evidence from witnesses:

- National Institute of Health and Care Excellence (NICE)
- Department of Health

Examination of witnesses

Witnesses: Dr Crabb, Dr Fielden and Dr Palmer.

Q191 **Chair:** Good morning, welcome and thank you for joining us. For the record, could you introduce yourselves by saying who you are and where you are from?

Dr Crabb: My name is Nick Crabb. I am the programme director for scientific affairs at NICE. I am responsible for the science policy and research programme that focuses mainly on NICE's research and methods needs. I am also responsible for the NICE scientific advice service and the Office for Market Access, which support life science companies in preparing for NICE appraisal. I was involved in the regenerative medicine expert group and co-chaired the evaluation and commissioning sub-group. I also led the NICE input to the study we did on the appraisal of regenerative medicines in collaboration with the University of York.

Dr Fielden: I am Dr Jonathan Fielden. I am director of specialised commissioning and deputy national medical director of NHS England.

Dr Palmer: I am James Palmer, clinical director of specialised services within specialised commissioning in NHS England. I represented NHS England on the regenerative medicine expert group during that process. My main responsibility is building the processes that allow NHS England to form national clinical policy around service development areas.

Q192 **Chair:** Where do you think regenerative medicine fits into the strategic vision for transforming the NHS?

Dr Fielden: NHS England absolutely sees regenerative medicine as an important aspect for the future. It links to specialised commissioning, because specialised commissioning is the area of NHS England where we directly commission for the rarer conditions for smaller numbers of patients, generally those that tend to be high cost or those that are within more specialised centres. We commission about 14% of the NHS budget, which relates to about 149 prescribed services set by the Secretary of State.

Regenerative medicine links very much to our strategy, which was published back in May. That has been developed, and now we are going into implementation. We feel it meets our approach to the health and wellbeing gap and the link to the five year forward view around precision and personalisation. For that, we feel that, importantly, we need clear clinically-led decision making about making the right products available and put into practice for our patients; that we work with industry in general to ensure we can get the best innovative pricing around that—our commercial directorate is looking very much towards that; that we make sure that, where they are commissioned, we get the uniformity of access

across England that we would expect our patients to want; and importantly that we continue to collate the data we need to make sure that the treatments are delivering in the way they are expected to. At this point that is, if you like, the receiving strategy as we wait for the relevant products to be available.

Q193 **Chair:** That is the vision. How ready are you to deliver it?

Dr Fielden: We are pretty ready to deliver that, in so far as we have already had early discussions with some of those most advanced in the process, and we have our processes of clinical prioritisation each year. We have the ability to bring treatments into practice in year, and we are currently consulting on the ways that can be done. We are also beefing up both our commercial ability to get the right deals for the right price and our business intelligence so that we can do the data monitoring.

Q194 **Chair:** What is the view within the NHS of regenerative medicine and cell therapy itself? Is it a fundamental step change in the way we are going to treat people, or is it a replacement for older therapies?

Dr Fielden: It can probably be both, depending on what you are talking about. We will see some products that in time will be transformative, maybe in the area of haemoglobinopathy, say thalassaemia. It could be completely transformative for disease states. Other areas, such as the ones closer to landing and how to improve corneal recovery post-burn, or something like that, may be more niche, but for those affected patients it is particularly important.

Dr Palmer: When we started looking at regenerative medicine as a whole system in the UK about a decade ago, we saw rat renal cells being clumped together and producing urine. We thought, "We're going to get a kidney soon." We thought we could have a whole organ that was going to produce urine, and that the transformative nature of that particular development would be huge. Dialysis, renal transplant—the whole system—would change. It is coming, but it is a fair way off, and the field has changed to being much more cell-based than organ-based, which is just as interesting and transformative but more complicated. It is now about what cells we can use rather than what whole organs we can use. That is what is immediately in front of us—what cells and what changes within them can be achieved to change medicine. I still think that in our lifetime we will see organ-related transformative change. It will still happen, but it might be in a combination of different technologies: regenerative medicine with emerging biotechnology fields.

Q195 **Chair:** The accelerated access review addressed the need for products with transformative features, which presumably includes regenerative medicine. What will be the barrier to implementing that? Is it going to be limited NHS budgets, or recreating or changing the patient pathway and reconstructing the NHS infrastructure around it?

Dr Fielden: Clearly, we are awaiting the Government's response to the accelerated access review, but what has been outlined is, first, that we

have to have very firm evidence of efficacy and safety. There was an article about it last week in the *New England Journal of Medicine.* We have to be sure that the evidence of benefit as well as of safety in this area is clear. Where we have that, it is a matter of identifying the patients most likely to benefit and working between particularly NHS England and NICE to ensure that we can bring those treatments speedily to patients. It is then for us to work with the industry or researchers about how to get the right price within the resources we have available so that they can be afforded, and then monitoring to make sure they deliver what the original proposal was.

Q196 **Chair:** You talked about industry. Presumably, you are working very closely with industry, or there are good ties with industry. Is there any evidence of the biotech or pharma industry not understanding the impact that emerging regenerative medicine will have on the NHS?

Dr Fielden: Generally, we have reasonably good and improving working relationships with industry. It depends on the products you are referring to and the degree of the positive nature of the relationship. As we go towards cell treatments in this area coming to market, we have already had probably the two closest discussions about how we might interact with them. There is an understanding, but as ever, once we get into the nitty-gritty of how much it might cost and the number of people it might affect, we need a more strategic way of delivering that with industry. There are early signs outside this area of how we are doing that, and positive conversations about it, but when we absolutely have something that is ready to come into the wider marketplace, that will be the test.

Q197 **Chair:** You stopped the routine commissioning of second stem cell transplants. Why was that?

Dr Fielden: Those transplants have not been commissioned. They came through to our clinical prioritisation advisory group, in which we have a published publicly consulted mechanism for how we prioritise; we relatively prioritise from high, medium and low clinical benefit. That is done with a group of clinicians, commissioners and public representatives. Once that is done, we add the high, medium and low costs, and, within that, we end up with five bands. Very positively, we were able to commission, this time, 10 treatments in the second round, having previously done eight, but there were three second cell transplant treatments that fell in the group of lowest relative clinical benefit and highest relative cost, and at that point we did not feel that in the relative prioritisation process they warranted a routine commission. There is still potential to go through our individual funding request route. Of course, we have another round happening in the spring, and towards the end of 2017 there will be another round for 2018-19. It is not correct to say that we have stopped, but they did not get through this year's round of clinical prioritisation.

Q198 **Chair:** But they might in future.

Dr Fielden: We met some of your colleague MPs only last night on this. We need to work with our clinical colleagues to beef up the evidence. We have to make sure we have the best and most focused evidence to give the best chance of moving in relative terms to the higher clinical benefit, which gives it more chance of getting through our clinical prioritisation process.

Q199 **Dr Mathias:** Dr Crabb, I completely appreciate that we are talking about high cost and a small number of patients. It is a very exciting part of medicine, but very emotional for those groups. A specific question came up with a constituent recently. Although it is not concerned with regenerative medicine, it concerns me because I think it will affect regenerative medicine. It is about enzyme therapy, which is transformational for patients with hyperphosphatasia. There was concern about a NICE managed access agreement that my constituent felt was being changed. It was an agreement NICE was going back on, and there is now a block on that treatment going forward to NHS England. Are there such blocks in the system, because surely this will happen for regenerative medicines as well? Apparently, the agreement was based on clinical need.

Dr Crabb: I am not fully familiar with all the issues of that particular case, but our highly specialised technologies programme comes with a funding requirement. The managed access arrangement associated with that product was to facilitate patient access. Having gone through that system, there should be a funding requirement such that patients get access to the product recommended through the highly specialised technologies programme.

Q200 **Dr Mathias:** There seems to be a problem about transparency and whether at that stage it was clinical or about funding. My understanding is that NHS England would look at the funding, and that was not part of the NICE agreement, but you are saying it is.

Dr Crabb: Where a product is recommended through the highly specialised technologies programme there is a funding requirement that goes with the programme.

Q201 **Dr Mathias:** At the NICE stage.

Dr Crabb: Yes.

Q202 **Dr Mathias:** That is the first block. When cell and gene therapies cannot gain approval because of their high cost, to what extent does incomplete data stop approvals for those therapies?

Dr Crabb: It is early days because there have not been many therapies that have gone through the system. To help clarify the issues, we did a study in collaboration with the University of York that was all about the appraisal of regenerative medicines to try to probe these sorts of issues. One of the key things evaluated in that study was the impact of evidence maturity. We included some scenarios where the minimum level of

evidence that would be required from a regulatory perspective to get a conditional marketing authorisation were considered. In the study we were able to illustrate the interplay between evidence maturity, price and the payment, so that provided some helpful insights.

Q203 **Dr Mathias:** Is evidence maturity an objective you can measure?

Dr Crabb: It is really important. As Jonathan said, it is reasonable to expect evidence that the products will be clinically effective and cost-effective. If products are addressing high unmet need, they may come to market through an expedited regulatory approval route. For example, they might come to market with a conditional marketing authorisation, and that means that the evidence available for doing the types of assessment NICE does will be limited.

