HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Antimicrobial resistance follow-up, HC 842

Wednesday 30 November 2016

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Watch the meeting

Members present: Stephen Metcalfe (Chair); Victoria Borwick; Jim Dowd; Chris Green; Carol Monaghan; Graham Stringer; Derek Thomas.

Questions 1 - 70

Witnesses

I: Lord O'Neill of Gatley; Helen Shirley-Quirk, Director, Emergency Preparedness and Health Protection Policy, Department of Health; Professor Paul Cosford, Director, Health Protection and Medical Director, Public Health England; Simon Hall, Veterinary Director, Animal and Plant Health Agency.

Examination of witnesses

Witnesses: Lord O'Neill of Gatley, Helen Shirley-Quirk, Professor Paul Cosford and Simon Hall.

Q1 **Chair:** Good morning, everyone. Welcome and thank you for joining us. For the record, could you state who you are and who you represent?

Simon Hall: I am Simon Hall, veterinary director for the Animal and Plant Health Agency, which is part of DEFRA. I am also deputy chief veterinary officer.

Lord O'Neill: I am Jim O'Neill—Lord O'Neill of Gatley. I represent me, I guess, and in this regard, the review into antimicrobial resistance, which I chair.

Helen Shirley-Quirk: I am Helen Shirley-Quirk. I am the director of emergency preparedness and health protection policy in the Department of Health.

Professor Cosford: I am Paul Cosford. I am the medical director for Public Health England.

Q2 **Chair:** Thank you very much for joining us and welcome. Very dramatically, Dame Sally told this Committee—or the previous Committee—that she was more concerned about dying from a routine operation in 20 years' time than she was about climate change. Following that, antimicrobial resistance got on to the national risk register and is deemed to be a serious long-term issue. How significant a threat is AMR?

Helen Shirley-Quirk: It is still a very significant threat, and it is one that we take very seriously indeed. As Lord O'Neill's review set out, AMR already causes up to 50,000 deaths a year in Europe and the US, and more than 700,000 globally. Resistance has a major impact on healthcare provision—lengthening prolonged illness, disability and, of course, death. As Sally said, if left unchecked, it could potentially put paid to medicine as we know it for surgery, cancer and infections. It is not just a healthcare issue; it is also an economic issue. That is why Lord O'Neill's report was so important. It highlighted that it has been estimated it could cost $100 trillion—US dollars—in lost production by 2050. These are serious numbers, serious concerns, and ones that the Government take seriously.

Q3 **Chair:** Can you say that number again for me?

Helen Shirley-Quirk: It is $100 trillion. Is that correct?

Lord O'Neill: Yes. It is more important for the world than the issues that most people in this building spend their time talking about these days, that's for sure. It is more important than whether we are in or out of the EU.

Graham Stringer: That is 14 zeros—100 trillion.

Lord O'Neill: We specifically estimated that if we do not do something about it by 2050—this is probably equally, if not more important, to focus on—10 million people a year could be dying around the world, more than those who are dying from cancer today around the world, with $100 trillion of potential output lost, which is bigger than the current size of the world economy.

Q4 **Chair:** You have put that into fairly stark terms for us. Are we talking about a sudden catastrophic event, or is it going to be potentially a gradually unfolding, and building, resistance problem?

Helen Shirley-Quirk: It could be both. At the moment, it is a gradually unfolding problem. To talk about the UK, levels of resistance to antibiotics are broadly constant. In Gram-negative infections, the ones that we worry about most, both the infections and the rate of resistance to the most commonly used antibiotics are rising. Obviously, resistance continues to evolve, and unless we tackle the problem, reduce infections, conserve the antibiotics we have and develop new ones, there will come a day when the existing antibiotics are no longer effective. That could happen quite quickly in terms of the way infection spreads. Paul may wish to say something from a surveillance point of view.

Professor Cosford: First, it is very important that we put this in the context of reducing the burden of infectious disease as a whole. We know that if we reduce the number of infections in the community, we reduce the harm from infection and we reduce the numbers of people with resistant infections, and we reduce the need to prescribe antibiotics, which in itself reduces the drive to develop new resistance. It is really important that we have that as the broadest context. On the bit about using antibiotics, we have good evidence that, if you or I have a course of antibiotics now, within three months we have three times the risk of getting a resistant infection of some sort, because we have had those antibiotics affecting all the organisms that are in our bodies. If you are a child, you are 12 times more likely to get a resistant infection in the three months after a course of antibiotics. It is really important that the course is only used when it is necessary. That increase occurs for 12 months afterwards.

The other point is that when we focus on specific infections that are causing a problem, we can be very successful. We saw it in MRSA. We had 7,000 cases of MRSA bloodstream infection at the peak in 2003. By consistent focus on the issue—making sure all the evidence was applied to reduce it—that is down to about 800 at the moment, but while we have done that, we have seen the problem of Gram-negative infections increase. That is the current biggest problem in the UK that we want to attend to.

