



Science and Technology Committee

Oral evidence: [Antimicrobial resistance](#), HC 848

Wednesday 26 February 2014

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Written evidence from witnesses:

- [Wellcome Trust](#)
- [Research Councils UK](#)
- [Universities Allied for Essential Medicines](#)
- [Antibiotic Discovery UK](#)
- [Discuva Ltd](#)
- [GlaxoSmithKline](#)
- [Association of the British Pharmaceutical Industry](#)
- [European Herbal and Traditional Medicine Practitioners Association](#)

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Members present: Andrew Miller (Chair); David Heath; Stephen Metcalfe; David Morris; Stephen Mosley; Graham Stringer; David Tredinnick

Questions 168-240

Witnesses: **Professor Jeremy Farrar**, Director, Wellcome Trust, **Professor Sir John Savill**, Chief Executive, Medical Research Council, **Kush Naker**, Advocacy and Campaign Co-ordinator, Universities Allied for Essential Medicines UK, and **Professor Sir Anthony Coates**, Professor of Medical Microbiology and Founder of Antibiotic Discovery UK, gave evidence.

Q168 Chair: Good morning, gentlemen. Thank you for coming here this morning. For the record, it would be helpful if the four of you quickly introduced yourselves.

Professor Farrar: I am Jeremy Farrar, director of the Wellcome Trust.

Sir John Savill: I am John Savill, the chief executive of the Medical Research Council. I am representing all seven research councils.

Kush Naker: I am Kush Naker. I am the policy and advocacy co-ordinator for Universities Allied for Essential Medicines UK.

Sir Anthony Coates: I am Anthony Coates, professor of medical microbiology at St George's and founder of Antibiotic Discovery UK.

Q169 Chair: I want to start off with a broad question to help contextualise your evidence. Would you describe the UK as having a world-leading research capability in antimicrobial discovery?

Professor Farrar: That is interesting. It has the potential to be world leading but, as I suspect we shall discuss, we have a problem with critical mass. However, we have some remarkable strengths outwith the normal suspects. We have the potential to be world leading, but that is a personal view.

Sir John Savill: The UK has been world leading. If you look back over the last 50 years, there have been periods when it has been absolutely stellar but, with the decrease in courses in pharmacology and microbiology around the UK, there will be long-term major implications if we do not address that, in terms of human skills.

Kush Naker: I largely agree. Historically, we have certainly been world class at times, but work needs to be done to ensure that we continue to stay there.

Sir Anthony Coates: I agree with everything that has been said.

Q170 Chair: If we got ourselves into a position through the work that you do on the development of skills or whatever is needed—that magic ingredient that got us back into world class—do you think that big pharma would respond differently? If there were a different set of drivers coming from within the key public sector organisations, would big pharma respond differently?

Professor Farrar: I think that they would. We have a major problem in pharma in the area of infectious diseases, because of the decrease over the last 20 years in the number of pharma, both big and small, engaged in it. Twenty or 25 years ago, there might have been 18 or 20 major pharma players in that space. There are now four.

There is no doubt that the UK is a very attractive place for pharma to work, and some of the changes made over the last few years have made a big difference to that. However, you have to understand that one of the problems in this space is that these are often short-term treatments. We may be developing drugs that we may not want to use on a routine basis. Therefore, the business model around development in this space really is a challenge, and that is where the Government have an absolutely critical role to play.

Sir John Savill: It is also a research question for organisations such as ESRC. Is there a novel business model? For example, I am not an economist and it does not immediately chime with me that selling plane tickets cheaper results in more people flying and bigger profits. There is some science to be done around the business models, as Jeremy suggests.

Kush Naker: Probably the key to driving antibiotic research in the UK is making sure that it is commercially viable for big pharma to get involved. With the current system as it stands, the profits that are generated by pharmaceutical companies off the back of antibiotics are linked to the units that they sell of the antibiotic. For antibiotics, that is probably not the best model, because you also want to be driving down prescriptions to tackle antimicrobial resistance; things like vaccines and public health initiatives also undermine that.

The solution, in terms of a commercial model, would be some way of delinking the cost of research and development, and the incentives that pharmaceutical companies have to perform that research and development, from the revenue that they get from selling large units of the product.

Sir Anthony Coates: I very much agree that the unit price, or the unit price equivalent, is key to getting pharma interested. For example, antibiotics are very cheap. The most expensive anti-cancer drugs are tens of thousands of dollars, even \$100,000, per course, whereas antibiotics are much cheaper at less than £100. Companies are not going to come into this area under those circumstances.

What can we do about unit price, for example, or patents? One of the things that has been suggested in the United States is something called the limited population antimicrobial drug pathway. This was suggested by the Infectious Diseases Society of America, and it has been discussed in Congress and in the Senate. The idea behind it is that you take your antibiotic through to market with small clinical trials, aimed for example at carbapenem-resistant organisms—very nasty bugs. You are then given a licence and you can use that drug, but you can use it only for these super-resistant bugs for which you have a licence. That is a very neat way forward.

What could the British Government do? NHS England could commission NICE to do a report on the limited population antimicrobial drug pathway. That is what I would suggest is the way forward. NICE could have a look at it and do an assessment for the Government.

The other way to look at this is what they have done in the GAIN Act in the United States, which is to alter the patent rules so that you get an extended patent if you are in antimicrobial drug therapy, either for the particular drug that you are working on or, indeed, as a wild card; the company that puts millions into antimicrobial drug discovery can use that wild card for another drug—in other words, to extend the patent life on another of their drugs. Those are some suggestions.

Q171 Chair: All four of you appear to be arguing that the key is the business model rather than, for example, Britain's skill base.

Professor Farrar: You cannot say that it is one or the other. They both go together. We are going to have to develop new business models, and I would agree with what has just been said. However, if we do not continue to invest in that skill base—it is a broad skill base; it is bioinformatics, computing, pharmacology, microbiology and infectious diseases—then those two things need to go together. It is not one or the other.

Sir John Savill: There are particular gaps in the skill base. Certainly, in academic medicine there is great concern over the lack of academics who work on bacteria, whether they are labelled medical microbiologists or even infectious disease experts. That is just one area where we are down on numbers. It is not simply a throw-money-at-it problem, because to train people you have to find the right environment in which to train them and there are now very few that offer that. There have also been concerns expressed by the chemistry community about the loss from Britain, because of disinvestment from pharma, of a lot of chemistry expertise, although EPSRC is trying to address that in partnership with its community. Those are two examples of significant gaps.

I agree entirely that the approach has to be interdisciplinary. Much of the trick will be to interest people who currently hold a slightly different card in their academic life, and draw them into this important issue.

Q172 Stephen Mosley: One way of reducing the use of antibiotics and making sure that we treat things in a better way is early diagnosis, a more accurate diagnosis, and having a more speedy result once you have done the tests. Is research in diagnostics a hot topic?

Sir John Savill: I spent 29 years in a high-resource health service in Britain treating immunosuppressed patients and acutely ill patients, and it was a source of frustration to me that we were using diagnostic techniques that Pasteur, Koch and Fleming would have recognised. We often had to make key decisions about which antibiotics to use on a best-guess basis; we would not have cultures for 24 or 48 hours, and we would not have sensitivities for another 24 hours, and we relied very much on the nous of our medical microbiology colleagues from the lab, who would look at the patient and advise us. As a jobbing physician nephrologist, it would be wonderful if we could make a point-of-care diagnosis of a serious bacterial infection or an infection with a multi-resistant organism.

Professor Farrar: I spent 20 years of my life working in a low-resource setting in Vietnam, but it was the same. Sir John is absolutely right that, the world over, you are still using things that Koch would have recognised in the 19th century

However, there has been major progress. The coming of the molecular revolution has changed some areas of infectious diseases, particularly viral infections, and point-of-care diagnostics are playing a huge role in HIV, in malaria globally and, increasingly, in TB, but it is not going to happen for everything. It depends partially on how many infectious agents you have in your body at the time. With malaria, we might have 10 to the 12th or 10 to the 14th parasites—that is a lot of pathogen—and with typhoid, we might have five. Spotting them is going to be difficult, but Britain is ahead of the game in diagnostics, and MRC, the Wellcome Trust and others are investing heavily in that area.

Q173 Stephen Mosley: In some of the evidence, we have seen some suggestion that money might be best spent on diagnostics—that you might get more bang for your buck with diagnostics than by developing therapeutic solutions. Is there anything in that?

Sir John Savill: There is a general belief that the route to market is quicker. Indeed, I have been involved in discussions with this Committee about the “valley of death” inquiry, and the belief that for diagnostics and devices the route to market is quicker. There is a

problem, in that there is not really a clear path to market in contrast with the development of small molecules or biologics for therapy.

Your question is one for research. Where is money best invested? Some of the most exciting science, however, is in the area of diagnostics. EPSRC—the Engineering, Physical Sciences Research Council—has two exciting interdisciplinary research centres, focused on early diagnosis of infection, bringing engineers and chemists together with medics and biologists. There is a tremendous opportunity in diagnostics. The TSB has plans for a catapult in the area, and it is now focused on precision medicine, which chimes beautifully with what we might need do with infection. I see this is as one of the areas of potential UK strength, based on our science and on the fact that we have the TSB articulated to this. Whether the money is better spent, however, I don't know—it is a research question.

Q174 Stephen Mosley: With respect, you are the guy who should be making that decision, given your position at the MRC.

Sir John Savill: Do not forget that I represent all seven research councils; we are driven by excellence as well as value for money. I go back to the point that we do have gaps and therefore we may have missing excellence at times. At the end of the day, however, diagnostics are not going to cure infections. Treatments and antibiotics cure infections, so my gut feeling is that the UK should maintain a major programme in trying to find new antibiotics, rescuing old antibiotics, or manipulating antibiotics with poor pharmacokinetics.