The study we did illustrates that there are ways round those things. If the early evidence suggests transformative benefits for patients, but that evidence is immature and we do not really know how much benefit the patients will get, managed access agreements and responsible pricing are all things that can help ensure patient access while the evidence is still developing.

Q204 **Dr Mathias:** Dr Fielden, what is NHS England's commissioning through evaluation programme?

Dr Fielden: We feel it is quite important that we can get products with a degree of potential but make them available while we are gaining more information. The idea of commissioning through evaluation is that we will commission earlier; we will work with industry, or the relevant organisations, to enable the product to be made available to a set number of patients. You need a set number to get the power of the evaluation right over a certain period of time, and then evaluation of that takes place. One of the difficulties around that is that you need to evaluate.

Q205 **Dr Mathias:** You are working with industry.

Dr Fielden: It will depend on the product. It might be working with researchers. If it is a particular technique, we may be working with a company on how to collate the data in that area. Once we have the number of patients we have decided we need to get an adequate amount of evidence, we need to evaluate, so there is a period of time when they will be commissioned and potentially a stop while we evaluate for a period of time, and then it will come back in. Sometimes there is a degree of difficulty about raising expectations for the first group, and then we have to evaluate it. When we are evaluating it for them, it is more difficult to manage.

Q206 **Dr Mathias:** That sounds a very valuable thing for the company. How do you work out the fee for that amazing collaboration? Who benefits financially?

Dr Fielden: Usually, it is early on in that process, but it will depend on the product. Looking forward, it would be a relatively low price at that point, and then we would evaluate to see how effective it was.

Dr Palmer: Entry into this has to be that we are not routinely commissioning it and NICE has not appraised it.

Dr Mathias: Understood.

Dr Palmer: It does not have a mandated NICE approval, or when we have assessed it as a potential treatment area we have said we are not routinely commissioning it.

Q207 **Dr Mathias:** But to have that evaluation sounds very valuable to a company.

Dr Palmer: It is valuable to an individual company, but where possible we want to make sure we are not working with individual companies but with all available companies for that particular technology area. We make absolutely sure that it is not a one-to-one relationship with an individual company, and we look at all technologies related to that particular therapy area.

Q208 **Dr Mathias:** Is there a benefit for NHS England?

Dr Palmer: It is a huge benefit.

Q209 **Dr Mathias:** Is there a financial benefit?

Dr Palmer: There is a financial benefit during that period. It has to be clear that this is outside our routine commissioning approach. NHS England forms this as a separate programme budget within which it prioritises work. There is prioritisation within routine commissioning, but there is a limited budget for commissioning through evaluation where we test whether we want to add or remove projects to take that through.

Q210 **Dr Mathias:** But you are saying there is a budget for it.

Dr Palmer: There is an allocation by NHS England for the amount of money we would want to spend on commissioning through evaluation, which importantly is separate from the decision making around the allocation for routine commissioning.

Q211 **Dr Mathias:** But it is absolutely priceless for those companies. Is it like a superior clinical trial?

Dr Palmer: A key element is that it is where you do not think you can conduct an appropriately run trial. It is not an alternative to research. It is a system of NICE and the NHS. We want good, well-funded and well-conducted research studies. There are some situations where it is very difficult to form a research study in the areas around specialised commissioning, because patient volumes are small and you have to build up certain expertise in order to deliver the treatment. Various questions

can be asked through a commissioning evaluation programme, not just pure efficacy questions.

Q212 **Dr Mathias:** It sounds great for NHS England, but it is invaluable for the companies.

Dr Palmer: It can be, of course, because they are getting market access outside routine commissioning.

Q213 **Dr Mathias:** But we are still paying for it.

Dr Palmer: We are still paying for it.

Q214 **Dr Tania Mathias:** How do the therapies appraised under specialised commissioning produce a return for the developers if only some clinical commissioning groups commission them?

Dr Palmer: The real beauty about specialised commissioning in the current situation is that since the Health and Social Care Act we have been able to form national policy. It does not relate to CCGs for the service areas that are defined as specialised commissioning. In the future, hopefully, some regenerative medicines will be for disease areas that are spread throughout and are not just specialised, but we think that in the first stages of evaluating those treatments it is likely that you would want to bring them into a specialised service to evaluate them. There are mechanisms by which we can do that. Even in the first phases of regenerative medicine we see specialised service. You do not have to be concerned about CCG decision making for funding, because if NHS England forms a national clinical policy, it is a mandated policy across the country with complete equitable access wherever you live.

Q215 **Chris Green:** Getting the regulatory and funding model right for regenerative medicine is important for its uptake and development. What steps have NHS England and NICE taken to develop a robust reimbursement model to support the adoption of regenerative medicine in the NHS?

Dr Fielden: Those models will depend on the products we are talking about. As yet, we do not have a product ready to come directly into the wider marketplace, but NHS England already has its commercial directorate working in a variety of areas across specialised commissioning to ensure that we get good value from those products, largely drugs but also things outside. You can see from the current clinical prioritisation round that we have managed to do that; you can see from the cancer drugs fund that we have managed to do that; and you can see from some of our rare disease areas that we have managed to do that. We are beefing up our commercial side so we are even more able both to do that in the general sense and look more strategically with companies at how to move from a price per treatment potentially, depending on what we are talking about, towards an outcome base. Depending on the product, we will move towards that so that we get the best outcomes for patients

at the best value. The detail will depend on the first products that get to the stage of being commissioned.

Dr Palmer: In our three phases, Jonathan has a commercial team that works really hard to get the best value for the NHS and for the country in terms of the price available for routine commissioning. We talked about commissioning through evaluation, which obviously has a phase of price discussion. The integration of the highly specialised technologies programme within NHS England has been really important. People worldwide are looking at that phase, because NICE and NHS England now have the ability to work together and form what is called a managed access scheme for individual products where we are not sure that the price is right for the value proposition, so it needs to be explored. That is different from commissioning through evaluation. The managed access scheme still collects data but it is also trying to evaluate the price the particular commercial entity wants for the product. Is it truly a value proposition for the NHS as a whole? With those three elements, as Jonathan says, we are ready to take any particular new proposal, and if it is offering us value we can work out the best model.

Dr Crabb: One of the things we looked at in the NICE-York study I talked about earlier was different payment methods that could help manage and share risk. One of the major recommendations from the study was in that area. It is important to remember that we already have a patient access scheme infrastructure in place, and that has been very effective in enabling products to get to patients. To date, there has been a tendency for most of the schemes to be confidential, simple discount-based, but there is provision for outcome-based approaches. In situations where early evidence suggests that products are transformative, but the evidence is very immature, more outcomes-based schemes to effectively to manage and share that risk could be very important. I am hopeful that the patient access scheme infrastructure can probably deal with a lot of that. I tend to think that, in addition to trying it on real products and making sure that the dialogue starts way in advance of products coming to market and NICE appraisal, there is probably some role for broader discussions between NICE, NHS England and the Department of Health on those types of payment methods.

Q216 **Chris Green:** Is there a tendency in the discount rates to emphasise that, if you cure someone or if you can help someone and reduce costs in the short term, that is perhaps preferential treatment over someone with a chronic condition who would have to be looked after for a far longer period? Is there concern that the funding may skew towards one and not the other?

Dr Crabb: When you refer to discount rates, do you mean the rates used in the health economic analyses that we do?

Chris Green: Yes.

Dr Crabb: That was one of the things we looked at in the NICE-York study. Discounting is widely applied in health economics, and economics more generally. It just values costs and benefits that occur in the future less than those that occur in the present. In situations where you have products that involve a very high up-front cost but then deliver benefits over a prolonged period, discounting can disproportionately impact the benefits. That was something we looked at. There is already some provision in NICE's methods for applying different discounting rates, depending on very specific criteria, but in this particular case our normal discounting of 3.5% was considered to be applicable to the hypothetical products we considered in the study; but there was a recommendation that, when thinking about policy on discounting, NICE should take account of the work undertaken by NICE and the University of York.

Q217 **Chris Green:** Based on the mock appraisal exercise that you published earlier this year, has the industry complained that NICE's data requirements to tackle uncertainty around therapies may be disproportionately burdensome compared with more traditional treatments?

Dr Crabb: As I mentioned earlier, one of the specific things that we looked at was the impact of evidence maturity, and the study should help to illustrate some of the issues there. It really is all about the interplay between evidence maturity, price and payment method. Bearing in mind that some of the scenarios we looked at were minimum evidence scenarios, I think the study should at least help to guide people in that area.

Q218 **Chris Green:** Are the complaints well founded?

Dr Crabb: It is fair to expect reasonable levels of evidence, combined with some sort of pricing agreement and managed access arrangement, bearing in mind the risks to the NHS of spending too much money on treatments that are not well understood. I think that is reasonable. Given that the study included what I would consider genuinely minimal evidence scenario, which would be the evidence needed for a conditional marketing authorisation, the NICE framework is broadly appropriate.

Q219 **Derek Thomas:** One thing we should welcome, but I imagine presents a challenge for you, is the sheer pace of development in medicine and technologies regarding people's health and how we treat them. With regenerative medicine at the forefront of curative therapies, how do you keep pace with change? How do you get the right people? Have you developed a workforce that has the right skills to look upstream at what is coming so you can move as quickly as the development itself?