Q5 **Chair:** You talked about MRSA. Are there other particular diseases that would pose a serious threat in the UK if they were to emerge in the same way as MRSA did in 2003, and would that potentially lead to greater use

of antibiotics, which would potentially exacerbate the problem as it stands at the moment?

Professor Cosford: One of the things we are most concerned about at the moment is the rise in Gram-negative infections. That is why we are so pleased that there is a national ambition around reducing Gram-negative bloodstream infections. They have risen over recent years, and, as they have risen, we have seen an increase in resistance. At the moment we have about 100,000, in ballpark terms, bloodstream infections every year. Roughly two thirds of those are Gram-negative infections and roughly 40,000—just under that figure—are due to a particular organism called E. coli. When you trace the source of that infection, the biggest source is urinary tract infections.

If we are trying to do something about the resistance, because that rise has been matched by the rise in resistance, attending to urinary infections and preventing them at the outset is one of the most important things that we need to do. I can give you the figures, but roughly about 11.5% are resistant to one of the key antibiotics, piperacillin and tazobactam, and as we have seen the increase we have seen that rise in infections. Our ambition is reducing Gram-negatives altogether, because by reducing them altogether and prescribing appropriately, we will see a reduction in the problem of resistant Gram-negatives.

Q6 **Chair:** The Government recently published the latest progress report into their strategy. Would anyone care to comment on how much progress the Government are making and how that is being measured, what metrics are being used?

Helen Shirley-Quirk: I will kick off and I am sure colleagues will wish to contribute. That was our second progress report. The strategy was launched at the end of 2013. I will not say we are complacent, as I would never want you to think we are complacent, but we are pleased with the progress that we are making. Over the last two years we have put the building blocks very much in place. You have already alluded to the fact that it is on the strategic risk register, which puts it squarely on the agenda of all Government Departments. We have a very comprehensive cross-sector approach, working very closely with colleagues from DEFRA, from the Foreign Office and from all Departments. We have unprecedented levels of research under way in this country, and we have expanded and made more accessible our surveillance data. Those are really important building blocks.

Alongside that, we have a comprehensive suite of professional resources in place for healthcare professionals—tools and guidance from NICE, from PHE and indeed from the professional bodies. We have refreshed our approach to training for healthcare professionals. We have incentives in place for clinicians to reduce inappropriate prescribing and we have action under way on behavioural change measures and public awareness.

You asked how we measure it. In the short term, we will keep a close eye on progress on reducing inappropriate prescribing, and we are starting to see progress on that. In data published just 10 days ago, we saw that prescribing had fallen by 4.3% across all parts of the health sector. That is the first time we have seen a fall in all parts of the health sector. Equally—my colleague from DEFRA may wish to speak—data also published 10 days ago show that the use of antibiotics in food-producing animals fell by 10% over the previous year from—I will not give you the details, but it fell by 10%. That is our short-term indicator. Clearly, we monitor trends in resistance very closely as well. That is why we have some cautious optimism.

Q7 **Chair:** As far as you are concerned, it is all going in exactly the right direction and we are winning the battle.

Helen Shirley-Quirk: There is always more that we can do. I said we have the building blocks in place, but that is only the start of the journey.

Chair: Fair enough. I am putting words in your mouth.

Helen Shirley-Quirk: It is only the start of the journey and we know there are plenty more things we want to do. We are commissioning an evaluation of the strategy so that we can review and really understand what progress we are making over its lifespan, to be able to prepare for the next period.

Q8 **Chair:** Does anyone disagree that the Government are doing enough?

Simon Hall: I will not disagree, but I was invited to agree. As my colleague said, we continue to monitor the overall consumption of antibiotics by animals, and from 2014 to 2015 it went down 10% and there is detail below that. For example, there are some critically important antibiotics that we monitor specifically, and they went down too. We very much encourage the livestock industries and their vets to take their own responsibility and they are stepping up. The poultry meat industry, for example, has its own scheme in place. That has seen a significant drop in overall antibiotic use, and some farms are now committed to using none at all. The pig sector has recently introduced its own scheme for monitoring at farm level the consumption and use of antibiotics, reporting to an electronic system from which we can see the outputs. The cattle sector is also important. They are at a slightly earlier stage, but they have made a commitment. There are plans in place that should come into action in 2017. I think the message has got through, and it is very pleasing that these industries are taking responsibility for themselves and delivering what we want.

Lord O'Neill: I have two quick things. I am sure we might come to this elsewhere, but on the Government's response to our recommendations in the review, as yet the UK has not announced that it is going to do all the things we suggested, including some of the most punchy ones, but generally speaking we, as a review, were positively surprised by what the Government have said so far. However, linking it to something earlier—it

is important that you understand, in my view—the second thing is that, because of the nature of this problem, it does not distinguish colour, borders, religion or anything. We can do whatever we want, but unless other places are doing things as well, it—

Chair: We are going to come to that. I wanted to keep going on whether or not the Government are doing all they can. Graham Stringer wants to come back on the point Simon Hall made and then I will come to you, Professor Cosford.