Sir Anthony Coates: Clearly, diagnostics have a great potential, but if you have an infection for which there is no drug you are much more likely to die.

I talked about carbapenem-resistance before. This country does not have a huge problem with carbapenem-resistance, but I assure you that in other countries—Asian countries, for example—there is a much bigger, much higher incidence of carbapenem-resistance, and they use an old drug called Colistin in very high amounts. If you ask me where the priority should be, yes, we should have better diagnostics but we need to put a big effort into making new drugs for antibacterial-resistant organisms.

Professor Farrar: I agree. Again, it is not a zero-sum game. If you can diagnose but not treat, the diagnosis has only so much value. On the development of new antibiotics—and, I would add, the better use of existing antibiotics; this comes to the loss of pharmacological skills in this country and how we best use drugs—many of the doses that we use today were designed for people living in the 1960s and 1970s. They were slightly smaller than people living today, and the doses that you use, whether loading doses or the time and duration, are critical to the relationship between the drug and the infectious agent, and we have not moved forward. We have been complacent in the way that we have used these drugs over the last 30 years.

Kush Naker: I echo the sentiment that improving diagnostics would improve prescribing practices and reduce the development of resistance, but the nature of antibiotics is that over time resistance will develop. Unless we invest in new drugs, we will face the challenge 10 or 15 years down the line.

Professor Farrar: May I add a point about the international agenda? I appreciate that the focus here is on the UK, but the UK will be totally dependent on what happens in the rest of the world in terms of what antimicrobial-resistant organisms end up here, or do not end up here. One country will not be able to take this forward on its own. The UK's role will be playing an international role in looking at the way in which these things are working, both in this country and outside it.

Q175 Stephen Mosley: Professor Savill, you mentioned the catapult centre. All the documentation that we have seen talks about the catapult centre and diagnostics for stratified medicine. You were talking about the precision medicine catapult. Is that a bit of a scoop, or is it public knowledge?

Sir John Savill: I believe that the proposal to focus the name away from stratified medicine towards precision medicine is in the public domain.

Q176 Chair: It is now.

Sir John Savill: I think it is already. I have certainly had discussions with the TSB, and it makes sense because we need precision medicine when treating bacterial infection.

Professor Farrar: In many ways, as we move toward precision or stratified medicine or whatever we are going to call it, infectious diseases is a model from which we can learn lessons for that future development. The business model around stratified medicine has not been fully made yet, and infectious diseases have something to teach stratified medicine, in how you develop drugs not to give to everybody but to give to a smaller group of people. This has implications beyond infectious diseases.

Q177 Chair: Before we move on, in the light of your answers, I am thinking about the 2013-18 strategy. Does it have the right approach to diagnostics? What more should it include?

Sir John Savill: Again, this is a personal view, but it is a useful high-level framework that covers a broad sweep of the interventions that are necessary to change the game. I draw your attention to the European document "Joint Programming initiative on Antimicrobial Resistance" that was published recently. That involves 19 countries, and the MRC is representing the UK, and it provides a detailed analysis of the problem and of the multiple research approaches that are required. Read together, they are very two valuable documents.

Q178 Mr Heath: I wish to follow up on something that Professor Farrar said, which I thought was interesting. Is there no organised revisiting of drug use protocols? You spoke about different dosages and so on, but is it not something that happens as a matter of course, from the pharmaceutical companies or from the research world, or is it something that is part of normal research practice?

Professor Farrar: It is not part of normal research practice. There are some areas where it is done, and some of the infectious diseases of the developing world have been where they have been mostly led. Malaria has done that well over the last 10 years, and as a result we

have seen remarkable changes in malaria incidents globally. There are examples where it has been done systematically and well, but it is not done routinely across the board.

Q179 Mr Heath: Is it normally resource driven, or research driven? Are people finding new ways of using it simply because of availability?

Professor Farrar: It is research driven by people interested in it, and of course there are not necessarily that many business model incentives to repackage, relook at and redevelop drugs that already exist.

Sir John Savill: May I respond to that really good question? The MRC enjoyed a world first, collaborating with AstraZeneca on a mechanisms of disease initiative. Our community of researchers were informed of, I think, 22 discontinued drugs that AstraZeneca no longer wanted to develop, but nevertheless powerful reagents. We ended up funding 15 projects. The principle was to understand human disease using these powerful antagonists of particular pathways.

The other general principle was that here was an academic organisation funding research on old drugs and trying to find new uses for them: repurposing. Indeed, the National Institutes of Health in the USA adopted this approach with a broader sweep of companies and medicines, and it could be highly applicable in this area of old or underused antibiotics. It is a very good point.

Professor Farrar: The other is not just repositioning the single therapy but the crucial importance of moving towards combination therapies. If you use drugs in combination, your chance of developing resistance to one of those drugs is less. That is another bit that adds on to what John was saying.

Q180 David Morris: What do you consider to be the most significant barrier to the development and commercialisation of new antimicrobials, and what should be done to resolve these issues?

Professor Farrar: It is the business model around which you develop drugs, which may not be used or which may be used sparingly in small populations. That applies to stratified medicine as well, which is why I make that link.

We have to address that business model for the development of new antibiotics, and appreciate that this is not going to be a short five-year fix. It is going to be with us for ever, because resistance is an inevitable consequence of the way that pathogens evolve, whether it is bacteria, viruses, parasites or fungus. Therefore, a complete paradigm shift in the way that we encourage and facilitate business models around antibiotic development is the crucial element.

Sir John Savill: I emphasise a point that Anthony made. “Business” is not just business; it is also the NHS. In our country, the main payer for drugs is the NHS, and it therefore has to be intimately involved in the development of a new business model.

Q181 David Morris: Because we have the NHS and because health care is free, would you say that we have a broader scope, a broader range to choose from, of information on how particular drugs work in a global market, because we are more condensed in the UK?

Sir John Savill: We have the discipline of NICE, and the health technology assessment discipline is one that is disseminating across the world. NICE often gets criticism, but again that is a world first for Britain. It is doing stuff that no one has done before, and it does it as well as it possibly can, based on the methodology, and it reviews and develops the methodology. Having that as a UK strength is to our advantage.

Q182 David Morris: What has been the impact of TSB funding, the biomedical research catalyst, on the field of antimicrobials and resistance?

Sir John Savill: That is quite interesting. We recently analysed the first few rounds of the MRC-TSB biomedical catalyst, and about a quarter of the awards had been made in the general area of infection, in both diagnostics and novel therapeutics. That is encouraging.

Sir Anthony Coates: May I comment more generally on the questions that you have been asking? I agree with everything that has been said, particularly what John has been saying. I know that we are going to come to co-ordination shortly, but there is a need for this global drive, and cross-council efforts in this country and in other European countries, and continental funds.

We have not really talked about this yet, but there is something called the emergency countermeasures drive in the United States, in which big organisations such as NIH and Baader get together and put large amounts of money—we are talking about very large amounts of money in antibiotic development—into the development of new antimicrobials. Europe does not have anything like that at the moment, but we need something like a European antimicrobial recovery programme to bring the infrastructure—all the things that we have been saying this morning—up to a level where we can start producing new antimicrobials. The level of the infrastructure in the industry and in academia is quite low at the moment; it is too low, actually.

Kush Naker: I come back to the question on barriers to commercialisation. There are probably three specific barriers affecting antibiotics. First, they have a limited shelf life. After the first dose, a new antibiotic that you bring out will start losing its efficacy over time in comparison to other drugs; you can repeatedly use the same drug and you will not have this loss of efficacy, but it means that the amount of time for which it can be useful on the market is reduced. Secondly, you have competition, in that the new antibiotics coming on to the market currently have to compete with generics that are already available for most infections. If, during the patent life of the drug, you do not regenerate it, then you have to price the new patented drug very competitively against the generics, and that reduces the incentive that pharmaceutical companies have to invest.

The only way around that is to wait until we have reached the point where we do not have any drugs to treat something, as there will be a market incentive to start about tackling it. That, combined with the lab time that it takes to develop the antibiotics, which in most cases is 10 to 15 years, means that we would have a long period with nothing to treat these cases.

Coming to solutions, as I mentioned before, delinking will be the key. If you can stimulate research and development into a drug without having to say that you need to sell this many to get your money back, then you can use tools such as prize funds. There could be a public pool of money, and strict criteria that would need to be met in terms of product, but the patent on the newly developed drug could be bought out by the public, using the money from that prize fund. That would also give the option, with newly developed antibiotics, of saving them for a rainy day, saying, “We have this new drug, but we don’t need to use it immediately because there is no time pressure on us to sell a certain amount before the patent runs out.”

Q183 David Morris: What problems do researchers encounter in securing funding for new technologies? You have answered most of the question, but do you find as a whole that a lot of these companies find it hard to secure funding to come up with a new generation of antimicrobials?

Kush Naker: It just comes down to a risk-benefit analysis on behalf of the pharmaceutical companies when deciding where to invest their research and development. They would rather go for markets where they can get away with charging higher amounts, because they know that the market will pay for it.

At the moment, antibiotics is not one of those markets. The solution that we have taken so far is trying to increase the number of product development partnerships, and that effectively is putting some public money towards privately developed products and reducing the cost of developing the drug. The effect of that is that the public are essentially paying for it twice; we are paying for a lot of the research that goes into developing it and then, at the end, once we have a product, the profits are going back to the pharmaceutical companies.

One of the mechanisms that was proposed by WHO was the antibiotic innovation fund; you could use the prize fund to stimulate research, and that could be funded through a tax on antibiotics. The money from the tax would also drive down prescribing, because the medicine would be slightly more expensive. The funding from that tax would then go into paying for the pool for the next generation. Although it would require initial public commitment, the idea is that it would become somewhat more self-sustaining.