Dr Fielden: We look at it in several ways. We try to pick up early so we scan for that. We are much more developed in pharma. With scans we can pick it up early on and have early discussions with pharmaceuticals. We are developing the device side, which probably would cover the regenerative medicine-type technologies, so that we can get early sight.

We already get early sight through interactions with our clinical teams, our clinical reference groups and their leadership, highlighting where we think things will be coming through.

We are then able to flex where we think there is a focus to move more quickly. Generally, bringing a clinical policy through can take many months, but we have managed to get some through within a day or a month when there has been real focus. It is key that we get early sight. We need to work with pharma, our researchers or otherwise, on what is happening so that as they develop closer to market we and NICE are working closely to get the right evidence base and then we can target.

I come back to the point made earlier. It is important that we have robust enough evidence before things go out more widely, to ensure that what is claimed is correct and safe. We have to get that balance. It is a really fine line. Not unreasonably—we are clinicians by background—we tend to trumpet the things that are going really well, but as we get more data or otherwise, the picture can change. It is critical that we have enough data, and that we continue to monitor it.

Dr Palmer: We have learned that we take our advice from our clinical body in England on commissioning, and we integrate clinicians in commissioning. Across our service areas, as Jonathan said, we have 41 clinical reference groups with eight clinical members in each group and a clinical chair. They feed into six programmes that are also clinically led, and they feed into a single clinical priorities advisory group, which has a lay chair and a clinical focus, and advises NHS England. We use the system to do the commissioning rather than trying to build in-house expertise. The expertise to help us is in our medical society and lay society.

Dr Fielden: Each of those groups also has three Patient and Public Voice members, and we have a Patient and Public Voice advisory group as well, which challenges us as well as supporting the decisions, so we aim to get both sides.

Q220 **Derek Thomas:** Obviously, there is pressure at every level in the system. Do you rely on experts from abroad to be part of that process?

Dr Palmer: In certain situations, yes. We commission some services that are provided by one provider in the country. When we are trying to take advice on whether we should have a service development in a particular area, we would take advice from abroad. We have some really small services that need to do that, but only when we need to. We do it when required.

Dr Crabb: We also have horizon scanning processes. In preparing for these types of medicines, we did the study with the University of York, and through our Office for Market Access, we provide opportunities for companies to come to talk to us way in advance of real products coming to market and being ready for appraisal. That helps us understand any

particular complexities that might be coming through related to specific products.

Q221 **Derek Thomas:** Has there been a shift in focus from regenerative medicines to what we would describe as precision medicine? If that is the case, does it matter? Is it a concern?

Dr Palmer: They go hand in hand; it is not one or the other. Our genomic strategy in this country is huge; with the 100,000 genomes project, we are making sure that we have a genomic strategy that identifies sub-types of tumours. I am a neurosurgeon by background. We do not deal now with a single type of malignant brain tumour; it is a malignant brain tumour with a chromosomal abnormality and a deletion on a particular bit of it, and it gets a particular stratified treatment. Regenerative medicine is going to come in with a treatment for that particular genotype, so they are entirely hand in hand. You need both. You need the genomic side first, before the medicines, because you want to identify it. We are not talking about organs anymore; we are talking about cells that can target individual genetic types of disease. It is so interlinked that it is right that the NHS has focused on the genomics side first, because the regenerative medicine side is still a way away from those big transformative curative treatments; they are not coming through thick and fast.

Derek Thomas: It is an exciting time to be doing that work.

Q222 **Dr Mathias:** Your insight and clear answers have been very valuable. Dr Fielden, you talked about the danger of trumpeting early results and the maturity of evidence. We have taken evidence about science communication, and I want your opinion about health journalism and journalists who write in daily newspapers. Do you think all those health journalists are helpful? If not, is there more NHS England can do, because I suspect those messages get through to more people than the kind of evidence we are taking from you today? It is also of concern politically.

Dr Fielden: On a question like that it is tempting to wax lyrical, particularly for someone with a clinical background. We live in an increasingly open society where people want to hear good news and what is transformative as early as possible. As commissioners, are we doing something? It is quite nice to be in the public spotlight for that. For companies, it helps their share prices and so on, which helps them to invest more in further development. There is a positive side to that, but we are absolutely obligated to work with the best quality evidence we have, so we focus on what is published.

What is the firm evidence that allows us to get something into commissioning? Where the evidence is not quite so firm, as you have already heard, we aim to work with organisations to get better evidence. Commissioning through evaluation and the cancer drugs fund are two examples where we can firm up the evidence. We work early on to try to

get better evidence, but that will never stop our health journalist colleagues picking out and perhaps trumpeting on the front page yet another cure for dementia or diabetes, because there is a huge appetite for that. We need to be assured that the evidence is out there and that, as we move these products into commissioning, we are as open and transparent about what we do to show why we say yes to some things and no to others, because of the weight of that evidence, balanced against the resources we have to bring things through.

Q223 **Dr Mathias:** Pardon my ignorance. Do you have regular media press releases?

Dr Fielden: Yes.

Q224 **Dr Mathias:** Are they picked up?

Dr Fielden: We have a very active media team and coms team. They are almost certainly monitoring us at this moment. They track and try to ensure that we get our goods news stories, sometimes less good news stories, into the public media. NICE does it similarly in an active, accurate way, but we also deal with the less accurate stories to try to ensure that the public are as informed as possible.

Dr Mathias: That was what I wanted to hear.

Q225 **Chair:** Dr Crabb, I think you said that NICE is able to apply different discounting rates to its appraisals. Did I understand that correctly? Do you determine those discount rates yourself, or do you have to get the Department of Health's permission? After all, they are the ones who ultimately have to pay for it.

Dr Crabb: The NICE reference case includes a discounting rate of 3.5% per annum on both benefits and costs. Within our methods guide, there is a provision for applying a discounting rate of 1.5% to benefits and costs where specific criteria are met. Those criteria have been very narrowly defined. We would not need permission to do that on a case-by-case basis; it would simply be that the stated criteria in the methods guide would have to be met before that 1.5% was applicable.

Q226 **Chair:** There is a system in place to govern that; it is not ad hoc.

Dr Crabb: No. There is an absolutely robust system in place.

Chair: Thank you very much indeed for your time this morning.

Examination of witnesses

Witnesses: Dr Mathur, Professor Nathwani and Professor Lombardi.

Q227 **Chair:** Good morning. Thank you for joining us. For the record, could you state who you are and where you are from?

Dr Mathur: I am Professor Anthony Mathur from Barts Hospital and Queen Mary's medical school.

Professor Lombardi: I am Professor Giovanna Lombardi from King's College London.

Professor Nathwani: I am Amit Nathwani from University College London, representing the National Blood Service.

Q228 **Chair:** Thank you very much indeed. Back in 2013 the Lords Science and Technology Committee produced its report on regenerative medicine. That was three years ago. What do you think the Government's response to that has been, and how would you rate them on their report card?

Dr Mathur: As an end user, 12 years of experience of clinical trials of autologous cell therapy in an NHS environment, and the recently established compassionate cell therapy unit at our hospital, suggests that we have felt a bit lonely for the past five years in trying to effect this. It is probably true to say that a lot of the report was focused on commercialisation and industry, and I am not sure how well academia and the end user with respect to patients in the health service came across in that process. We struggled to effect the means to deliver a basic form of cell therapy or regenerative medicine in the healthcare system, such as even the manufacturing of cells. For instance, I think we are running the first phase 3 trial of autologous cell therapy—the patient's own cells—which is a pan-European study funded by the EU. We have to ship the cells out to Germany to be processed to come back. That has not been without trying to establish a mechanism for doing it in the UK.

From my perspective, which is obviously highly biased, there are two tracks, one of which is a commercialisation track. I am not sure that the leadership in that particular aspect has fed back into the strategic leadership on what is going on in the NHS. There is also the NHS track where we are trying to treat patients with this potentially amazing new technology.

Professor Lombardi: I can mention my own experience. Essentially, I am an immunologist and I hope the cell product that we get is instrumental in regenerative medicine, but they are not strictly stem cells. The NIHR and the Medical Research Council have created in the past few years infrastructure for an improvement in cell therapy, and that is where we are now. I am dealing with at least three clinical trials with cell therapy, although it is not stem cell. As has already been said, commercialisation is a big issue. We may speak about the gene and cell therapy catapult, which in my view has been extremely helpful for that.

Chair: We will come to that shortly.

Professor Nathwani: I echo some of the things that have been mentioned. As a haematologist and a gene therapy enthusiast using cells that have been gene modified, I feel academia is making substantial advances, but our efforts to make successful medicines that can be universally available are, essentially, not supported to the extent they

need to be by improvement in infrastructure—for example, support for manufacturing facilities that would help us move forward.

At the moment, I have a very nice idea for a cellular therapy for cancer. I will have to move my production requirements to the United States to get the product made, which I find extremely frustrating. The UK was the first to create successful gene therapies; we are very impactful in developing successful medicines that involve cellular products. We are pioneering the way with IPS-derived regenerative medicine in the UK and Europe, but we receive very little support, other than the fact there is a catapult that is swamped with demands and requirements.

Q229 **Chair:** You said you may have to move your manufacturing to the US. Is the barrier to doing it here purely funding? Is it framework? Do you not have the right people to approach to say, "Help me to set this up"?