Q9 **Graham Stringer:** A 10% reduction might sound impressive, but we had our inquiry when tetracyclines and penicillin were banned from use on farms for growth, and the increase in the use for veterinary purposes of those two antibiotics went up tenfold—not 10%, but tenfold. You are starting from a huge base, aren't you? A 10% reduction is not very impressive when the use of those antibiotics went up tenfold about five years ago.

Simon Hall: By global standards, we are pretty good.

Q10 **Graham Stringer:** We are between three and five times the level of the Nordic countries.

Simon Hall: We are, but in terms of overall consumption, corrected for livestock population, we are the best in the G7. Yes, the Nordic countries are better, but other countries in Europe use a lot more than we do. I do not think it is true that we are in a particularly bad place to start with. We have made a commitment to improve and we are improving.

Q11 **Graham Stringer:** Don't you think we should be aiming at least at the Nordic standards? If they can do it, why can't we get to their level or better, rather than looking at averages?

Simon Hall: We have a big, important livestock industry, much more so than, for example, Sweden; Denmark is different. Lord O'Neill recommended 50 milligrams per kilogram of a certain measure as achievable and worth while, and that is what we are aiming for, so we are in line with that recommendation.

Lord O'Neill: We indeed suggested as one of our strongest ideas in agriculture the Danish success. Denmark, in our view, is the most successful place in the world on agricultural reduction. Because of that, we recommended a target of 50 milligrams per kilogram phased in all over the world, starting in 2018. The UK has announced it is going to do that from now. That is important, because the people who briefed me did not seem to be aware of it. It is one thing that the UK is doing more aggressively than we suggested. No other country I am aware of has yet decided to do that, other than those that have achieved it.

Graham Stringer: I can either do a follow-up now or later.

Q12 **Chair:** We can come to it later. I want to bring in Professor Cosford.

Professor Cosford: I want to make a couple of comments on progress so far. We are very pleased with much of the progress that we have managed to make across the healthcare system, with leadership from the Government and so on. The enemy, of course, is always complacency and it is sometimes a bit like squeezing a balloon. The very young and the very elderly, or people in the last year or so of life, are particularly vulnerable to infection. We tackled C. Diff, we tackled MRSA and we have now seen the increase in Gram-negatives, so we have to attend to that. We will tackle it, I am sure, but then there will be another problem that we will need to attend to. That is why we are putting a particularly strong focus on infection prevention and control and basic hygiene across the whole system and in the community.

On the prescribing side, we are delighted that we have seen a significant reduction in prescribing of antibiotics. In our primary care system last year, alongside our quality premium, there is some suggestion that there are three or four years of reductions if you take account of age and sex, but there is huge variability that we need to attend to. In the hospital sector we have seen reductions, and we are pleased with them, but there are increases in the use of some of the antibiotics of last resort. That is where we need to focus, because if we drive resistance further to antibiotics of last resort, we get into much more significant problems in the future. I want to give you a picture that, yes, we are absolutely delighted with the progress that we have made, but there is a huge amount for us still to do and some real concerns where we must keep an absolutely close eye on what is happening in the future.

Q13 **Chair:** How do we compare with European countries? We are going to deal with the international aspect later, but the European Commission has announced a five-year AMR action plan. How does the progress that we are making compare with what is happening in the rest of Europe?

Professor Cosford: I would encapsulate it as our having a much less significant problem than some and much better patterns of antimicrobial prescribing than some. You can particularly see problems of carbapenem resistance in southern European countries and different ways that antimicrobials are used in some of those countries. Again, I hesitate to compare ourselves with Scandinavian countries all the time, but they have seen much more significant reductions in antibiotic use for humans than we have yet seen. We are pleased that we have made the progress we have made, but there are some good examples where we should be able to do more.

Q14 **Victoria Borwick:** Can I follow up on that point before we move to the other questions I have? If somebody goes to the GP and the GP thinks, on reflection, it is the right thing to do to help that person get over an infection now, although I think most GPs are very aware in this country of the overall thrust, surely they have to try to help the person in front of them. What advice would you give to people who are receiving antibiotics today?

Professor Cosford: I was discussing this very issue with GPs and microbiologists in hospitals in the south-west of England yesterday. It is clear that we have to understand why GPs prescribe. They prescribe largely for three reasons: first, to reduce symptoms that are of concern; secondly, because they are worried about things developing if they do not prescribe, and serious complications; and, thirdly, because they think their patients want it. We tackle all three of those things to make sure that GPs have the tools to be able to have the best possible discussion with their patients. One way we are doing that is a programme called TARGET, which many GPs are now using, where, when they see a patient, the TARGET system provides them with the tools to have a discussion with the patient about what the likely benefit of antibiotics may be and what to look out for if they become more significantly ill. It also gives guidance on the likelihood that the infection may be due to bacteria and, therefore, may be susceptible to antibiotics, and helps them with some tools.