Sir Anthony Coates: I support all of that. These are good ideas. On antivirals, we might be able to learn from the experience of the United States; the emergency countermeasures drive, for example, gives large grants for the development of antivirals—I mean hundreds of millions of dollars. They then make a commitment to buy a certain amount. You have probably seen this sort of thing in the press. The Government make a commitment to buy a large amount of the drug, which gives a guaranteed market for the drug once it has been produced. These are things that are taking place now in the United States in the antiviral area, but there is no reason why it could not be done for the antibacterial area.

David Morris: Thank you, gentlemen.

Q184 David Tredinnick: Does the UK five-year 2013-18 antimicrobial resistance strategy focus too much on bacteria—that it is perhaps more of an antibiotic strategy than an antimicrobial one?

Sir John Savill: In short, no. It has the right focus, because what is dangerous to the most people is, in my view, multi-resistant bacteria. In my clinical practice, I have treated fungal infection in immunosuppressed patients, and generally you have to be pretty unlucky to die of a fungal infection unless you are immunosuppressed. There are others much better placed than me to talk about lethal viruses, but one of the approaches to HIV therapy that was successful was using combination therapy specifically to address the issue of resistance arising during treatment. That, of course, was a principle established by the MRC 60 years ago, with its ground-breaking trials on tuberculosis. Again, we had to use multiple drugs to achieve a therapeutic effect. I would not denigrate the importance of fungi or viruses, but I think that the big issue at the moment is bacteria, although I might be wrong.

Professor Farrar: The report has got the balance about right. I grew up as a young doctor here in London before the advent of treatment for HIV, and to see young individuals dying of an untreatable infection in London was an appalling experience, so we absolutely should not forget viruses—HIV, influenza and many others. In the absence of a vaccine for those, and a vaccine for HIV is a long way off, we are going to be dependent on behavioural change and therapeutics. We should not forget, and your question is well put.

I think that the balance is about right, because the coming wave of bacterial resistance coming to this country has been underestimated.

Sir Anthony Coates: I strongly agree with what has been said.

Q185 David Tredinnick: Will we be better prepared for resistance emerging to antiviral and antifungal drugs than we have been for antibiotic resistance? You have already touched on this.

Professor Farrar: I shall start with the virals. It was mentioned in passing, but there are really important lessons to be learned from the way that the world dealt with HIV, and the pull and push in developing antiretroviral drugs. We do not celebrate enough where we went from 1983-84 to today in terms of antiretroviral drugs and of learning the lessons of how we incentivised the industry, academics, the research community and the population. The public should not be underestimated in terms of the pressure that they can bring to bear. The HIV committee had a huge role to play in the development of antiretroviral drugs. I would be hugely worried, in our working lives, of the coming of real HIV drug resistance. That is a major concern. The other viral resistance—hepatitis and influenza—should not be underestimated.

Q186 David Tredinnick: In our terms of reference, we ask whether there is sufficient research and investment into other treatments and methods “to ensure continued protection against infection”. According to research that I have from the House of Commons Library, a report in *Drug Discovery Today* in 2008 said that between 1994 and 2008 “almost half of the drugs approved since 1994 are based on natural products.” Have you looked at the possibility

of a greater use of herbal medicine and acupuncture as a way of reducing the need for antibiotics?

Professor Farrar: I shall start with the first one. There are a number of issues in your question, and there is a lot to be teased out of it.

Most of the anti-infective agents that we have today come from some sort of natural product. For instance, the one that I have worked in extensively over the last few years, artemisinin for the treatment of malaria, is a natural product, as were quinine and many others, and huge efforts have been made by the traditional pharma industry and those such as the Chinese Academy of Sciences in developing drugs from natural products. That work is ongoing; it has been extraordinarily difficult, but it is a very active area. I do not believe that there is a role for homeopathy in the narrow definition, unless it is proven to be of benefit by what I regard as traditional means.

Sir Anthony Coates: There is a bit of a misconception about what new drugs are coming forward for bacteria, particularly the biggest threat at the moment, which is gram-negatives. The truth of the matter is that there has not been a new class of anti-gram-negative drug reaching the market for 40 years. We are not talking about new drugs coming to market; there have not been any. The first new class that has used against anything that is remotely gram-negative was something called beta-quinine against tuberculosis last year, but there have not been any new classes for 40 years against gram-negatives.

Q187 David Tredinnick: Sir John, you mentioned fungal infection earlier. According to the Library research, tea tree, an Australian herb, is effective in treating athlete's foot, wounds and infections. Should we not be looking more carefully at this range of natural products as part of the battle that we are fighting?

Sir John Savill: I am sure you are right that we need to cast the net wide. What immediately occurs to me is the importance of genomic science. We are now seeing the sequencing of more and more organisms in their entirety, and we have immensely powerful investments in the analysis of this genomic information—for example, in the Wellcome Trust Sanger Institute. A way of finding new things would be by comparative bioinformatics. We found this fungus in the Antarctic and sequenced it, and, lo and behold, it has a thing that looks like tetracycline. Your point is well taken, and genomic science spreading right across the research base is one cause for hope.

Q188 David Tredinnick: Professor Farrar, you raised the subject of homeopathic medicine, not me, but I have a question for Professor Sir John Savill.

Sir John, you are vice-principal and head of the College of Medicine and Veterinary Medicine at the university of Edinburgh. Are you aware of the European Parliament's resolution on the public health threat of antimicrobial resistance, and its call to phase out the prophylactic use of antibiotics in livestock farming, and the £1.8 million that it voted for a pilot research project to examine the effectiveness of homeopathic treatments on farm animals?

Sir John Savill: Yes. My colleagues in the vet school would wince at the idea that I am speaking on their behalf as a humble medic, but you raise a really important issue, which is the concept of one health—namely that the health of animals and humans is inextricably intertwined. We have not discussed much the importance of animal husbandry and the use of antibiotics, which is featured in the Government's AMR strategy. I want to draw attention to it. In particular, the BBSRC is very active in this area as it holds the animal health card, and it is collaborating internationally with US and European organisations. You have touched on an important area, and we cannot take a human-centric view of this.

Going further, the National Environment Research Council says that if we sampled the Thames now we would find several antibiotics in it. The issue of going beyond the hospital and medical care is crucial.

Q189 David Tredinnick: The last Science Committee did an evidence check on homeopathy, and said that it did not work despite the fact that it did not call any homeopaths to present their case. Since then, a lot of research has been done by the Homeopathic Research Institute and there is some promising research in France. I put it to you that, if we are going to deal with this subject scientifically, we have to think out of the box and look at the natural remedies that are around, and look at the small but popular science of homeopathy. We have to grip this and put it in the pot.

Sir John Savill: It is an interesting point. Clearly, views about homeopathy vary from strong support to strong objection. The principle might work for stimulating the innate immune response to infection, but it is harder to see how sub-molecular concentrations of anything are going to kill a bacterium and stop it in its tracks. However, the principle of not dismissing anything is well taken.

Q190 Stephen Metcalfe: I want to talk about the co-ordination of research, if I may. The Society of Biology has called for centres of excellence. What do you imagine a centre of excellence to be? What would it look like?

Sir John Savill: The MRC has been able to establish such a centre at Imperial College under Professor David Holden, a distinguished microbiologist. There is a focus on molecular bacteriology and infection. There are at least 20 research groups, which hold in excess of £25 million in research grants. The MRC has invested an additional £3.8 million. That, by any definition, is a centre of excellence, and it is something that we should be proud of.

The question is a good one, because the MRC hopes to find similar strength in one place for translational bacteriology, particularly on the issue of antibiotics and antibiotic resistance, but we were not able to find such a centre in the UK. The approach initially has to be based much more on bringing experts together from different cities into UK-wide consortiums. That is certainly what six of the research councils have been discussing with the Minister, and we have identified substantial funding from our own resources to do that.

The direction of travel is that, if we could scale up the resources, then we could develop a range of centres of excellence, by training more people, by attracting scientists to the UK, and by bringing people from other disciplines to the cause. One of the concerns that I have

is that we lack a large number of centres of excellence compared, for example, with cancer research, cardiovascular research or genomics. You cannot say that there are six or seven places doing this; we lack the strength, in my view.

Sir Anthony Coates: May I comment on that, particularly on the translational aspects? Sir John is absolutely right that there is a gap between academia and industry. Industry is in bad shape as well, but let us say that industry was in good shape. How could we get drugs from academia through to industry?

A number of models have been quite effective in the past. For example, embedding small companies in universities has been done a lot in the United States. It has been done in the UK as well, but more so in the United States, where perhaps academics spin out companies and ideas, and they start off by being embedded in the universities. It is important to have a legal contract that covers the rights of both parties—not so easy to get, I can tell you—and that will do the early stage development, say up to phase 1 and possibly phase 2 and clinical trials. It is at that stage that you need much more money; the average cost of a clinical trial is about £50 million. You need big pharma to come in at that stage. That is where someone from outside would definitely have to come in with a large amount of money. That gap needs much more effort, and embedding of SMEs.

We have also suggested that chemistry, which has not been talked about much this morning, is key. With small chemical molecules, you could have centres of excellence of chemistry with nodes throughout the country, for example, and that could form a good basis for pushing academia towards the industry and translational side of things.

Sir John Savill: The EPSRC is doing just that. It is starting with grants to develop chemistry. You make important points, Anthony, and the Committee has discussed this before in the “valley of death” inquiry, but there is a general trend now towards incubating companies for longer within research-intensive universities, and the availability of funding—for example, from the biomedical catalyst, soon to be joined by Agri-Tech, another catalyst—which encourages that closer relationship between universities and SMEs. The BBSRC has a particularly strong model of campuses where SMEs cluster with research strengths. At the MRC, we are interested in the concept of proximity to discovery, and encouraging such campuses, which might include a medical school, a hospital and a research park, so that SMEs are clustered close to the research. That will apply to all therapies, not just to antimicrobial, but you make important points.