Professor Nathwani: Funding is a very important criterion. We are generously funded through the Medical Research Council, but that is the main source of funding. The big limitation is infrastructure. The facilities to manufacture the vectors to manufacture the cellular products we need are few and far between. I could join the queue for having my vectors and cells manufactured in the UK, but I would be waiting for two years. In the meantime, my competition will obviously make substantial headway. The funding of infrastructure just has not come through.

Q230 **Chair:** This strikes me as a technology that is developing faster than the infrastructure around it can support it. It sounds as if we need some proper strategic leadership and someone to take control of it. Who should be providing that?

Professor Nathwani: It needs to be co-ordinated. My personal view as an end user of some of these facilities and as a person who is developing the new therapies is that we need a co-ordinated strategy. We need to exploit areas of excellence in the UK, such as the National Blood Service, which has had a substantial track record of providing personalised cellular products for many years. It is very good at developing cell products to the standards required by the EU, which by the way are higher than those required by the FDA, but it needs to be empowered to do more and not be in competition with new ventures, such as the catapult, where it feels there is a bit of a threat. It should be working together with the catapult. This needs to be co-ordinated through a Government body, as opposed to leaving it to charities, the medical councils or other funders.

The other big problem with this area is getting the people to do the work. Training in the UK in regenerative medicine, cellular medicine or gene therapy is not fantastic. Getting the staff here to do the work is difficult now, even though we can get people from Europe, and it will get more difficult as we understand the impacts of Brexit.

Q231 **Chair:** That was something we addressed in an earlier report on the impact of Brexit on science and research. We are fully aware of that

point, but thank you for making it again. To go back to providing leadership, presumably both of you have a view on it.

Professor Lombardi: I agree that probably it is not the general situation, but in my own experience at King's College London, thanks to the NIHR providing infrastructure through the Biomedical Research Centre, we have a fantastic GMP facility where products are made, not only for my clinical trials but for other clinical trials, and the BRC employs the right people to provide a service to have the product ready to treat patients. It is probably specific for some centres, but there is some movement.

Dr Mathur: I see it as a partnership. From my perspective, it is about the end beneficiary, the patient. I do not feel that they are represented particularly well in what we have at the moment, because it is too biased towards the commercial. The answer would be a clinical academic in partnership with an industry champion, because obviously the strategic output has to be with respect to commercialisation, as well as delivering within the NHS. That is what is currently lacking in our strategy.

Q232 **Chair:** That would provide the leadership. Would they then develop the nationwide strategy?

Dr Mathur: Absolutely, yes.

Q233 **Chair:** What should that strategy focus on?

Dr Mathur: My perspective is incredibly biased, because I have been through a lot of pain to get to where we are. There is talk about all these manufacturing facilities that we personally have not been able to access, hence the comment that we have to go through an inordinate process to get cells out of this country to Germany, processed and back, which is frankly embarrassing. When you are the chief investigator in a pan-European study and have to move the cells out of the UK, it is not easy to run with in meetings.

With respect to what needs to be done, certainly it has to feed in what is going on commercially. Industry has approached us with various strategies for trials of cell therapy for the heart; we have seen phase 3 studies come to the UK and go. Most never actually started, because a lot of the time the definition of success from a commercial perspective is different from the patient's perspective. That is why we made the big mistake of going for the autologous cell therapy route; it is very cheap and there is no IP associated with it, so we have been unable to engage in any industry partnerships to get us where we need to be—for instance, to do our phase 3 study which will involve several millions of pounds. There is no readily accessible funding structure to do that, yet if you look at the data with respect to heart disease that is out there, the studies we have done in the UK are some of the most powerful studies for that very simple first step in regenerative medicine. Those are the things that are lacking.

Q234 **Chris Green:** What are the good and bad parts of the clinical trial landscape for regenerative medicine in the UK?

Professor Nathwani: We have taken two trials to phase 1 and have had the great pleasure of working with our institutional regulatory officers, as well as the MHRA and the FDA. What is refreshing in the UK is the interaction with the MHRA compared with the FDA. The MHRA has in the last few years taken a very pragmatic view in helping us move forward, at least in the context of an academic-led phase 1 study, to a clinical trial to establish proof of concept. That has been very useful. As we negotiate with the MHRA and the FDA you can see a significant contrast. Our authority is very well informed and proactive in trying to help us, whereas by contrast the FDA is very involved in following protocols and processes but is not necessarily well informed in this area.

Q235 **Chris Green:** You said earlier that the expectations in terms of the standards between the FDA and EU are different.

Professor Nathwani: They are different; they are higher in the UK and Europe for cellular and gene therapy.

Q236 **Chris Green:** Is that necessarily a good thing, or are we perhaps expecting too high a standard?

Professor Nathwani: When it comes to phase 1, the MHRA, at least for our products, has definitely shown a degree of leniency, as it were, to enable us to move forward to clinical trials to establish proof of concept. I have to be honest and say that our gene therapy trial in haemophilia would not have been a success if we had not been helped in that way by the MHRA, because in the manufacturing process—it was the first time we were doing it—there were clearly some problems that we had to resolve. The MHRA recognised that and helped us move forward with the trial, which has been a great success.

Professor Lombardi: I completely agree. It is exactly the same experience as we had with the MHRA. They are extremely available and competent, and it is an easy journey. I completely agree with what has been said.

Dr Mathur: Again, the experience is slightly different from the heart perspective. Of the three phase 3 studies that have hit the UK, two originated in the US. They went through the FDA process and spread to Europe, and our study started here. It is not as bad as it might be. The MHRA is absolutely fine; I am in agreement. Certainly for cardiovascular disease, the FDA seems to have a slightly different approach and is more advisory. We are struggling to get advice as to exactly what a phase 3 study would look like to get regulatory approval here, whereas I think the FDA has already done that. Like my colleague, the issue about our phase 3 study is that we are likely to take it to the US, probably because of issues to do with funding, and using the private healthcare system there to try to establish the money to do that.

Q237 **Chris Green:** I think phase 3 studies will be picked up later on. To what extent is research in regenerative medicine capitalised on by UK industry? Is the UK at risk of losing its market share or competitive edge in this field?

Professor Nathwani: We are in the process of developing cellular products from IPS cells. These are skin biopsies that we have taken and reprogrammed into pluripotent stem cells and then differentiated into retinal progenitors. That is personalised medicine. Industry will have a hard time getting involved with personalised medicine, even if we establish that it works very well. There is a great chance that it will work, but because the costs involved in making patient-specific products are so high, industry will struggle if it is not supported in some way or other by the Government to move forward. That is part of the reason why, at least in the UK, all the cellular products are procured for patient-specific use through a national organisation such as the National Blood Service, for example, which also provides all the organs for transplantation. We need a similar body with a similar structure that can help us move forward in the future. The one thing we do not want to do as academics is to continue making these cellular products in our garage at home for use in the clinic. We want to exploit the expertise in the UK, and the larger-scale manufacture that organisations in the UK can provide, to reduce the pressure on academics so that we can concentrate on some of the other issues.

Professor Lombardi: Again, I agree completely. I know we are going to speak later on about the catapult, but I do not know what the plan is for this new huge GMP facility that they are going to build, and how we will have access to a structure like that.

Q238 **Chris Green:** Do we have enough understanding at the moment of the size and profile of the population that needs to be treated to inform us what cells need to be manufactured to meet demand?

Dr Mathur: From the heart perspective, yes. That is with 12 years of working in the field and identifying where we start with a no-option patient and move back. I guess that would be true of any new high-risk technology. To go back to your previous question, the other bit is the evidence. In cardiovascular, we are bypassed in the UK by a commercial entity in Europe. It was perceived as too difficult to set up a trial here, so it ran as an extra-UK European study. I have already answered the bit about the two American studies.

Q239 **Chris Green:** Are there any particular road blocks that could be addressed for changes in the systems or processes in the national health service? What needs to be changed there or could be improved?

Professor Nathwani: We need an organised structured approach to help inventors, the academics and universities to move forward with these cellular products. That requires a dedicated good quality GMP facility and good people to operate it, who understand the standards required and

are able to reach those standards. To me, that is very important. Investment in that area would be fantastic, but it has to be done in such a way that we can all access it, provided we have good quality research to support what we are trying to do, which currently is not necessarily the case. You need to be friends with certain people to be able to access some of the GMP facilities, and that is just crazy; it is not driven by science.

Q240 **Chris Green:** It is done on a who-you-know basis.

Professor Nathwani: Yes.

Dr Mathur: On the NHS side of things, there is a cultural bit about it too, which I think the 2013 paper tried to address. You certainly feel like an alien in a strange environment when you try to do this within the NHS. You are trying to secure beds to do treatment. I suppose it is true of most clinical trials as well. It is a combination of trying to use access to NHS resources, which are particularly stretched at this time of year generally—admitting patients to beds, and other difficulties—even contractual ones.

From our perspective, the autologous approach is pretty straightforward. NHSBT has a great manufacturing chain across the UK that potentially could disseminate this to patients all over the country, if indeed it worked out to be what I would call the first step of regenerative medicine, not where we are hoping to get to. We have been in two years of contract negotiations with the NHSBT to try to achieve that. I do not think there are any particular obstacles; it is just a cultural thing. We need to do this quickly; we need to move it through, and the money is there. It is not about building new facilities or anything like that. It comes down to cultural acceptance, not just of regenerative medicine in the NHS but how we do clinical research, because it is so focused, for obvious reasons, on the delivery of clinical care.