One particular thing many GPs are now doing is giving a prescription that is postdated for 24, 48 hours or a little longer. That goes along with a detailed explanation that if you have bronchitis, for instance, it is likely to last for 22 days anyway, on average—20 to 22 days—and antibiotics, on average, only bring that down by 24 hours. If you have that conversation with the patient and give them information, instead of what currently happens, where about 70% of people with bronchitis get a prescription, it comes down to just over 30%, and it does not seem to be associated with increased significant harm.

Q15 **Victoria Borwick:** I am mindful that we have lots of other questions, but the instance you gave earlier was urinary tract infections, which if you can get to them early reduces a great deal of misery for people.

Professor Cosford: Absolutely, very much so. Again, the tools that we have provided to GPs help them to have a discussion with patients about when antibiotics for urinary tract infections are particularly needed.

I can give you another example from care homes, if it is helpful; I do not want to take too much time. A study has just been done in north Somerset in care homes, for instance, where the usual practice is to put a dipstick in people's urine and, if it is positive, you do a test and then you give an antibiotic. The evidence suggests that, if you use an algorithm of appropriate questions and appropriate clinical signs that the patient may have and instead of routinely using the dipstick you go through that and then refer people as appropriate according to that, you reduce antibiotic use by 50%. In fact, it was greater than 50%, in an early study; they are early indications. Not only that; you increase the number of people who get the appropriate management of their urinary tract symptoms. You get increased attention to things like hydration, which is terribly important, and other things, and you reduce the number of people who get complications of urinary tract infections. By stimulating a better clinical engagement between the clinician and the patient, in that case care

home staff, you get better outcomes and less prescribing. Giving people the evidence that that works is really important to help them not just to reach for the prescription, but to have that discussion with their patients.

Q16 **Victoria Borwick:** As long as they are given relief, I hope. If people are in a care home, it is presumably because they need care and they are not necessarily going to affect the next trillion that we are going to talk about, so I want to fight for those people to be looked after properly. If I may, because of time, I will turn to the questions I wanted to ask Lord O'Neill. You published the final report of your review in May. What do you see as the main concerns for AMR internationally, to take you back to the point you started to touch on in the introduction?

Lord O'Neill: How long have we got? Linked to the previous topic, at the absolute core we need to stop treating these things like sweets. We all need to be re-educated. I could not even pronounce antimicrobial resistance two and a half years ago. After I accepted this role I was speaking, in my previous guise, to 500 highly sophisticated international business people. I said, "I am only going to talk to you if I can mention this topic," and I asked for a show of hands as to how many knew what AMR was, and probably less than 10% of that audience knew. If you go around vast swathes of the emerging world, people have no idea that it is a problem.

There is an enormous number of challenges, but the core is that we all need to be re-educated that these things are not a magical solution for as many things as everybody thinks. They are really useful in the right case, including in care homes, but they have to be treated in the right way in the right circumstances. It is extremely problematical in agriculture. In many parts of the world, such as the US, it is worse in agriculture than in humans. In China and India—the two most important countries in the world for the next 30 years, in my opinion—it is hard to know which is worse. It is bad in both.

Q17 **Victoria Borwick:** You touched on it briefly earlier, but were you satisfied with the Government's response to your report? You said there are some things you were pleased with. Do you want to talk about what you feel they had made progress with and where you think there is still progress to be made, and then perhaps internationally?

Lord O'Neill: There are three quick things. First, it is important for this Committee to know that the leadership role the UK has taken, not least through the remarkable efforts of Sally Davies, and with that, tangentially, the setting up of our review, has been enormously respected all over the world, with some surprise actually, especially in a sort of post-Brexit world, in my judgment. It is a brilliant example of soft power at its greatest. The UK played a huge role in the UN high-level agreements on antimicrobial resistance in September. It is only the fourth time there has ever been anything to do with health at the UN. That is the first point.

On the specifics of our recommendations, as I said, we were generally positively surprised by the scale and seriousness of the British Government's response. I am slightly disappointed that they did not try to give it more publicity than they did, linked to my first point, because a lot of people in the medical world probably still do not actually know what the Government's response has been. They have not responded to the most aggressive things we said, again linked to not treating them like sweets, going to your previous question. Probably our single most aggressive recommendation for the developed world is that, by 2020, antibiotics should not be prescribed without state-of-the-art diagnostics, otherwise you will not be able to achieve a lot of the other things that need to be done. Of course, it is very difficult for a Government to say that we are going to do that now, because the affordable diagnostics are not ready, which we knew, but you need to kick-start in a bigger way the affordable diagnostics market to really make a difference.