Professor Farrar: On co-ordination, the MRC has led on this, but we are happy to be part of it. The MR Funders Forum is getting together to encourage a more joined-up approach in this space, bringing SMEs, and small and large companies as well, in closer proximity. There are a lot of so-called targets within the academic sector. Drug targets on the antimicrobial space may or may not be targets, and bringing the rigour of industrial input to our thinking on what is a target is crucial.

We keep coming back to the issue of the economic case. Through the forum, I would like to see a much more hard-nosed look. Many of us have ideas about the business model for the development of antimicrobial agents, but a really hard-nosed economic assessment of that at the global level would be invaluable.

Q191 Stephen Metcalfe: Who should conduct that?

Professor Farrar: The UK already has an international reputation for leading on this. It has put things to the World Health Organisation, through Sally Davies, and will do so to the World Health Assembly later this year. The UK would be in a position to take a lead on that.

Q192 Stephen Metcalfe: Presumably, yours is not a lone voice in calling for the model to be redefined.

Professor Farrar: We are not a lone voice, no.

Q193 Stephen Metcalfe: Why have we not yet taken those steps?

Professor Farrar: I have worked with emerging infections diseases, and if you have a nasty virus coming out of south-east Asia and it is going to hit you here in London, it creates a wave of excitement and interest, and then films like “Contagion” are made. Antimicrobial resistance is a much more insidious, slow thing; it is burning in the background, and it will hit us like a brick wall at some point. It has already hit places such as Ho Chi Minh City in a bad way. TB drug resistance was discussed recently in the news in London. It is much more difficult to get a momentum behind it than it is for an emerging virus coming out of somewhere nasty. There is a change now, and the UK has played an important role in leading that, but we need to push it much harder and that is why this Committee has become so important.

Kush Naker: May I add to the point about co-ordination? It has certainly been done quite well with regard to the surveillance of disease, but, in terms of funding, although there has been co-ordination within research councils and even Europe-wide, we need a global strategy.

WHO published a report on this in 2012, looking at how we can finance and co-ordinate research, particularly as it affects markets that have been failed by traditional pharmaceutical models. It made a series of recommendations, but one of the leading ones was a binding global research and development treaty, where every country would commit to spending 0.01% of their GDP on research and development where it has been failed by traditional market incentives. That was thrown out by a previous WHO assembly, which said that it would revisit it in 2016. In the meantime, demonstration projects have been set up to look into the concept of how international co-ordination on funding might work. Unfortunately, none of those demonstration projects relate to antimicrobial resistance, but some of the proposals that were sent to the Committee include the antibiotic innovation funding mechanism that I mentioned earlier.

Q194 Stephen Metcalfe: When creating these centres of excellence, whether they are global, regional or national, do the scientists themselves physically need to be in close proximity, or is it something that you can do virtually, or remotely? This is a subject that we have visited on various occasions; is it the personal contact that is important, or the quality of the research that is being done?

Sir John Savill: The answer is yes and yes. It works best if there is a grass-roots-up coming together in one university or hospital of a bunch of people that are like-minded, who fire off each other. That is probably the best model, but the virtual network, particularly in this era of Skyping and e-mailing, also works well. It works across nations, and Jeremy has led such an effective collaboration, and he might want to talk about it.

Professor Farrar: I am a great believer in coffee rooms and people sharing corridors and meetings. Thankfully, the world has not yet moved beyond that sort of contact, and there is huge benefit to be gained from it. The Wellcome Trust Sanger Institute has been a fantastic success over 20 years or so, and it is a campus, but much of its work is done virtually, throughout this country and globally. I would not suggest that you had one model or the other. You are going to need both.

Q195 Stephen Metcalfe: Does the Norwich Research Park centre fulfil the model that you all have in mind?

Sir John Savill: It is a powerful campus in plant science and related genomics. It is a good example of a campus. Another good one in the BBSRC's territory is Babraham, which has a more biomedical emphasis and a greater concentration of small companies. This model of working closely with small companies is important and will be required to help crack the problem that we are discussing.

Q196 Stephen Metcalfe: Professor Coates, you talked about a cross-research council to tackle this, and I know that there is some work going on. Would you expand on that a little; on how you would see it working? What will the strategy be, and how would you initiate this?

Sir Anthony Coates: This is already happening. Discussions are already taking place for this to happen in the UK. Each research council has, as it were, its own speciality. Antimicrobial resistance and discovery is a broad church, and it is a bit too broad for any one council to take on board, so the concept is being discussed on how one can take this forward as a group of cross-councils. Sir John would know more about this than I do.

Sir John Savill: I have said before to the Committee that health research requires all seven research councils—and I shall say it again—and there is nowhere more obvious than in the case of antimicrobial resistance. Time is short, but I could run down each council and articulate what it might contribute, but even the arts and humanities have something to contribute. In fact, the AHRC did not fund the work that the Wellcome Trust did a couple of years ago, which was a really interesting exhibition on cultural attitudes to dirt, with a fascinating book, which some of us were given. I agree entirely that all seven councils need to get together to bring their strengths to this, and we are doing that with encouragement from David Willetts.

Q197 Stephen Metcalfe: Going slightly off subject for a moment, do you think that there is still a need for seven different research councils if there is going to be so much cross-collaboration?

Sir John Savill: This has been examined carefully during the triennial review of the research councils. The final conclusions have not yet been published, but we think that it works. So, “If it ain’t broke, don’t fix it.”

Q198 Chair: Given your earlier comments about the TSB and so on, is there a case for a catapult specialising in antimicrobial resistance?

Sir John Savill: You would need to ask the TSB.

Q199 Chair: I am asking you.

Sir John Savill: I think that we can go an awful long way with a precision medicine catapult if it has a strand within it of infection. A catapult works best when there is a clear market to take the innovation to. That was highlighted in Hauser’s report, and we have been discussing that there is not a clear market. You really need to ask the TSB that question. I am not convinced at the moment that it would be the panacea that you hope it would be.

Professor Farrar: I agree. It could be, but there are bits in the criteria for a catapult that do not quite fit with the infectious disease models at the moment, and we would need to address that before I could push for a catapult.

Q200 Mr Heath: It is a wonder of Somerset that we have the cultural latitude to do it—and water, but do not start me on that.

I want to ask about data collection. As was mentioned earlier, we have a good surveillance of disease incidence, but I wonder whether we have sufficiently good surveillance for failed treatment and whether there is a limiting factor in terms of data collection, which could be improved upon.

Sir John Savill: This is the subject of enthusiasm for a number of us. The UK has parts where we have tremendous strengths. For example, I reside in Scotland and I was the chief scientist in the Scottish health directorate. We have enormous strengths, and we could answer the question of who has had antibiotics, who had an effective response. We now have tremendous strength developing across the UK. The MRC has collaborated with nine funders to establish the Farr Institute, and the issue of harvesting NHS data every day, analysing the information carefully and discovering things is very much at the front of our minds.

I would be failing in my duty if I did not say that much of the research done on potentially identifiable data without consent could be threatened by the amendments before the European Parliament in relation to the European Data Protection Regulation. A number of us are concerned about that, but the general point of data sharing being catalytic in this area is well taken.

I finish by saying that the Department of Health in England has established Genomics England as a company that will undertake the sequencing of 100,000 whole genomes, and many of those genomes will be bacterial—they will be to do with infection. Again, those

data have to be made available and widely accessible. I agree that the data-sharing issue is key to cracking the problem.

Professor Farrar: The way you phrased the question was interesting. At a global level, since SARS, there has been an absolute sea-change in the way that data are shared around the world in terms of emerging priorities but also around drug resistance. It is not perfect and there are many countries around the world with absolutely no facilities for making any diagnosis.

You raised the question in a different way. You asked whether the data are sufficient not just for the start of patients with an illness but what happens to them at the end with infectious diseases. You are right that there is a gap. Often, an infection is thought of at the start, and you get a pathogen—it is malaria, it is a bacteria, it is a virus and so on—but the link to the patient's outcome and what happens often gets taken off by the infection and the immune response. Those data do get lost, and it is not being systematically kept.

Q201 Mr Heath: It is valuable.

Professor Farrar: It is invaluable. It is absolutely crucial.

The other bit of data, which I keep going back to and which is never recorded and is often never part of clinical care, is pharmacology. If you know what the infection is, you know what drug was given but you do not know how much of the drug reached the patient and site of action, then your ability to interpret all those data is missing.

Q202 Mr Heath: Are there ways in which we can improve that data flow? Let us start in our own country rather than on a global scale. The NHS is the biggest single repository of health information anywhere, as far as I know. Are there things that we could be doing better?

Sir John Savill: One thing that we could clearly be doing better is communicating the importance of sharing data to developing health care and research. We have seen a storm of protest in some of the tabloid newspapers in the last couple of weeks about the English initiative care.data, and the first thing that we have to do is to explain how important it is.

Q203 Mr Heath: Why have you scientists not been shouting about it? You leave it to politicians to defend what seems worthwhile.

Sir John Savill: I reside in Scotland, and I have joined the share initiatives. The Scottish approach has been grass-roots-up, with people volunteering to share their data. It is a powerful model. It is a complex issue, but we have to get the public onside about this.

Mr Heath: Any further views? No? Well, I'm happy with that.

Q204 Graham Stringer: May I ask Professor Farrar a question? I am sorry to have missed the first few minutes of your submission. You said earlier that there has been a loss of pharmacological skills in this country, and you just referred to a lack of pharmacological information from the treatment of patients. Would you expand on those two points?