Q241 **Chris Green:** It is all about now rather than developing things for the future.

Dr Mathur: Yes.

Q242 **Chris Green:** In terms of academic trials and trials led by industry, are there significant differences between the two approaches?

Professor Nathwani: I am involved in a spin-out company for gene therapy, which stems from our success in the past. I do not see a big difference. The obstacles are pretty similar. Some of the studies we want to do are easier because the money is made available and it is in the interests of the company, but the challenges are the same. The product we are manufacturing for the spin-out at UCL is going to be made in Belgium, not the UK. That was the only place where we could find a facility that could manufacture for a phase 3 trial. It goes back to the issue we raised earlier.

If we are going to be serious about this, we need to set up centres of excellence. Typically, I would not say that, because we do not want to create new ivory towers, but this is such a niche area that if you do not bring in the scientists, the manufacturing base and the regulatory requirements and support, together with the NHS, you will not make the impact at the speed you need to. In contrast with what Japan is doing with IPS, they are doing exactly that; there is a Government-led initiative to make IPS-derived cells into medicines. There is huge support, and it is moving at a rapid pace.

Chris Green: The Japanese example is a good model.

Professor Nathwani: Yes.

Q243 **Dr Mathias:** Dr Mathur, has there been progress in getting funding to cover excess treatment costs in cell therapy trials?

Dr Mathur: Not in our experience. Our compassionate unit, which started two months ago, is using a charity to raise the NHS costs to pay for that.

Professor Lombardi: My own experience is that it is mostly European funding. The Medical Research Council provides support, and the NHS provides support for normal care provision.

Professor Nathwani: I have a very similar experience. The funding for patient treatment comes from the MRC, but it is substantially discounted by the institutions. In our case, the Royal Free Hospital, for the studies we have done, has waived many of the charges so we can make progress. There is real support locally to move these things forward.

Q244 **Dr Mathias:** Do you know whether there is a central registry of patients who have received cell therapies?

Professor Nathwani: There is a registry for bone marrow transplants, tissue and organs. That is the only registry. These registries are getting better and better. Whereas in the past there would be just a registry of the donated product and the characterisation of it, now the registries are also looking at outcomes, which is very important, because that is obviously the measure we are all interested in.

Q245 **Dr Mathias:** There is a model of how to have a useful registry, even though it does not exist at the moment.

Professor Nathwani: I would not say it does not exist; there is a registry, but it does not capture everything that has been done in academia. It captures what has been issued, for example by Anthony Nolan or the blood service with regard to stem cell products, or tissues and organs from the transplant service as part of the NHSBT organisation.

Dr Mathias: But not everything.

Professor Nathwani: Not everything, and not the gene therapies or the crazy things we do in academia. They are not necessarily captured, and they need to be.

Q246 **Dr Mathias:** What do you call them?

Professor Nathwani: Crazy, but successful.

Dr Mathias: I like that.

Professor Lombardi: I suppose that the only information we can have is through publication. When a trial is written up we can have all the information about the outcome.

Q247 **Dr Mathias:** But not a registry or go-to place. The challenge is to try to make the UK a clinical trial hub. Is the challenge in trying to make us a hub investment or getting research done?

Dr Mathur: That is a big question because it is all sorts of things, which include the investment and leadership we spoke about. Unfortunately, the recent changes in how clinical trials are approved, which were thought to be facilitatory, seem to have run into a number of issues for us. In our close contacts with industry, not with respect to regenerative medicine but the other stuff we do in cardiology, there is a tendency to shy away from the UK because of that perception. Our approach to it in my hospital is to set up our own unit which is designed to break down the obstacles in the system as it stands, because I do not think we have gone far enough at the moment to make it work as well as it could.

Q248 **Dr Mathias:** Professor Lombardi, would you add anything to that?

Professor Lombardi: No. I agree.

Professor Nathwani: I agree. I think co-ordination in investment is important, and education is very important. If we do not create home-grown scientists to work in our GMP facility and in our science labs, which is not happening at the moment, we will struggle.

Q249 **Dr Mathias:** That is a very good point. We have heard about manufacturing problems and investment in progressing trials to phase 3. Are any other factors involved? Are those the great obstacles?

Professor Nathwani: The difficulty with phase 3 trials is that the bar in terms of product quality is much higher. Reaching that bar is quite often a challenge and requires a substantial amount of investment. This is why, when we look at the cost of the gene and cellular therapy products that have been licensed and eventually get to market, we are talking about sums like £800 million. That is a lot of money. You will not do that lightly. You need cast-iron guarantees that there is a market. For some of the personalised medical products, that is going to be a very difficult market to service, so we have to be cognisant of that.

Dr Mathur: There are two answers to your question from my perspective. One of them goes back to a previous question about the

difference between academic and industry studies. In cardiology, we see a difference, and I end up in a difficult dilemma. Our big phase 3 study was designed through academia as a 3,000-patient pan-European study, and the studies that have come to the UK from the US for treatments for heart failure using cell therapy are in the order of 300 to 500 patients and are commercial studies. There is clearly an issue as to what satisfies the regulators. It could be that our academic approach, which was a purist approach about mortality—whether patients live or die with respect to the cell therapy—is too extreme, but I think that is what our scientific colleagues would want to pursue from where we are at with phase 3 autologous cell therapy, whereas my suspicion from the commercial approaches we have seen from the US is that the end points in their studies are very mixed. Most clinicians scratch their heads wondering what they are getting at. What they are getting at is the regulatory approval to sell their product and get some returns.

We need clear leadership guidance, and that is why I think there should be partnership with academia and industry in the UK on the parameters we need to identify for it to be licensed as a cell therapy: the answer being 400 to 500-patient studies, for the reasons you have heard about. Given the cost of manufacturing all these cells, that would make a big difference, rather than the 3,000 pan-European study that is a logistical nightmare.

Q250 **Dr Mathias:** That is very well described. Professor Lombardi, what do you say?

Professor Lombardi: My experience is mostly with phases 1 and 2.

Q251 **Carol Monaghan:** Last week we had a visit to the UCL Institute of Ophthalmology. Professor Nathwani, some of the things you said about the international nature of the sector were very apparent. The doors had on them the flags of the home countries of the researchers. That in itself was a great eye-opener. They spoke to us about the role of philanthropy. How much is your research dependent on philanthropy?

Professor Nathwani: A lot of the eye work we do is funded through charities and philanthropists, but the work we are doing with leukaemia and gene therapy in general is funded mostly through CRUK or the MRC. Overall, about 10% of all the money we have comes from philanthropy and charity.

Professor Lombardi: For us, it is entirely MRC and MHRA, not philanthropy, or not yet.

Dr Mathur: Of the £20 million we have raised, £5 million has come from philanthropy, but with it has come the drive particularly from a patient perspective, with the media and all the rest of it, which brings in all sorts of other things, not just money but interest with respect to what we are doing. It is about a quarter.

Q252 **Carol Monaghan:** That is fairly significant.

Dr Mathur: Yes.

Q253 **Carol Monaghan:** Should research in this area be milestone-driven, as opposed to bidding for grants and getting a lump sum up front?

Professor Nathwani: I think it needs to be milestone-driven. All the funding we get from the MRC is milestone-driven and very strictly policed. I think that is very important. If it is not, we will not develop the evidence base required for the efficacy and toxicity of these new medicines. It is very important that it is milestone-driven and that we achieve those milestones.

Q254 **Carol Monaghan:** Do you think having those milestones keeps the pressure on the researchers?

Professor Nathwani: It keeps it focused. We have a target, which we are allowed to set. It is not as though somebody imposes the targets on us, and we strive to reach them. In the most recent study, we did not reach one of the milestones and we had a discussion with the MRC. They are totally understanding of the problems we have had to encounter and we will change those milestones, but we have to have that dialogue and provide proof and rationale for the delays; otherwise, money is given and you do not really know what happens to it and where it goes. At least this way we can show through the milestones that some good has come from that money.

Professor Lombardi: I completely agree. We have a dialogue with the MRC and essentially everything is driven by the milestones. If they are not met, there is a conversation with MRC and something will change. It is absolutely milestone-driven.

Dr Mathur: I agree with the milestone bit. My problem is with the funding mechanism in the UK through grants. I think that determines strategy, and it is not the way to determine strategy. To go back to the leadership aspect, we determine the national strategy, set milestones and the grants are the facilitatory mechanism for getting there. At the moment I think the direction of the research is often guided too much by individual research councils' views of what is being submitted to them in grant format. A lot of people put in grants as a means to an end. They actually want to do something else but the way they will get money is to do that. That is why you need to dissociate strategy from the grant side of things as purely facilitatory. We need a clear-cut strategy with milestones.

Q255 **Carol Monaghan:** We have heard about the need to support later stages of clinical development. Who should be funding that?