The third generalised thing is that you need ongoing international co-operation. As good as the UN agreement was, I like to describe it as the end of the beginning. As we know with so many other things to do with the UN, or many entities, it is one thing to say, "This is what we have agreed", but then you have to get on and do it. An additional thing is that this is a big year for the German hosting of the G20, which is going to be brought forward because of the German election. The Germans have shown a lot of intent for taking this seriously, but given the fact that there was an important statement—I think it was paragraph 46 in the Chinese-hosted G20—it is important, particularly for new drugs, that the Germans deliver something of substance.

Q18 **Victoria Borwick:** With a view to your relationship with this Government, as opposed to having been commissioned by David Cameron, have you managed to make sure that your views are being carried forward?

Lord O'Neill: I am no longer a member of the Government, so I am not in a position to do that in the same way as I was before, but whenever the chance is there, I try. I think there is interest, if not perhaps with the same passion as under David Cameron, to maintain the momentum.

Q19 **Victoria Borwick:** But it is still on the agenda.

Lord O'Neill: I should hope so. It is certainly in the election manifesto, so it is in so far as the elected Government's job is to deliver what is in the manifesto. I will throw in one other thing that is important, however, and it is why I emphasise Germany. The world is not going to deal with it just by the UK telling everybody what to do. It is equally important that we somehow make space for other countries to share the leadership model, which the Scandinavians are very good at, in my view.

Q20 **Victoria Borwick:** You predicted my next question. The Government's response seems to focus very much on the G20 and the G7. Is that the right approach, or how would you make it more global?

Lord O'Neill: Because of the commitment through ODA, and the role of DFID, we could probably play a more active role. I know that, under the new leadership there, some discussion is taking place about the interplay with infectious diseases. Of the 10 million deaths that we suggested could happen, one third approximately would be TB, and there appear to be some interesting developments on drugs where, with a bit of momentum, there could be some breakthroughs, to break the very worrying rapid escalation of drug-resistant TB in many highly populated emerging countries.

Q21 **Victoria Borwick:** I thought we were doing quite well at getting rid of TB. Does anybody else want to comment on that as it has been raised?

Professor Cosford: In the UK, we are doing very well. We have a reduction of 35% or so in the number of new cases in the last four years, and that has not been associated with an increase in resistance. In fact, we have seen, as I mentioned before, that if you focus on a specific disease and put in place all the evidence-based actions everywhere all the time, you get a reduction in infections and a reduction in the rates of resistance as you do so, as a general rule. The picture on TB is slightly different globally. It remains one of the biggest infectious disease threats at a global level.

Q22 **Victoria Borwick:** I am sure we will come back to that some other time. Finally, how well do you think the AMR agenda has been taken forward on the international stage? Are there any risks of unhelpful efforts in the sense of duplication of effort? How do you see the international agenda? Your message was not only about the UK but about the international need. Do you feel there is duplication of effort in the UN and the WHO? Can you give us your view?

Lord O'Neill: For the purposes of the goal of our review, close to two years ago I was set a challenge of coming up with ideas that could contribute to a UN agreement. At the time, most people thought the idea of a UN agreement on AMR was close to impossible, but there was one. In that sense, it is a fantastic development. Linked to aspects of what I have said, and so many other things that I do not have time to say, it is only the beginning. There was no reference to agriculture at all in the UN agreement, which was a specific disappointment from our perspective, because it is such a huge problem. For example, in that regard, and something that we did not think we would see evidence of until future years, as I am sure people here are aware, a so-called last-in-line antibiotic known as colistin has been so overused in some places that there is evidence of humans being resistant to it in some cases. There are many things that need to be treated a lot more seriously in key parts of the world. To pretend that just by having a UN agreement we have cracked it is dangerous.

Q23 **Victoria Borwick:** Do you want to talk about the duplication of effort at all—the WHO?

Lord O'Neill: I am not so worried about duplication of effort. I am more concerned about how entities that have some bureaucratic aspects to them can genuinely, collectively focus and co-ordinate because of the connectivity. One of the fascinating aspects of studying this is how it involves everything. There is no one entity. You could not just give it to the WHO to solve. You need the OIE and you need the others. That is the reason why the specifics of the UN statement, particularly the part where they requested feedback in two years' time from each of the three key international agencies, was an important part of it.

Helen Shirley-Quirk: I have a couple of points. In terms of co-ordination at international level, picking up on the point Lord O'Neill has just made, the declaration called for the establishment of a co-ordinating mechanism to drive forward work on AMR across the UN agencies. WHO, OIE and FAO are core, but there are others as well. I understand that the plans for that are in development. We wait to see those, but they will play a critical role in ensuring that there is the right co-ordination and the right continuing momentum.