Professor Farrar: It goes back to the original question, when you asked if Britain was leading, and some of us said that we thought that Britain had been. If you look back to what the MRC funded in the 1950s around TB, there is no doubt that at that stage Britain was leading the world in the combination of microbiology, infectious diseases and TB in particular, and in pharmacology.

Over the last 20 to 30 years, those disciplines within our universities, pharmacology in particular, have become less than they were. The teaching in medical schools around pharmacology is less even than when I was a medical student, and pharmacology is not thought of in sufficient levels, particularly around infectious diseases, in clinical practice. That is something that we would need to seek out, and enhance and improve it. You cannot just think of this as the pathogen, the infectious agent. You have to think of it, as well as the patient and the intervention that you give—the drug. Those have to go together.

In the animal sector, which we have not talked about much today, it is even more poorly developed.

Sir John Savill: Funders have recognised the general weakness in pharmacology over the last five years. Both the Medical Research Council and the Wellcome Trust have initiatives focused on young clinician scientists, to attract them back to the discipline of clinical pharmacology. Those schemes are now fully recruited and we are going to need to evaluate the impact of that. They were not focused specifically on infections.

Sir Anthony Coates: Thank you for that question. I work in a medical school, and there is constant pressure on pharmacology teaching and antibiotic teaching. If the Government could do anything to enhance the right of teachers in that area to make space in the programmes and courses for teaching pharmacology and antibiotic resistance, it would be welcome indeed, and extremely important. At the moment, we are judged as being less important than most other areas in medicine, and that is wrong. We should now change with the times, and emphasise how important antibiotic resistance and pharmacology are in medical schools.

Chair: Gentlemen, thank you very much for an extremely interesting session.

Examination of Witnesses

Witnesses: **Dr Louise Leong**, Head of Research and Development, Association of the British Pharmaceutical Industry, **James Anderson**, European Partnerships Director, GlaxoSmithKline, **Dr David Williams**, Chief Executive Officer, Discuva, and **Michael McIntyre**, Chair, European Herbal and Traditional Medicine Practitioners Association, gave evidence.

Q205 Chair: I welcome the second panel to this morning's session, and I invite you to introduce yourselves.

Dr Williams: Hello. I am David Williams. I represent a small biotechnology company called Discuva, which is focused solely on antibiotic research.

James Anderson: I am James Anderson from GlaxoSmithKline. I am in the public policy team there, and I have worked in the sphere of antibiotics for a number of years. I

participated in the chief medical officer's global forum on AMR last year, and I was also involved in negotiating with the Europe Commission the IMI new drugs for bad bugs programme.

Dr Leong: My name is Dr Louise Leong. I am head of R and D policy at the ABPI, the Association of the British Pharmaceutical Industry. We represent research-based industry.

Michael McIntyre: Good morning. I am Michael McIntyre, and I am chairman of the European Herbal and Traditional Medicine Practitioners Association.

Q206 Chair: Thank you for coming here this morning. I want to start by looking at markets. How different are the markets for antivirals, antifungals and antibiotics, and do Government initiatives match the needs of those markets?

Dr Williams: That is an interesting question. The markets for antivirals are perceived as bigger, because there are a lot of new medicines there. In antibiotics, currently there is space, and a lot of traditional old medicines that are perceived as being very cheap. We have a situation at the moment where we have the ability to put new medicines through clinical trials and on to the market, but we are waiting for a market to appear.

Even in hospitals, when you talk to clinicians and the expectation is that they are going to use an antibiotic to cure a patient and stop them dying, it has to be something that is a pound or two per treatment, which is wrong. We have to change that.

James Anderson: I fully agree with that. There are some unexplainable differences, when you look between those segments, and particularly where that comes through in price. The price points for treatments for HIV, for example, are orders of magnitude higher than what you would see for antibiotics, even for the new ones, which should be used in small volumes.

Currently, we have an interesting situation where some companies are launching new hepatitis C products. The prices that are being charged there are extremely high, and that will potentially raise some questions on how this works, but from the point of view of antibiotics, it comes back to a number of the points made earlier—that the economics as they are today for developing antibiotics are broken. There is a market failure there.

Dr Leong: I would agree with that. Antibiotics are unique. The dynamics of the market are very different from those of other medicines that we are more familiar with. Certainly, they are undervalued for the value that they bring to the health care system, and to society. We have heard about the three main factors in that—that they are used sparingly, that the courses of treatment are short, and that the price is low. Therefore, it is not an attractive model for investing, when you consider that it takes about £1 billion and 10 to 12 years to develop a new medicine.

Michael McIntyre: Herbal medicines are an unexplored resource, I would say, and they have significant potential to produce cheap medicines. They are used in other countries across the world as a matter of course, and they have a good track record in helping antimicrobial resistance. There is research showing that relatively cheap herbal medicines can be used with drugs that are on the market to which bacteria have developed resistance. When combined with a herb, some of these antibiotics become active again. I would argue

that there is a good business reason for looking again at natural products, herbal medicines, to solve some of these problems.

Q207 Chair: I want to start with you, Dr Leong, on this question. In discussions with many of the members of the ABPI—I have crossed paths with them in different guises—I hear different answers to the question. How effective are the various R and D initiatives, such as tax credits, the Stevenage biomedical catalyst, at encouraging antimicrobial development?

Dr Leong: If we look at research in general, we can see that there are two types of mechanisms; they are push and pull incentives. Tax credits, and R and D funding are examples of push mechanisms; and TSB support for SMEs and the biomedical catalyst fund fall into that arena as well. Tax credits are useful. What we are seeing is an evolving industry, one that is interacting and collaborating much more outside its walls with other sectors, such as academia, SMEs and so on. Anything that supports each of those sectors would be vital.

Q208 Chair: Let's go to the different parts of the industry.

Dr Williams: Louise has made a good point. It is a joined-up problem. You have an ecosystem here. You have the academics at one end, doing blue-sky research; you have the biotechs, where I sit, doing innovative drug discovery research; you have the pharmas doing discovery and development and on to the market; and you have the NHS and the public. Each of those components has to be stimulated.

In the biotech sector, we find R and D tax credits essential to operate, and our company would not exist without them as we would not be able to fund our research. The biomedical catalyst has been an enormous injection of money into the biotech sector. We should remember that the biotech sector is the next pharma companies; it grows and creates its own pharma companies. If you do not have the biotech and the pharma, you do not have the need to educate people in your academic institutions because there are no jobs for them to go to. The whole thing is joined up, and you have to stimulate every component.

James Anderson: I agree with what has been said. What is interesting when it comes specifically to antibiotics is that there is a need to do something more. As we have heard, what we have today has not delivered sufficient investment into R and D in this area. We feel that public-private partnerships can play an important role in this specific area. The IMI new drugs for bad bugs, which I mentioned earlier, at a European level starts to address a number of the issues, and we see that as an interesting model that can be rolled out. Our strategy also involves partnerships with other funding organisations, such as Wellcome. We have an interesting partnership with the US Government in the form of BARDA, the biodefence funding agency. There is a need to do more, and perhaps we can learn from some of those approaches.

Q209 Chair: Your sector, Mr McIntyre?

Michael McIntyre: Again, this is something that needs development. I heard one of the professors talking about the lack of pharmacology training. Pharmacognosy, which is a special area looking at natural medicine development and plant medicines, has disappeared almost entirely in the last 50 years from British universities. That is a great shame. We have several universities training people in herbal medicines. We are the world leader in training people in herbal medicine. There are a lot of experts in this country, who represent a significant resource that I argue should be tapped into.

Q210 Chair: Mr Anderson, you mentioned the US connection. Thinking about the US framework, there are different legislative arrangements, such as the GAIN Act. Do you think that there are lessons to be learned here from that kind of legislative approach, as far as antimicrobials are concerned?

James Anderson: There are several parts to that question. The main incentive of the GAIN Act is that it provides five years of extra data exclusivity on top of what already exists, specifically for qualifying new antibiotics. That has a certain level of benefit, but from our perspective it is not sufficient. In fact, it will have a rather limited impact, partly because the patent term that we will have when bringing a new product to market will typically span that increased period anyway. However, it has put the whole debate on to the agenda of Congress, and we have seen continued interest from the FDA, particularly to address the use of antibiotics in animals in the States which is much more heavily done than here.

There is not a direct parallel, but they are elevating it up to the senior levels in the political infrastructure or hierarchy. For example, the President's committee of scientific advisers is doing a project on it right now, and there is a personal interest from the President. He mentioned this problem during his State of the Union address last month. If we could have that step of progress here, in terms of David Cameron talking about it, we would see it as being a very positive step.

Q211 Chair: That is a case for political leadership rather than legislative change.

James Anderson: We believe that political leadership is absolutely what is needed here. You heard in the earlier session some of the things that need to be done, as I would describe them, and we can go into them in more detail, but they are really hard and there are all sorts of confounding factors. From the bottom-up point of view, we can go so far, and that is what we are trying to do but, given the leadership already shown by the chief medical officer, that starts to put some big lines in the sand that everyone can start to move towards, not only in the UK but on a more global basis.

Q212 Chair: Does anyone wish to add to that?

Dr Leong: Yes. We totally feel that it is an international problem. The UK cannot do anything on its own. We really welcome this continuing momentum in raising this as an issue with willing international partners.

Coming back to the value of antibiotics, we may value them but the demand is for them to be available, not necessarily to be used. Therefore, extending the patent term might help

only to a certain extent, because there would not be the high volume to recover that. On some options for mechanisms, we would be happy to sit down with Government officials to look at the real economics and so on. A potential model might be likened to an insurance system, where you have a new effective antibiotic available, but not necessarily used, you have it there for when you need it, and therefore some of the options are something like an advanced market commitment, where Governments might purchase in advance a new antibiotic that has proven to be effective, licensed and been through the regulators.