Dr Mathur: Our frustration is that we have the autologous approach, which is dirt cheap compared with all the other engineered things. I admit that is not particularly great for UK industry and the rest of it, but it is great for UK patients, if it works. The frustration is that we do not have anyone we can go to to raise the £6 million to £14 million,

depending upon your 300-patient study or 3,000-patient study, and put that across to the NHS. You would argue that, in the absence of that commercial outlet but the potential to make a big difference to healthcare in the UK, essentially it should come, in that small part, from the Government, whereas for things that have IP associated with them and are commercial it would come from other potential streams. Currently, there is no outlet for what could be the most cost-effective and biggest game-changer in UK medicine. Until we answer that question, you will just have to take my word for that statement.

Q256 **Carol Monaghan:** Your feeling is that with greater Government funding it would be of huge economic benefit in the long run.

Dr Mathur: For particular areas in which there is clearly a funding problem. If you have a cell therapy that does not have intellectual property and cannot be commercialised but could change the health of the nation, you need a mechanism for solving that.

Professor Lombardi: I agree. Without IP it is very difficult to move to the commercialisation side. The Government should support progress for some of the cell therapies.

Q257 **Carol Monaghan:** Professor Nathwani, you straddle the two—Government and industry.

Professor Nathwani: Yes, that has to be the way forward. You need to have a relationship between academia, industry and Government to be able to drive the creative parts of the UK in medicines. Without that partnership, those medicines will go elsewhere for sure.

Q258 **Carol Monaghan:** Where should we strike the balance between initial basic scientific research and more translational research? Which is more important?

Professor Nathwani: If that question had been asked five or 10 years ago, I would have said scientific research, because we still had a long way to go. I am not suggesting we have resolved all the barriers when it comes to regenerative medicine, but we are making progress. We now need to make that progress into something tangible, and without support from Government or organisations that can pour in money and support industry we are not going to get there.

Q259 **Carol Monaghan:** I take it that it is specific to regenerative medicine where you feel translational support is required.

Professor Nathwani: Yes. As we move out of phase 1 studies, where we have shown initial proof of concept, we need big investment to get to the 200-patient studies, and that requires a huge amount of product, which is very expensive to manufacture.

Q260 **Carol Monaghan:** We cannot do it in this country.

Professor Nathwani: Yes. That is where it is important that the investment comes.

Professor Lombardi: There should be equilibrium. We should keep supporting research but there should also be big support for clinical trials, phase 2 and upward, from the Government.

Dr Mathur: I sort of agree. The problem is that there is a great danger that regenerative medicine will fall flat on its face very shortly in the world of cardiology. There have been 10 years of promise and no achievement from what my colleagues perceive. I see a pipeline that has been going for 10 years with some successes. The field has moved forward, but for your jobbing clinician who will potentially deliver this to patients in due course, as we can see by the number of presentations given at cardiology clinical conferences, the spotlight on it has disappeared. There is a need to focus more on the translational side for the time being, but not with total exclusion of the basic side, which is incredibly important. It is a bi-directional process to get more promising therapies into the clinic and try to look for a win, because certainly in cardiology there is now tremendous scepticism about whether regenerative medicine has anything to deliver in our lifetime.

Carol Monaghan: That is interesting, because on the ophthalmology side what we saw on our visit was extremely exciting.

Q261 **Derek Thomas:** We have covered most of what I was going to ask, but perhaps it would help to clarify it. The cell and gene therapy catapult is intended to speed up the process to commercialisation, as I understand it. Does it perform? That question probably does not have a yes or no answer.

Professor Nathwani: We have had some interactions with it. It is an organisation that has not been around for long enough to say for sure. It needs to be given a chance. Some of the things it has been trying to do of late are certainly very interesting and exciting, but access to the facilities and its expertise needs to be much more open than is the case, at least for some of us.

Q262 **Derek Thomas:** That is helpful. It is early days and hopefully there is scope for it to evolve, mature and do the job it needs to do. From your perspective, how do you change the access that you are not getting at the moment? What do you believe is the process for deciding who should benefit from the catapult, or not? Is there a process, or is it just too cumbersome to understand?

Professor Nathwani: Up to now, I have not been aware of the process they used. Of late, that has changed; they have started to become more interested and transparent about their intentions and drives, but even then it is not obvious that they are open for business and happy to help anyone who has a good idea. How one accesses the catapult is not very clearly defined. One needs to search quite hard for the key individuals to

whom you need to talk about your great idea. Those sorts of things should be obvious for an organisation that is supposed to support us, but it is not terribly easy to follow for somebody like myself who is a little dim.

Q263 **Derek Thomas:** That is really helpful, although not the last bit because I am sure you are far brighter than all of us collected together. Does anyone else want to comment?

Professor Lombardi: I interacted with the catapult a lot at the beginning of my first clinical trial, and it is a co-applicant in the Medical Research Council grant that I have for phase 1 and phase 2. Their contribution has been to define the commercialisation of those. They put together a very nice document, but unfortunately it is very clear that if you do not have IP you cannot move on very easily. That is where we are stuck at the moment. They have been available, but if I need to go back I do not know who to contact, or how to set up a meeting. I know a few people individually, but there is not a clear structure that we can easily approach.

Derek Thomas: That is useful.

Dr Mathur: The nub of the problem is the word "commercialisation." In theory, they should be a great resource for all types of regenerative medicine in this country but if you are not commercial or commercialising they do not help. I have had some very nice interactions. I know the people there and have had some early phase regulatory-type advice, but with respect to the size of the phase 2 and phase 3 studies we are doing in the UK they have absolutely no involvement and have not helped to do them at all. That is a bit of a missed opportunity. Even if the output is supposed to be commercial, it should be about bringing the whole of regenerative medicine to the fore for the UK.

Q264 **Derek Thomas:** To wrap this up, I am a constituency MP, and I meet people in the medical profession all the time. When we talk about ideas or models to try to improve healthcare, some just do not believe any of it; they have seen so many new initiatives, so it is about creating confidence that an idea will work. Do you feel the same about the catapult? Do you think it is part of the solution, or do you feel that pessimism?

Dr Mathur: Its remit is clear. Talking to the guys there and trying to understand why they could not help us as academics in the way we want, it was all about shares and trying to demonstrate revenue income, whereas what we are trying to do is help people and, I guess, the health of the nation, which will ultimately lead to a reduction in healthcare costs if it all comes off. They cannot do that; it is all about return, so part of the way they are set up limits their ability to help us all.

Q265 **Derek Thomas:** Do you have any confidence that it might be part of the solution?

Professor Nathwani: The most recent arrangements seem encouraging. Initiatives like the catapult are definitely needed. It is not that it was a bad idea. Its execution has not been to our expectations. Perhaps we had unrealistic expectations. Perhaps it is our fault.

Professor Lombardi: Their budget is limited. They finance some of the clinical trials that are immuno-related, but I do not know about that. We tried to offer our clinical trial but there was not much response. It is about economic support as well.

Q266 **Chair:** Dr Mathur, you said that the grant-giving system was not informed by an overarching strategy, so there is potentially an over-reliance on charitable donations. While welcome, does that act as a barrier to forming an overarching strategy? Is it going to hinder us moving forward?

Dr Mathur: At the moment it is. How research is funded and set up in the UK is quite a fundamental thing. My frustrations are that basically it is directed very much by how you perform on a grant panel rather than an academic-cum-industry partnership that says, "This is the UK strategy, and this is how we go about doing it." The evidence from my perspective is that our research is funded in large part by philanthropy because we are doing the research that patients have asked us to do, not what the research councils have funded us to do. We are lucky that we have funding. Most of it is from the EU; £12 million of the £20 million has come from Europe, not the UK. There has been £1.2 million from the UK Stem Cell Foundation, and the rest is philanthropy. It is philanthropy and patients that have driven our trajectory, not the research councils.

Q267 **Chair:** What you are saying, therefore, is that those two are not necessarily heading in the same direction.

Dr Mathur: That would be my suspicion.

Q268 **Chair:** Are we losing something through that? From the patients' point of view, they are funding valuable research that they want to fund through philanthropy, but are we missing areas because it is not at a point where it would benefit an individual patient?

Dr Mathur: I think so. It is just about redressing the balance, and that means bringing patients and what they want into it a lot more.

Chair: Dr Mathur, Professor Lombardi and Professor Nathwani, thank you very much indeed for your time this morning.

Examination of witness

Witness: Lord Prior of Brampton

Q269 **Chair:** Lord Prior, good morning. For the record, please state who you are and your responsibilities.

Lord Prior of Brampton: I am David Prior. I have responsibility for life sciences, but not for science. I am standing in for Nicola. She would have been here but felt she should not be because she was so recently among you.

Q270 **Chair:** We are grateful to you for stepping in and coming along. I can assure you that we would have been very gentle. Obviously, we are looking at regenerative medicine. It was listed as one of the great eight technologies, which presumably led to the establishment of the cell and gene therapy catapult. What more can the Government do, or are they doing, to support regenerative medicine?

Lord Prior of Brampton: As you know, we are developing an industrial strategy, which is something we have not done for quite a long time. A key part of that industrial strategy will be a focus on life sciences for a number of reasons. First, we have two fairly unique long-term, sustainable, competitive advantages. One is our extraordinary research base in regenerative medicine but in other areas as well, not just in the golden triangle, where it is absolutely world class, but in other parts of the country, whether it is Leeds or Manchester. It is fairly well spread, although Oxford, Cambridge and London are at its heart. That is very hard for any other country to copy. If you do not have it already, it is very hard to copy. We have four universities in the top 10 and all the rest of it, with lots of Nobel prize winners, papers, patents and the like.