The second point is about what we do in the UK to try to help foster co-ordination. We work very closely with other countries who are similarly seized of the importance, particularly through something called the Global Health Security Agenda, which has an antimicrobial resistance working group of which we have been the leading chair for the last year—the chair has now been taken over by the Netherlands. That brings together some 20 countries across the globe to co-ordinate and align our work, and indeed, coming to my third point, to support other countries that are perhaps less far down the line.

On that last point, in the UK we have a £265 million programme called the Fleming Fund, which is specifically intended to support low and middle-income countries to develop and take forward laboratory capacity and surveillance for antimicrobial resistance. We are just setting up that fund now. We already have some pilot projects under way—over five years—but that is part of something that we can do as the UK to help countries that would otherwise be struggling to get to first base.

Q24 **Derek Thomas:** We talked briefly about the World Health Organisation. Their global action plan on AMR refers to the need for a "whole-of-society engagement including a One-health approach." How should the concept of that One Health approach be interpreted in practice in the UK? Are we engaged in that process? How do we understand that?

Helen Shirley-Quirk: Is that particularly just to Lord O'Neill?

Derek Thomas: Simon seems to want to answer.

Simon Hall: I might as well. Any of us could answer it. One Health is a concept that is now well embedded, and really took off with avian influenza, being both an animal and a public health threat. It is about human health, animal health and the environment all being considered as

a whole. In the UK, we work seamlessly together. AMR is just the latest thing. There are other infections, such as salmonella or BSE, where there is human-animal crossover, so there is a lot of joint working, from political senior official level meetings down to working level. My Animal and Plant Health Agency works very closely with Public Health England, with shared laboratories and that kind of thing. That is how it feels.

It is interesting that you said the global action plan was the WHO's global action plan. Actually, it is the WHO, the OIE, which is the World Organisation for Animal Health, and the FAO, so it is joined up at that level. We on the veterinary side play our part internationally as well. Where it is a One Health agenda, we are there with public health colleagues, but we have our own place to work as well, so at the OIE—the World Organisation for Animal Health—meeting in May this year, AMR was top of the agenda. All the countries there, which are most of the countries in the world, committed to action plans. Another body, which comes under FAO, is called the Codex Alimentarius, the global standards-setting body for food, including its production and international trade, and the UK, led by the Food Standards Agency, is this week hosting a meeting here in London and co-chairing it. They have a very long process, but they are getting the work plan for that scoped. That is important in respect of food-producing animals being part of the food chain, possibly then converting it into risk for people and attacking it at a global level.

Helen Shirley-Quirk: I absolutely echo—I am sure Paul would too—the way we work across human and animal health. As a tangible example, we published—I think it was last year—the first joint animal and human surveillance report called the "UK One Health Report" on AMR. If you keep publishing separately, it keeps the impression that we do not work together, so bringing together and publishing for the first time a One Health report, to my mind, is a very important visible sign of an ongoing and very close relationship.

Professor Cosford: I echo that many of our national specialist advisory systems and surveillance systems are joint between the animal health world and the human health world. We know that new emerging infections for humans are very often from an animal origin, so we need to be very close in that. For instance, in the south-west yesterday, as I mentioned, I was meeting both veterinary colleagues and human health colleagues about practical AMR actions that they may wish to take at a local level. There is more to do, but there is engagement at a local level as well.

Q25 **Derek Thomas:** In terms of public awareness, it seems quite clear that, while we need to work with GPs, doctors and others to reduce use or prescribing, we also need to get the public on side. You have talked about the sheer scale of the problem and how it is so much worse than everything we are talking about at the moment. What is the solution? Why are we not screaming through TV adverts to try to get awareness?

You referred to the fact that you spoke to a number of bright business people, and only a small group had any idea what you were talking about. What is the solution? Is there a strategy to communicate and raise awareness?

Helen Shirley-Quirk: Absolutely, there is. Perhaps Paul would like to talk about it.

Professor Cosford: There is no single solution but there are a number of different things that we are doing. At the point of the conversation between clinician and patient, there are a lot of tools that we are providing for them to be able to explain and use the evidence that we have to help patients understand when an antibiotic might be appropriate or not appropriate. That includes things like leaflets and posters that may be in waiting areas for general practices and so on.

At a national level, we are at the moment commissioning a pilot of a very rigorous public information campaign. It will be piloted in the north-west in the new year, and it will include television, radio, social media and other forms of advertising. We will be evaluating that very carefully. If the evaluation is successful, we will look to roll that out next year. We are very keen on that. I have seen some early mock-ups of what it looks like and it looks very exciting. I hope it works as well as we hope it will. There are other things such as European antibiotic awareness day, which we have just had in the last month or so, and we put a lot of publicity behind that. We work with media medics and others to make sure there is publicity going out, but as you say, it does not yet hit public awareness quite as much as it needs to.