Dr Williams: I agree with Louise on her last point about the licensing model for funding antibiotic prescriptions, but we need a little bit more work on the patent life extension. We are looking at the current situation and the way that we prescribe antibiotics. In the previous session, Jeremy mentioned the need for combination therapy. That means that you could have drugs with a longer market life than they currently have, because you put them into different combinations. In that case, it would be a financial incentive to have a longer patent life. We should remember that it is a long process to get a drug to the clinic. It can be 10 years before it even sees a patient, so that leaves just 10 years to get all of your money back.

Q213 Stephen Metcalfe: With the previous panel, we discussed the creation of centres of excellence, as called for by the Society of Biology. What would your vision of centres of excellence be, and do you think that the Norwich Research Park is a model for that?

Dr Williams: The Norwich Research Park is a fantastic centre for microbial expertise, and it also has a teaching hospital. That is significant because, going back to the previous session, if we are going to have a centre, precision medicine focused on antimicrobial resistance would be a good use of the Norwich Research Park. I do not think for drug discovery that it has the core skills; nor can it attract the right people to the area, because it is a bit cut off.

Q214 Stephen Metcalfe: What would a centre of excellence that was working on those wider issues look like?

Dr Williams: It would have to be very joined up, and it would have to be well funded. It could not just be a university department extension.

A real centre of excellence for me, in therapy in the UK—we do not talk about it enough—is the ICR down in Sutton, which is a cancer research establishment. That centre of excellence has a different model for funding its research, so it has longer-term contracts and a goal at the end. They get two development candidates for therapy each year, which is better than anything else in the world.

You need a focus for a centre of excellence, and you need to stop the people-coming-through-and-leaving mentality that you have in university departments, where you do your PhD and leave. You need some continuity.

James Anderson: I fully agree with those points. We see a particular opportunity that we would like to explore within the UK context, which is looking at alternative approaches to

treating bacterial infections. These would not be the standard approach of small chemical molecules; we see a need to focus research on things such as bacteriophages, more of the host-immune response types of approach, and potentially monoclonal antibodies as well.

There are a number of different scientific techniques that, for reasons that I am not sure about, have not really been able to flourish. By bringing them together, both physically and virtually, there could be a real opportunity to create some critical mass, with a long-term approach and backing. We also see that there is an important role for multiple companies to work together on this with the academic researchers. We see that as important, because it would help smooth the transition from one side to the other.

Dr Leong: A centre would need to be interdisciplinary—microbiology, epidemiology, pharmacology and medicinal chemistry, and crucially bioinformatics, genomics and the use of diagnostics. Certainly, there needs to be clinical and basic science well integrated with hospital clinical sites and universities.

The second important factor is that any initiative or a centre that has a translational pull into the development of real new antibiotics would be welcomed. Such a centre would bring a great deal of focus to this important area, and would be a fertile training ground for new scientists and clinicians to develop the skills that we need in the UK.

At the same time, in addition to a central approach, the network approach is also important. In pharmaceutical companies, R and D is global. If we come back to the IMI, which is a €2 billion collaboration between European pharmaceutical companies and the European Commission, that takes place across EU member states. It has many pharmaceutical companies working there. Companies will collaborate where the science is good, so the network aspect is also important.

Michael McIntyre: I add the simple plea that we should be open-minded and think outside the box—I use somebody else’s phrase from earlier—and to use all means to explore the world at large, not just the UK. The director general of WHO called for the integration of traditional medicine systems with conventional medicine. She has done so twice recently in public, and we should listen to her.

Q215 Stephen Metcalfe: Thank you for that. There are some interesting models there. You talked about skills. Do you think that we have the skills base to be able to achieve our goal of realising these centres of excellence? If not, what do we need to do to build up our skills base so that we lead the world in antimicrobial research?

Dr Williams: The really good thing about Europe is this. Europe is fantastic for us because it means that we can hire people from anywhere from a pool of 350 million people. It has been very useful for our company. You can get some of the best scientists in the world by doing that. That is important for any organisation going forward.

The skills that have gone were from the merger of different pharmaceutical companies and pharmaceutical companies leaving the area. That is where we have lost pharmaceutical experience, but it can come back. I do not see that being gone for ever. We have a core set of capabilities in this country, and we have a lot of people who were in the industry who are still here—they have not all left. Reinvigorating the community and putting funding

into the biotech sector to grow those companies, replenishing the skills, I think is essential. I come back to the biomedical catalyst, and how useful that is.

James Anderson: Another area of skills that I think is vital for bringing drugs all the way through to market is on the clinical side. We need clinical centres that are expert in managing infections. Because there have not been many clinical studies on antibiotics recently in the UK or Europe, it is a real need. That was recognised as a key goal for the IMI project.

A network is in the process of being established, with 280 centres around Europe, 11 of which are in the UK. They need to have a really good grasp on the epidemiology locally, in order to help put clinical trials there that fit with the epidemiology and the resistance factors that they have. They need experts and high levels of capability across all the disciplines that we have talked about, and they need to have in place clear approaches to stewardship in terms of how they manage their infections.

Dr Leong: The UK historically has been seen to be strong in basic microbiology skills. One area that could be beefed up is the use of data, so that we have linked datasets. We can then come to an evidence-based formation of policy in health care. For example, we do not necessarily have the data that we need in terms of the incidence or prevalence of multi-drug resistance, infection and so on, linked to prescribing information that is then linked to the treatment outcomes. Having an understanding of that would build a good evidence base for health care policy.

Q216 Stephen Metcalfe: We heard mention of the fact that the biomedical catapult has been successful. Do you think that there is a role for a catapult centre directed specifically at antimicrobial technologies and research? Would industry welcome that, do you think?

James Anderson: I very much echo the comments of the previous panel on that point. In principle, a proposal for a catapult such as you describe would be something that we would look at, for sure. However, to the extent that catapults are designed to commercialise, to bring in commercialisable technologies, and that we have a market that does not reward innovation at the moment, that is going to remain a problem. The answer is yes, if we can create a new model that does three things.

First, it needs to reward in a way that attracts investment for new innovative antibiotics; we are talking about new classes, as all the existing classes are kind of reaching the end of their innovation life cycles. Secondly, we want the model to better align with the conservation of the resulting products, which means breaking the price-volume mechanism. It makes no sense for anybody, not only companies but doctors and pharmacists, to have incentives to use more of a product when from a public health point of view we should be trying to use less. The third thing that the new model needs to do is to ensure that patients anywhere in the world can access these new products, because we do not know where the outbreaks of new resistance will be.

It comes back to that model. We have some frameworks that are coalescing, and it was pleasing to hear many of the earlier speakers saying things that are exactly in line with how we articulate it. Once we have that in progress, or even a clear place where we

believe it is going to end up, then there are many things like a catapult that would be an ideal way to pull it through—but potentially not before.

Dr Williams: It is push and pull, as we have said before. It is not all doom and gloom out there. When you look at the pharma companies that got out of antibiotic research during the 1990s and the early noughties, it seemed quite depressing, but when you look at what they are doing now, they are making strategic investments and licensing new products. Some of them have got back in again, but they are poised, waiting for the financial incentives to make the full commitment. That is the pull. As we mentioned, catapult centres are the push, but if there is no pull there is no point in push.

Q217 Chair: Before we move on, Dr Williams, in response to an earlier question you slightly criticised the come-and-go nature of university research. Rather than them doing something about it, what is industry going to do? What do you think the solution is? Where can industry help to create a more direct approach?

Dr Williams: We are successful in our own company. When you look at the number of antibiotic classes on the market or that have been discovered, there are something like 20 or 25 within our own company, and we have thousands of new classes. We are being helped by TSB biomedical catalyst funding to take some of those through to the next phase. Our model is to partner those with pharmaceutical companies, which take them to the market. We will not be able to partner those products with pharmaceutical companies if there is no market. We are trying our best, and we are interacting with academia. I am not criticising academia—it does a fantastic job in seeding ideas and seeding research—but I am saying that academic institutions are not the best place for translational research.

Q218 Stephen Mosley: One of the things that we saw from the written evidence was the difficulty of conducting clinical trials when it comes to antimicrobial resistance. What are the main differences between clinical trials in antimicrobials and normal clinical trials?

Dr Leong: We need more rapid diagnostics. Some of the difficulties in terms of getting people into trials for antibiotics are that you need to know what they are suffering from and what pathogens and disease resistance there is. It does not help to have to wait several days for cultures to be grown, so more rapid diagnostics would help.

Traditionally, over the past two decades, we have seen increasing regulatory hurdles. When you look at antibiotics that were launched in the 1970s and 1980s, they were perhaps launched on the basis of 900 patients in trials, and the studies cost much less. As each decade has passed—the last antibiotics, the more recent ones launched in the 2000s, required 9,000 patients. If we are looking at patients that are specific to what you are trying to develop, they are fairly diluted in terms of needing to find that they are suffering from particular pathogens. Those are the difficulties.

Having said that, there has been a lot of movement in the last two years by the FDA, the US Federal Food and Drug Administration, and in Europe by the EMA, of which the MHRA is part, from which we derive our regulations in the UK. Both agencies are looking at accelerating clinical development programmes for the development of new antibiotics for multi-drug resistance pathogens, to allow them for use much earlier in the restricted

and specified population, with data from a smaller number of patients in trials but with the requirement for continued collection of evidence once they are available. Those would help very much. We would ask the UK Government to request the European Commission to ratify the EMA's proposals for such an accelerated clinical development programme.

Where we are seeing things that have worked for other areas, such as orphan or neglected diseases, there is a fast-tracked licensing regime as well, where new antibiotics are prioritised for review, with protocol assistance in terms of scientific advice at an early stage between the regulator and the drug developer. There is movement, and we are hopeful that these new requirements can be put into place.