The second competitive advantage we have in the area of life sciences is the biggest single-payer health system in the world, which gives you access to data—at least theoretically. If we can allow the people doing the research to have access to that data in a way that respects privacy and confidentiality and gives confidence to the people providing that data, that is also a huge source of competitive advantage.

The final point is that we all know that England has a productivity problem. We are a low-productivity country. Life sciences is high productivity. What we have missed in the past is the inability to translate this fantastic new technology, new ideas, new patents and new IP into manufacturing in this country. Much of the manufacturing has gone to other countries: Ireland, Singapore, Belgium, Switzerland or wherever. A key part of our industrial strategy will be to try to keep more of the value chain in the UK. So, regenerative medicine forms a very important part of that overall strategy.

Q271 **Chair:** Yes, it will hopefully form, I presume, part of that strategy. If it does form a key part of that industrial strategy, what will that actually mean? What additional support will the Government give to that area that they would not give to others?

Lord Prior of Brampton: I think the role of government here is to create an environment that encourages research into cell and gene therapy and the take-up of those therapies within the NHS in an accelerated, speedier way; to have a regulatory regime that is

competitive, fast and allows clinical trials to happen; that allows our regulatory system maybe to have a slightly more nuanced relationship between risk and safety, and enables newer products to come on board quicker; and to have a fiscal regime that encourages long-term patient capital and entrepreneurs to take risks. I think the lack of long-term capital has been widely recognised as a problem in the UK, and that is gradually changing. If we can address those overall at a more macro level, that will have a direct impact not just on cell and gene therapies but on robotics, nanotechnology and all the other digital technologies that are coming along as well.

Q272 **Chair:** You hit on a couple of things. Is change to regulation one of the opportunities that may come out of the UK exiting the EU? Are there other opportunities and, presumably, challenges/threats as well?

Lord Prior of Brampton: There are risks as well as potential rewards. On regulation, the EMA is clearly going to leave London, which is a risk; it will probably go to Italy, Sweden or one of the other European countries. That is a risk for us. On the other hand, the MHRA provides 40% of all the work that is done by the EMA. Therefore, the EMA, wherever it is going to be, will need the MHRA.

We do have an opportunity to develop our own regulatory system. We have to be very careful that it is not just duplicatory. If it just requires pharma and medtech companies to jump through two hoops rather than one that will be a disaster, but it may be we can come up with a system where we have a very close relationship with the EMA, and maybe the FDA and other licensing organisations around the world, but also have our own system that enables drugs to be tested earlier, but still safely, and gives British patients earlier access to new innovative drugs. I think there is an opportunity there.

The biggest risk post-Brexit, which I think is one we can address, will be if it in any way impacted adversely on our ability to attract the world's best talent to the UK. Between 30% and 40% of all trials and research projects done by Cancer Research UK, Wellcome and the others have EU nationals involved. This is a global business. If you want to know the biggest risk of Brexit that is it, but it is certainly within our own powers to address it.

Q273 **Chair:** I am sure you will have welcomed one of the recommendations in our recent report on the impact of Brexit asking for early reassurance to EU citizens, particularly researchers and students. Perhaps you could take that back and point your colleagues towards it.

Lord Prior of Brampton: I do not think anyone in the Government disputes the fact that attracting the world's best talent is really important.

Q274 **Chair:** It is early reassurance that the Committee would seek, so there is no harm in reminding the Government of it. I presume that the role of

the independent sector is going to be key to this. First, how do you envisage the relationship between the independent sector and the NHS working? Will they develop alongside each other? Secondly, are there areas where the NHS is dependent upon the independent sector?

Lord Prior of Brampton: By independent sector, do you mean the pharmaceutical industry?

Q275 **Chair:** The pharmaceutical industry and commercial side.

Lord Prior of Brampton: The NHS is not in the pharma business at all; it is a customer. At one level, there has always been an adversarial relationship between any healthcare system and the pharma industry, because the pharma industry means high-cost drugs. On the other hand, the extraordinary breakthroughs that have been made by pharma have been transformational, and the NHS has a huge incentive to ensure that our patients have access to the world's best drugs.

Interestingly, at the moment, 80% of global pharma profits are made in the US. The US is doing us all a huge favour in Europe because it is paying for a lot of the research for which we get the benefit. I am not sure for how long we can rely upon that happening. It is a bit like defence spending. We do not do as much as the US and yet we get the benefit of it. Therefore, the relationship between the NHS and pharma at one level is a quite difficult commercial one; at the other level it can be done sensibly only on the basis of a long-term partnership. Certainly, at the research level those relationships are incredibly close. The UK punches well above its weight when it comes to research and working with big global pharma, and, as it happens, that is also true of medtech.

Q276 **Chair:** I agree with that. Are there any areas where the NHS is dependent upon the independent sector to deliver?

Lord Prior of Brampton: If you take branded pharmaceuticals, by definition it is nearly a monopoly. Sometimes two drugs might come along to treat the same condition, but, by and large, branded drugs are protected by IP, so we are not in a competitive marketplace. In generics it is different, but for branded pharmaceutical products we are dependent upon big pharma.

Q277 **Chair:** Do you see a difference particularly around regenerative medicine?

Lord Prior of Brampton: There are now a number of companies involved in this field. The manufacturing process for cell and gene therapies is very different from conventional pharma. In a way, the need for close partnership working between the companies developing regenerative medicines and the NHS as a customer, if you like, is more important than for more conventional synthetic drugs.

Q278 **Dr Mathias:** I want to pick up what you said about industrial strategy—that we had not had it for a long time—and manufacturing. I do not know

whether you heard the evidence we took earlier this morning, but there is a dire problem about manufacturing. There is an obstacle in this field because of the lack of manufacturing in cellular and gene therapy in this country. We had evidence before about lack of vaccine manufacturing. What are the Government's plans to address this? Is there a plan?

Lord Prior of Brampton: Yes, there will be a plan.

Q279 **Dr Mathias:** There is not one right now.

Lord Prior of Brampton: To say that would be too simplistic.

Q280 **Dr Mathias:** Is there a plan?

Lord Prior of Brampton: I will give you an example. We are developing a plan to encourage more high-value manufacturing in the UK. That will be a key part of our strategy. Interestingly, I was talking to one of the big global companies that was looking to put a new manufacturing plant into Europe. It had not decided whether it would go to Belgium, the UK, Ireland or wherever.

Q281 **Dr Mathias:** That is very critical right now.

Lord Prior of Brampton: It is absolutely critical.

Q282 **Dr Mathias:** So you are working on it.

Lord Prior of Brampton: We are absolutely working on it.

Q283 **Dr Mathias:** The cell and gene therapy catapult wrote to the Department of Health to report progress against recommendations made by the regenerative medicine expert group. When is the Government's response coming to that?

Lord Prior of Brampton: Are you referring to the letter of 25 April?

Q284 **Dr Mathias:** I believe so.

Lord Prior of Brampton: We will be giving a response to that early in the new year.

Q285 **Dr Mathias:** What is your assessment of the catapult?

Lord Prior of Brampton: I have a view, but it is not a view that—

Q286 **Dr Mathias:** You were not here earlier. I flag up that there were some criticisms. Although the scientists were very respectful of the staff, they said it is not doing what they would have wanted. Somebody said that maybe they had unrealistic expectations.

Lord Prior of Brampton: I think it would be unfair of me to give a view because it would not be sufficiently backed up by analysis. I hear good and bad things about it, and, if I had a view, I would like to consider it.

Q287 **Dr Mathias:** Come back to us on that. Do you think the regulatory system needs to be rebalanced to focus more on pre-clinical evidence of

efficacy rather than the current approach?

Lord Prior of Brampton: The regulatory system has had quite a lot of difficulties in dealing with cell therapies, because the period is longer and getting an evidence base has been difficult. I think the MHRA and NICE have made a lot of progress over the last year. I think we are moving towards a regulatory system that will be better, but we are not finally there yet.

Q288 **Dr Mathias:** How do you envisage the independent sector playing a role with the NHS in regenerative medicine?

Lord Prior of Brampton: Do you mean the pharma industry?

Dr Mathias: A provider, yes.

Lord Prior of Brampton: I think it is going to be a very close partnership relationship.

Q289 **Dr Mathias:** Do you think it is more for regenerative medicine than other treatments?

Lord Prior of Brampton: It is a newer technology and inevitably that relationship will develop over time. I have not been doing this job for very long and this science is more Nicola's area than mine, but the long-term relationship that has been developed by the independent sector, as you put it, and the universities in this country goes back many years. It is a very close symbiotic relationship, and that is true of cell therapies as well as other drugs.

Q290 **Chris Green:** Do you have an opinion on the recommendations provided by the regenerative medicine expert group?

Lord Prior of Brampton: Do you mean the report it produced?

Chris Green: Yes.

Lord Prior of Brampton: I know Mike Rawlins, who chaired the group, very well, and we have had a number of conversations about it. I thought it was a very sensible paper. I think the response to George Freeman, who was at the Department in April, was very sensible. We will be responding more formally to that in the new year.