A point I want to make relates to the question from your colleague about making sure that this is not just about reducing and not using antibiotics. It is about using antibiotics appropriately, and that includes knowing when you really need them and need them quickly—the work that we do around sepsis, for instance. We have a public information campaign coming up in December around sepsis to help parents of young children know when they really do need to seek help, as opposed to when they need not to worry because their child has a cough or a cold. We have that coming on as well.

Q26 **Derek Thomas:** Mr Hall, finally, can I come back to you? You mentioned earlier that there are some poultry farms that do not use any antibiotics at all. In terms of public awareness, do you see a time when we will be looking at packaging to see whether a farm or a producer has used antibiotics? Can you see that as part of public engagement?

Simon Hall: It is an area that needs great care, because there is potential for misleading and confusing people. The ideal is that all our livestock industries make prudent use of antibiotics, using them only when required, and certainly observing withdrawal periods and that sort of thing. To go further and create, say, a benchmark of zero antibiotic use would create risk for animal health and welfare. When individual

animals or groups of animals are suffering from a serious bacterial infection that needs to be treated, it should be treated, and the sort of labelling idea that you put forward could compromise that.

Q27 **Derek Thomas:** Does the antibacterial, whatever it does to the body—I am not a medical person—sit in the flesh indefinitely, or is there a time when it would work its way out?

Simon Hall: In the UK, and in every other European country, there is definitely the possibility that using any medicine on a food-producing animal—antibiotics and other things as well—will get into the meat, milk or eggs. Before the medicine can be approved for use in animals, it has to go through trials to make sure that we understand at what point the level decays below the acceptable minimum. Then part of the authorisation is that the meat, milk or whatever cannot be used for human consumption until past that point. That is well regulated and enforced, not least by testing food at the abattoir or point of production to make sure that it does not contain excess residue levels.

Q28 **Chair:** Can I pick up on the pilot TV and social media campaign? I think Professor Cosford mentioned it. Is that something that is unique to the UK or is it picking up on best practice somewhere else in the world?

Professor Cosford: I am not intimately aware of all the public information campaigns that go on elsewhere in the world. I would have to come back to you on whether it is something completely different. It feels pretty unique, but I would hesitate to say it is completely different from what anybody else has done.

Q29 **Chair:** Would anyone care to comment on how successful world antibiotic awareness week was, which finished a couple of weeks ago?

Professor Cosford: We can come back to you with some figures about take-up, but in general our evaluation of the world antibiotic awareness week in this country shows positive penetration through public consciousness of the issue.

Chair: But you have no idea—

Professor Cosford: I do not have specific evaluation figures with me.

Q30 **Chair:** I accept that. The issue is on everyone's agenda here in the UK, but we are only a relatively small percentage—1%—of the world's population. It is getting the message globally that is going to be the key to this, isn't it?

Lord O'Neill: One of our four overriding broad recommendations is the need for major global awareness.

Chair: Thank you.

Q31 **Chris Green:** Professor Cosford, where in the health system does the highest antibiotic use or prescribing occur?

Professor Cosford: Eighty per cent of all prescribing takes place in primary care. The other 20% is divided between hospital care out-patients and other parts of the health system. Inevitably, much of our focus on making sure that there is good consistent prescribing will be directed at primary care.

Q32 **Chris Green:** The Government response to the Science and Technology Committee report in 2014 said that prescribing rates for coughs and colds were higher in 2011 than in the 1990s. Have you seen an improvement since then?

Professor Cosford: In terms of all prescribing, there is something called a STAR-PU, which is basically a measure of the needs of the patients in a practice. The number of antibiotics dispensed per STAR-PU has been going down for the past four years, and has now just got below the 2011 levels. There is, as I was saying at the outset, some cause for optimism. As a result of our monitoring of the quality premium that we put in place in primary care last year—that the NHS put in place—we have a reduction of over 7% in the number of prescriptions dispensed, but it also brought the UK to the lowest use of broad-spectrum antibiotics. Those are particularly important in driving resistance. There is a lot of change that has happened, but there is still wide variability.

Q33 **Chris Green:** The quality premium is based on the 2013-14 figures.

Professor Cosford: The quality premium was for 2015-16, and we have a new one for 2016-17. It looked at the prescribing data during that financial year compared with the previous year.

Q34 **Chris Green:** But it is starting from a relatively high base.

Professor Cosford: The 7.3% reduction was from between 2014-15 and 2015-16. The answer to your question is yes, but underpinning that we have the reduction in prescribing per STAR-PU—forgive the acronym—which suggests that we have had some longer term reductions.

Q35 **Chris Green:** Is the public information side of things more for the professionals, or is it also for the users of the antibiotics? Pester power in primary care is an important or significant factor in why there are so many prescriptions. Is it reducing on both sides: the professionals and the users?