James Anderson: I would add a couple of points specific to your question. One of the challenges is where new drugs are needed to treat serious hospital infections, typically. We have heard about the gram-negative side in particular. If you are a doctor with a patient that might be eligible for a trial, they are going to be really ill and are probably coming into the intensive care unit at the hospital, and it is practically challenging to talk about informed consent and enrolment into a clinical trial. That is a practical issue that does not have a straightforward solution, but we see the expedited approach that Louise talked about as a very important component of how to overcome that. It also should be emphasised that the more these approaches can be harmonised globally, not only by the FDA and the EMA but the rest of the world, the more efficient these approaches can be to enabling the clinical trials to take place.

One other challenge that we regrettably saw last year was the emergence of resistance to a product that we were testing during the process of clinical trials. That is a specific challenge that is clearly unique to this area. It caused us big problems, and we had to terminate one of our investigational programmes last year.

Dr Williams: It is worth reinforcing that what Louise mentioned about the FDA's accelerated approval for much-needed drug resistant antibiotics is also linked to pricing. There is a perception that you can charge much more than we currently pay for our antibiotics for these sorts of treatment. There has to be an embracing culture by the various paying bodies to pay those costs.

We see some evidence that even medicines that are approved by NICE are not prescribed by clinicians. Perhaps it is not good prescribing, or it may be a lack of knowledge—or a lack of health economic knowledge. That is something that we need to address.

Q219 Stephen Mosley: Thank you for those very full answers. I wanted to drill down on the difficulty of getting people to come forward for clinical trials and the need to speed the trials up and allow them to be conducted, and then for people to use medicines while the trials are continuing, but those questions have been fully answered. I move on to something else with my next question.

There has been a lot of talk about costings, and the economics and finances of the situation, so I move on to reimbursement strategies, in particular the new pharmaceutical price regulation scheme and the value-based assessment incentives. Do you think that they will help companies to develop new antibiotics?

James Anderson: There is a really interesting point here. Our hope for the new PPRS scheme is that it will enable a much more rapid uptake by the NHS of new products. In every case, apart from antibiotics, that would make a big difference to patients coming through. However, in antibiotics you almost want the opposite. You do not want a rapid uptake of new products; you want them to be used only by those patients who really need them, for whom none of the other products will work.

In the case of antibiotics, no, we do not believe that this will solve the problem. In fact, some companies are asking simply for higher pricing for antibiotics. Although we believe that that could make a short-term difference, in terms of attracting more investment into the area, we think that it could lead to other problems down the line, because it does not solve the issues of unpredictability, and that is specifically attached to the resistance. How resistance develops is largely unpredictable at this point, so when you are making a product you need to decide whether to invest the large amounts needed, particularly in the phase 3 studies, but you do not know whether the product should be used a lot or a little. Simply having a potentially higher price for it does not help to predict the revenue that encourages you to make that investment.

The final thing that a higher price could lead to is that it will increase the incentive for companies and other players to use more of a product, which should be used rather less from a public health point of view. For all those reasons, we do not think that price is the only answer. It may play a role, but the key thing for us is the concept of delinking that came up earlier, whereby the payments made to a company that successfully develops a new product are separate or delinked from the amount of the product that gets used.

Q220 Stephen Mosley: On that specific point, the ABPI has talked about decoupling a fair amount.

Dr Leong: Absolutely.

Q221 Stephen Mosley: You say that is essential when looking at the evidence. How can that be achieved?

Dr Leong: May I add two things? First, it is essential to decouple the volume of sales from reimbursement. Secondly, on pricing, antibiotics are still undervalued, but the price alone will not solve the problem, simply because one does not know the period within which one can sell enough to recover the cost.

The question is how to take a new model that takes account of price, value and reimbursement as well as promoting good stewardship, because we would not want to see new antibiotics overprescribed; we want to conserve existing ones as well as reserve new ones. Therefore, a potential mechanism might be an advance market commitment, which we have seen used in other arenas, where Governments will commit to paying a certain amount on the development of a successful and effective antibiotic against drug-resistant infection, and it has to have gone through the regulatory process and be proven to be effective and safe.

Q222 Stephen Mosley: Is that the licence fee agreement?

Dr Leong: It could be a combination of a licence fee plus an element of pricing. It is quite a complex area, but we are happy to talk in a little more detail or supply a more detailed briefing around that. That would be operating as a pull mechanism, where you reward success and effectiveness. Push mechanisms tend not to take success into account. Pull mechanisms, such as licence fee arrangements or the insurance-type model, take success into account and reimburse for an effective new antibiotic.

Q223 Stephen Mosley: What do the other panel members think of the licence fee agreement, in terms of reinsurance models? Would they work?

Dr Williams: I agree with both of the previous two speakers. You cannot link this to volume and the number of sales. The predictability of the market life is absolutely impossible at this time.

Dr Leong: This over-rides local variation, because it can happen on a national or international scale. One cannot predict when or where an outbreak may occur, so there may be a particular burden in a certain region or country. Hence, an agreed reimbursement or licence fee model would get around those considerations.

Michael McIntyre: When we come to using herbal medicines as a resource, we need to bear in mind that they are almost entirely orphan medicines, so there is no way to the market for many of them through the normal channels. There really has to be thinking outside the box if they are going to become part of the treatment. The reason for that is that you cannot patent natural products. If you put a lot of research into something, you cannot then own the result. That has been a huge problem with the development of these kinds of product on the market.

Q224 Chair: You are not arguing in favour of patenting.

Michael McIntyre: I am arguing in favour of some new way of thinking about licensing or dealing with orphan products, such as herbal medicines, because the current system does not suit the development of that. That is what I am saying.

Q225 Chair: In terms of the ABPI position, post the successful trial and licensing of a product, the model that you would be looking for is one where a fee is paid by the health provider—the NHS, in the UK—for having access to that medicine, but with a two-way arrangement between yourselves as the research experts and the clinicians about how it is administered.

Dr Leong: Yes.

Q226 Chair: That fee has nothing to do with volume.

Dr Leong: It is essential when there is a new antibiotic that there is collaboration between the drug developer who knows about the medicine and infection specialists, so that there is no over-prescribing.

James Anderson: May I make a final point on this? We fully support this approach, but it would be much more effective if it could be done on a global basis, or at least on a coalition of the willing. This is a place where the UK trying to create that new market on its own is probably not going to be sufficient. Some other countries have a more progressive approach, and recognise this as a big issue, and we believe that there could be an opportunity for the UK to take the lead, in terms of proposing a model, and then working bilaterally with eight or 10 other Governments around the world to agree on how to make it work. It does not need to be everybody in the first case.

Q227 Mr Heath: I was going to ask this question later, but I am not clear who the influences are that we can lever in on a worldwide basis, because it seems to me that we, on these small islands, despite the fact that we have a centre of excellence, cannot influence the global response.

James Anderson: Dame Sally Davies has done a fantastic job of starting to bring together some of those players. In the forum last year, which I mentioned earlier, the CMOs of Australia and Sweden, and representatives from Norway and the United States, made a start. We see strong levels of interest from the northern European countries.

You probably only need—the G8 would be a great forum for this type of discussion, because if you have that set of countries committing to even the set of principles that we laid out just now, then you could have more of a bottom-up approach, such as we are pursuing under the IMI. Part of the IMI is dedicated to bringing together health economists, academic experts, epidemiologists and industry folk to figure out what the model should look like, and how it can work. That work is just starting. The UK has strong representation; the LSE is involved, and the London School of Tropical Medicine, Imperial and Chatham House. A lot of the pieces are there already. The bilateral outreach is starting, and that is probably the way to go. The WHO would be the other possible forum, but I do not see that it would be able to operationalise it in the near term.

Q228 Mr Heath: I am encouraged by the fact that the London School for Tropical Medicine is involved, because it occurred to me that there was a danger of a first-world bias in thinking about how we deal with MRSA and not thinking about how we deal with what we consider to be exotics. Are you convinced that the balance is right?

James Anderson: Absolutely, and a delinked model goes some way towards helping ensure global access. That was one of the three principles that I said the new model needs to have. That is because the companies get their returns from the coalition of the willing Governments, which are western Governments, but after that the way that products are distributed globally is not dependent on price. An IP becomes much less relevant; you have a mechanism that manages that. However, it needs to manage it really carefully because what you do not want is the product being used poorly in less developed countries, with resistance building up there that then gets transferred everywhere else

around the world. It is not easy, but this sort of model takes a big step towards delivering a global solution.

Q229 Mr Heath: Thank you. You don't need to come back to me on that.

Dr Leong: May I suggest a specific mechanism? Europe is a good place to start. There is a legislative mechanism in place that can be used. That is the joint medical procurement tool for cross-border health threats, and I believe that antimicrobial resistance is in there. The European Commission would be a good place to start for the UK's CMO to talk with.

Q230 David Tredinnick: I would like to ask about herbal medicine. I referred in the last session, if you were here, to the fact that information from the House of Commons Library showed that almost half the drugs approved between 1994 and 2008 were based on natural products. With that in mind, what is the potential of herbal medicines to combat antimicrobial resistance?

Michael McIntyre: We have provided a paper to the Committee that shows the research on this. It shows that there are various ways in which plant medicines, in combination with antibiotics, can make antibiotics that have lost their efficacy more active once again. That is through well-known biochemical pathways—for example, by disrupting the quorum-sensing process of bacteria and also by disabling the efflux pump by which the bacteria pump out the antibiotic, and so on and so forth. These modes of action are well known. What we need is more research into this so that we can develop it.