Q291 **Chris Green:** The government strategy being developed might be coming forward in the new year.

Lord Prior of Brampton: We are very conscious about not wanting to pick winners and what new technology will be successful in the future, but clearly cell and gene therapy is very much on our radar.

Q292 **Chris Green:** Presumably, it will form part of the developing industrial strategy. It is not about picking winners but setting up a framework.

Lord Prior of Brampton: Yes, it will. In particular, we are now seeing that a lot of these new technologies are not just chemistry or biology;

they are also computer science and engineering. You may have seen the joint venture announced a couple of weeks ago between GSK and Google, for example, combining a lot of very different technologies. We want to be sure going forward that our universities are producing the graduates and PhD students who will be able to work with these new technologies.

Q293 **Chris Green:** Witnesses have consistently raised concerns about the skills and talent coming through, so one aspect is being able to bring in people from the EU and the rest of the world but also developing our own talent. Is it more on the university side, or does more work need to be done in the schools prior to university?

Lord Prior of Brampton: If we want to have a competitive manufacturing base, it is about what is coming out of schools; it is having degree-based apprenticeships in some of these very fundamental and newer technologies. That is absolutely essential. For example, I know one company has just opened up a big factory in Ireland because it has access to a lot of people there who are trained in 3D technology. You have to have a skilled workforce.

Q294 **Chris Green:** How do you think the industrial strategy as it develops will differ from the existing national innovation plan?

Lord Prior of Brampton: I think it is going to be more comprehensive. There is a strange thing about Brexit. I was a remainer, as it happens, but I also feel quite energised by it. Change does energise people. We are trying to use Brexit as a catalyst for addressing some of these issues, such as having more productive manufacturing in this country, for example. We could have done these things without Brexit, frankly, but we did not, for whatever reason, and now we are using it as a reason for doing some of the things we should have done anyway.

Q295 **Chris Green:** The final point is about developing centres of excellence and the delivery of regenerative medicine on a regional basis. How do you think this will link to Jo Johnson's work on regional audits of research and innovation?

Lord Prior of Brampton: I think it will very much link in with that. Through NHS Blood and Transplant we have a very logistical system across the UK for delivering cells and skeletons that you can grow cells on around the country. All the evidence is that centres of excellence, whether they are clusters like Oxford, Cambridge and London or those based around an academic health science centre, are probably the right way to go.

Q296 **Chair:** If I interpret this correctly, you said there is no strategy for regenerative medicine, but there is a Government strategy for genomics. The NHS said earlier that they go hand in hand. Why do the Government not think that?

Lord Prior of Brampton: I did not mean to say there was no strategy for regenerative medicine. We have an overall strategy that will

encourage all these new technologies, of which regenerative medicine is one.

Q297 **Chair:** But you do not think it needs a specific strategy of its own.

Lord Prior of Brampton: The catapult is, I suppose, an example of a tailor-made strategy. The jury is out on whether that is going to deliver what it was intended to deliver. I do not have a considered view to give you on that at the moment.

Q298 **Derek Thomas:** The accelerated access review was recently published. Many of its recommendations could mark a positive step for regenerative medicine. When are the Government planning to respond to the review? Who assumes leadership in taking forward these recommendations? Are you aware of that?

Lord Prior of Brampton: I think we have pretty much decided that we are going to respond to the accelerated access review within our industrial strategy for life sciences, so the response to it will be included in that. As to timing, the industrial strategy is due to be published in March around the time of the Budget. Therefore, we would expect to respond to the AAR within that timeframe.[1]

Q299 **Derek Thomas:** Moving slightly sideways, commissioning through evaluation—the CTE—was a really positive piece of work.

Lord Prior of Brampton: Is this the catapult?

Q300 **Derek Thomas:** No. Commissioning through evaluation was a very positive piece of work. My understanding from Nicola, the Minister, is that the accelerated access review in a way replaces it. I may have misunderstood that. It seems that there are some gaps between the two, but am I right in saying that the accelerated access review focuses a lot on pharma and not so much on medtech? Is that fair?

Lord Prior of Brampton: Inevitably, it is largely. It is not totally unfair. The thinking applies to medtech as much as it does to pharma, but the driver has largely been pharma, so that would be a fair point.

Q301 **Derek Thomas:** Are you able to have a look at how we can do a similar thing for medtech?

Lord Prior of Brampton: I think the principles that apply are exactly the same.

Q302 **Derek Thomas:** They just need to shout louder.

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[1] Note by witness: Lord Prior was more precise about the exact timing of the publication of the Government's industrial strategy than he intended to be. He can now confirm that the Government intends to publish a consultation paper, followed by a White Paper in 2017.

Lord Prior of Brampton: Very often, we talk about pharma when we mean pharma and medtech. We ought to refer to medtech as well as pharma because it is equally important.

Q303 **Derek Thomas:** That is interesting; I will feed that back. How do you envisage affordability influencing the implementation of the accelerated access review? The whole issue is about what money is available, even though we like what we see sometimes. Do you think the review is likely to be a net saving or net cost to the NHS?

Lord Prior of Brampton: We have to live within the money we have got, so affordability is always crucial. In a way, one of the most important things to come out of the accelerated access review was the recommendation that NHS England should develop a commercial unit so that we could have slightly more sophisticated reimbursement discussions in particular with big pharma, particularly around outcome-based pricing so that we are paying only for those patients who benefit from a drug rather than all those who take it and do not have any benefit.

We are also looking at annuitised payment processes so that in the case of the hep C drug, for example, you can use much more of it earlier but pay for it over a longer period of time. Therefore, you annuitise the cost of the drug. There are lots of ways we can cut the cake in a more intelligent way which for the same money will enable earlier access for patients.

Q304 **Derek Thomas:** If we go back to the medtech debate, what you have said to us makes sense, because, if we are going to give these companies some money and an ability to accelerate what they are doing, the return for pharma in particular could be over 25 years. That is quite profitable, or there is certainly money there. With medtech it is much more difficult; the lifespan is shorter because other technology comes along. Can you see the problem that, if we want a return from some medtech stuff where we have developed training that has not necessarily benefited the patient, that makes it more difficult to accelerate medtech?

Lord Prior of Brampton: To a point, but the cost of developing new medtech products is considerably less than developing new pharmaceutical drugs. My observation is that medtech is a much more competitive market for most of their products, so pricing is more market-driven than NICE-driven pricing, if you like.

Derek Thomas: That is really helpful.

Q305 **Carol Monaghan:** Regenerative medicine has received considerable funding from the National Institute for Health Research. Is the current funding model that NIHR uses the right approach to support emerging technologies and therapies?

Lord Prior of Brampton: NIHR is quite a new organisation, and I think it has done a remarkably good job, particularly on translational research. It is interesting that you should ask about NIHR. We often think of

America as the land of the free, small government and all the rest of it. In the US, public spend by the Federal Government on life science research is $32 billion a year. That compares with the UK's spend of about $3.7 billion. The private investment going into the US is huge. Therefore, the US is in a massively dominant position when it comes to research spending, but, in answer to your particular question about NIHR, I think we get a lot out of what we spend.

Q306 **Carol Monaghan:** We heard from the previous panel about the importance of using milestone-driven targets. They felt that the current model for some funding of a lump sum up front was not as useful for driving the expertise to which you are referring. We do extremely well, but would funding that was dependent on milestones make a difference?

Lord Prior of Brampton: I do not think I am really qualified to give you an intelligent answer to that. It would seem intuitively sensible to have milestones on any research project. If you look at overall outputs, however you measure them—whether it is patents, learned papers or whatever—we are very productive on research. As to whether we could be made more productive by a different method of funding, I am not really qualified to give an answer.

Q307 **Carol Monaghan:** They mentioned the Wellcome Trust whose funding was dependent on achieving milestones, and they felt that was a useful method to use.

Lord Prior of Brampton: That is interesting. We are incredibly lucky as a country to have the Wellcome Trust. It plays a pivotal role in research.

Q308 **Carol Monaghan:** So, there is potential for the NIHR to look at different funding models that might be more productive.

Lord Prior of Brampton: Have you had Sally, the chief medical officer, before you in this inquiry? She is responsible for the NIHR. If you have not, I will certainly put that point to her.

Q309 **Chair:** In response to Derek Thomas, when commenting on the accelerated access review, you said that would come out in March 2017.

Lord Prior of Brampton: Yes.

Q310 **Chair:** I think you said, unless I misheard, that it would be at the same time as the industrial strategy is published.

Lord Prior of Brampton: It will be incorporated into our life science strategy.

Q311 **Chair:** Is that the first time we have had a date associated with the publication of the industrial strategy? Is March 2017 the date we should use?

Lord Prior of Brampton: I hope I have not let the cat out of the bag.

Q312 **Chair:** There is that danger. That is what I am trying to get at.

Lord Prior of Brampton: I think it will be in March. The time of the Budget is, I hope, generally already well understood. It will be about that time.[2]

Chair: Unless there are any further questions, I thank you for your attendance this morning.

[2] Note by witness: Lord Prior was more precise about the exact timing of the publication of the Government's industrial strategy than he intended to be. He can now confirm that the Government intends to publish a consultation paper, followed by a White Paper in 2017.