You asked me about resources, and here is another real resource. One of the reasons that we have antibiotic resistance is that antibiotics have been overused. We all know of people who have taken antibiotics when they should not have. I know that doctors are now doing far less of that, but the genie is out of the bottle and, as somebody said, this is going to continue. One real resource that herbal medicines offer to GPs and other hospital doctors is to use them when somebody has a mild infection or is in the early stages of infection.

I had personal experience of this two years ago; I had a serious accident to my foot and I got a very bad ulcer. I was told by the physician at the hospital that I was attending that no antibiotic was going to work, and my foot got better as a result of using the herbal medicines in my clinic—rather interestingly, myrrh and frankincense and calendula, a herb that grows in most people's gardens, played a major role. That might sound rather fanciful, but where is the research into these? These things have been used for centuries, effectively, and we need to go back and look, and reintroduce them into general practice. It is not a laughable idea that honeysuckle flowers can cure sore throats; there is research showing that it can. Farmers should be growing these things, and we should be using them when we do not have a need for antibiotics. I am a great fan of antibiotics, by the way.

James Anderson: There are two different things that we should not confuse. One is that the original source of many of today's antibiotics is naturally occurring products that have gone through the standard research and development process to end up in medicines. That continues to be an important source of investigation for us and other companies.

The other piece is an area that I am much less familiar with and which Dr McIntyre has been talking about. You mentioned already that the lack of ability to get intellectual property protection on some of these approaches will probably limit the research investment that private companies are prepared to make, but from what you have said it seems that it is one of these potential areas of untapped opportunity, a bit like some of the others that I mentioned earlier in terms of bacteriophages. That fascinating scientific approach has not had the level of investment and investigation that it warrants, partially because of the challenges around securing the intellectual property behind it.

Dr Williams: I agree with Dr McIntyre that there are some extremely useful medicines in the herbal environment, but we must not forget that anything that we give patients has to be safe. That is why we have the regulatory approval of the clinical trials that we have. It is well known that there are many toxic things in the herbal environment. I would not want to chomp my way through belladonna, for example. It is essential to make sure that they are safe but, as James said, we already look at natural products. We treat them as a rich resource, and we would love to exploit them.

The slight issue in antibiotic research is that, if those antibiotics are out there, and we know that a number of the antibiotics that we use—indeed, many of them—already come from natural sources, then the environment has already found a way to resist them. A lot of the resistance genes that we see now are natural; they have been around for millennia. The gut feeling is that, if we come from a synthetic and completely non-natural start point, we might just have some medicines that can resist the resistance mechanisms, certainly in combinations.

Q231 David Tredinnick: Do you want to come back on that, Mr McIntyre?

Michael McIntyre: Yes, please. In the earlier session, Professor Farrar made a good point about combination therapies and how important they are. One of the innate strengths of plant medicines is that that combination is already implicit in them—they contain a multitude of plant chemicals. The history of traditional use is often combining several plants together. This is combination therapy.

I note that it was said that combination therapy experimentation dated back to 60 years when looking at TB, but it is thousands of years old when using plant medicines. There is a huge amount of experience of using plant medicines. I completely understand and take on board that plants can kill as well as heal, and there are some very toxic plants out there, even in our gardens in the spring, such as aconite. Nobody would think of that as something sensible to take on a regular basis, or even on an occasional basis. We need to combine the traditional skills with science, and pharmacognosists, if they exist, working with herbalists could do a good job working with conventional medics, and I would like to see that happen.

Q232 David Tredinnick: If we are going to go down this route, and it is the case that, as I think you said earlier, herbal medicine can assist in reducing the use of antibiotics, and that it can, in certain circumstances, reactivate antibiotics—

Michael McIntyre: There is research saying that, yes.

Q233 David Tredinnick: Then how do we go forward? How is this to be explored and exploited? What is necessary?

Michael McIntyre: One thing that we need to do is to recognise herbal practitioners who are properly trained, and to have them regulated. That is an opportunity that faces the UK at the moment. The Department of Health has spent 15 years thinking about it, and we are now asking it to make up its mind and get on with it. We could then see the people who are properly trained. As I said before, that training is at university level.

Q234 David Tredinnick: As you know, there is a herbal working group, of which I am vice-chair, and we are hoping to get that sorted out.

Professor Farrar and Professor Sir John Savill both touched on homeopathic medicine. It is my understanding that there is a relationship between homeopathic medicine and herbal medicine. We have had a submission from the Homeopathic Research Institute. Do you have a view on homeopathic medicine? I address this to Michael McIntyre.

Michael McIntyre: First, herbal medicine and homeopathy are really different, and I am not a homeopath, so I speak as an interested observer and not an expert in any way. I have seen the submission and, as I have argued from the start, we should keep an open mind and look at everything a priori and not with prejudice.

Q235 Chair: Let us be clear. On the basis of what you said earlier, that when you take certain herbs from the gardens not to do it in large volumes because that would kill you, the converse must equally be the case. The concept in some part of homeopathy that infinite dilution will do you good does not make any logical sense, does it?

Michael McIntyre: There isn't any science behind it, and I repeat that I am not a homeopath. It is rather like asking a doctor about vets. I am not really able to talk at length about homeopathy.

Q236 David Tredinnick: I just touched on it—it is a controversial subject.

Michael McIntyre: I do think that, if there is research showing that something works, we should have a look at it. That is all.

Dr Williams: If the emperor is naked, I see no point in doing it. One of the things that we have seen—I have seen it before in clinical trials—is the enormous placebo effect. In immune therapies that I have worked on, we have seen placebo effects of up to 40%. That means that the patients are getting nothing, but 40% are getting better. To see proper experimental scientific evidence on homeopathy dissociated from the placebo effect, you would convince me, and the emperor might have some clothes on.

Q237 David Tredinnick: In an earlier session, I raised the studies that have been conducted on animals, in particular to do with mastitis.

Dr Williams: They are sentient beings as well. Again, there could be an element of placebo effect, so it has to be properly controlled.

David Tredinnick: Well, the jury is out. Thank you very much.

Q238 Graham Stringer: Dr Leong, in answer to an earlier question you mentioned that there were processes to be learned on how the orphan regulations of 1999 had been applied to rare diseases. Would you expand on that, for the Committee?

Dr Leong: There was a set of US regulations and European regulations that were designed to stimulate the number of new drugs that would be developed for orphan diseases. There were two aspects to this. One was an extension of patent life, market or data exclusivity, for new medicines for orphan diseases. There is a specific definition what is an orphan disease, in terms of the frequency of occurrence per 100,000 of the population. That spoke to the extension of patent life. There was an element of pricing, which is a local issue, and that was not legislated for. Those two factors resulted in a healthier and growing pipeline of candidates that went through the EMA for regulatory approval.

Antibiotics are quite a different matter. Again, we come back to the decoupling of usage and volume to reimbursements and the recovery of investment. For orphan medicines, although it is a smaller population, so this is a similar concept to our position on stratified medicines, what happens is that, when you identify the population that is likely to respond, you would like to have a medicine to administer to that population or to the patients to make them better. For antibiotics, it is somewhat different. It is unique in the sense of needing to decouple the volume of use and prescribing to reimbursement. The patent extension alone will not help, in the same way that we talked about the GAIN Act, earlier. Pricing is important, but that alone would not address the economic incentive issue.

Q239 Graham Stringer: In the same answer, you also talked about increasing the regulatory hurdles and making it more difficult. Would you tell us which regulatory hurdles have been introduced and whether you would want them to be removed?

Dr Leong: There are ways in which clinical development can be made more efficient, while safeguarding safety. That aspect would be restricting use, and being specific about what a new antibiotic would be developed for, in terms of use against multi-drug resistance bacteria, and then, following a phase 3 study, to enable it to be used on that restricted population so that enough data are collected on its efficacy—in other words, whether it will be effective. Further data and another phase 3 study are to be collected once it is in use by that patient population. The regulators—the EMA and the FDA—have looked at that and they have safety in mind and believe that that can be done.

Graham Stringer: I missed the last bit.

Dr Leong: That can be done. These proposals are from the EMA and the FDA. The EMA proposals remain to be ratified by the European Commission in this framework by the summer of this year. The MHRA plays a lead role in that.

James Anderson: On your first point, the orphan drug was a package of measures that was designed to address a specific market failure in the area of rare diseases. It has had a successful result, in the sense of attracting massive investment, with many new products for rare treatments. Antibiotics is a market failure, but it has a different set of specific causes and issues within that. If a package can be put together to address those, companies will respond in a similar way.

On the side of the regulatory piece, we also believe that it will make a fundamental difference to the ability and the speed with which new products come to the market. There is a delicate balance to be found, and the regulators are trying to make sure that they get the balance right. If you get it wrong, which nobody wants, the risk is that you have products being launched too early, when the safety profile is not well understood. In the US, in particular, it has not been finalised either; the FDA has made proposals and discussions are ongoing. We believe that it is the right way to go, but we recognise how difficult it is to get it right.

Q240 Graham Stringer: If I may summarise, you are saying that there is an analogy with the orphan drugs regulations but that you need different things in the package than there are for the orphan drugs. I suppose that you are also saying that you are not sure yet what that package should be.

James Anderson: We have a pretty good idea of what the sorts of things are, and some of them we have touched on today in terms of the idea of a fixed payment that is agreed up front, and so on. What we are not so sure about, and what we want to work together with Governments on this, not only here but elsewhere is: who does it and how decisions are made? When are the decisions made, and where does the funding flow from? How is the use of those eventually resulting products controlled? Particularly when we are thinking about global development programmes but also global needs, people are dying from resistant infections all around the world, so the model needs to deliver to everybody. That is where there are pieces that industry can bring, to help solve that problem, but it really needs a joined-up approach.

Chair: Dr Leong and gentlemen, thank you very much for your attendance this morning.