Professor Cosford: I have two points. The first is that there is some data that suggests that around 40% of patients attending their GPs with particular sorts of illness actually want an antibiotic. It is slightly below that. A slightly higher proportion say they want a diagnosis and they want their symptoms relieved; they want to understand what is happening and they want an explanation. Much of what we are trying to do is to shift people from wanting an antibiotic, and GPs from feeling that they are being pressured into prescribing an antibiotic, to a discussion about an explanation of symptoms and what they might mean and what

can be expected. That is the first point. It is not quite as high, and 39% is lower than I expected it to be when I looked at the data.

The second point is about our new system—TARGET. It has information for primary care practitioners, for GPs, to use but included in it is data on their prescribing practice compared with others. That is helpful for them. Included within it are patient leaflets, which they can print off during the consultation, specific to the patient to say, essentially, "With the symptoms you've got, this is what you can expect. You've got bronchitis, so this is what you can expect. This is when antibiotics are appropriate and if we are in the position of giving a delayed prescription, for instance, these are the circumstances in which it would be sensible for you to cash that prescription in and take those antibiotics." It includes that, it includes resources for the practice—posters on the walls and leaflets in the waiting area—as well as specific guidance, the NICE guidance and our guidance to GPs on what to prescribe in what circumstances, given our current state of surveillance and our current state of antimicrobial resistance. It does both those things.

Q36 **Chris Green:** In food production, where does antibiotic use occur most?

Simon Hall: The big users are the pig and poultry farmers. We need the schemes that I was describing earlier to come into full effect, so that we can understand usage at farm level. The data we now have, and have had for some time, are very much about sales. To the extent that many of these products are approved for use in more than one species, we would not want to claim false precision in knowing exactly where they are being used. When, for example, the e-medicines book for pigs starts generating a year's worth of data, we will understand that better, but it is pigs and poultry.

Q37 **Chris Green:** Is it solely used to cure disease?

Simon Hall: The straight answer is yes. The marketing authorisations for these products do not allow them for growth-promotion purposes, but they will often be used at the herd or flock level, which means that, for example, if you have a group of animals and an infection takes hold, you would not necessarily just treat the individual animals that are sick today. You would make a judgment that the infection was in fact going to go through the whole lot within the next week or so and you would treat the whole group, not necessarily solely individual sick animals, but groups of animals that are at some defined risk of becoming ill.

Lord O'Neill: The main reason we recommended for all countries around the world a milligrams per kilogram target is that it is more sophisticated than the rather proud thing that European countries say about how they ban the use of growth promotion, because it is very easy to get around that. If you have a tough overall limit, it makes it more difficult, as well as allowing people to have more choice as to how they are used. There are many countries where people are easily getting around the apparent

ban on growth promotion—there is, unfortunately, evidence of it in the UK.

Q38 **Chris Green:** Are there more diagnostic tests that can be applied so that we can be better informed?

Simon Hall: Yes. In terms of individual sick animals, including pets and farm animals, the story is similar to the human situation, so I will not repeat it, but what should and generally does happen is that you look at the herd health situation; the farmer will have a herd health plan and that will take into account the infections known to be prevalent on the farm. The farmer should know, through applying the appropriate tests—they need not be particularly new high-tech tests, but tests that have been available for many years—what infections are present, including viruses, which are not bacteria. Where there are vaccines available, they can apply vaccines to each new generation of animal that comes along, but where there are bacteria present, for example mastitis, which is infection of dairy cows, they should understand what the antibiotic sensitivity is of the bugs they have on the farm, and then they can pick the right treatments and use them in the right way.

Q39 **Chris Green:** Professor Cosford, are there new developments, new tests being developed at the moment, or can we rely on established tests?

Professor Cosford: Do you mean for human cases of infection?

Chris Green: Yes.

Professor Cosford: Yes, of course; there are always new tests being developed and considered. At the moment there is no consistent point-of-care test that is well evaluated that can be used in all circumstances. In the interaction between the doctor and the patient, we are very much focusing still on diagnostic tools that are about an algorithm of the pattern of symptoms, and the pattern of things you are faced with, to decide whether an antibiotic is appropriate or not, together with an explanation to the patient. If one becomes available, we want it to be introduced routinely.

Helen Shirley-Quirk: Perhaps I can add to that, and clearly Lord O'Neill has alluded to it several times already. Diagnostics tests are a potential and important part of the armoury for tackling antimicrobial resistance, but, as his report makes clear, many of the tests currently available are not appropriate or sufficiently sensitive or specific, and they do not have enough data. We are investing in research to help drive forward the development of new tests, as well as research to evaluate how best we could use the tests that are available.

There is scope for making the best use of what we have, even if it is not broad ranging. We are investing in that research. There are some other issues that we need to look at in terms of supporting the adoption of the tests that are available, and NHS England has a programme of work under way on precisely that—a joint programme with the industry, NICE

and the research funders—to look at how we make sure that we are making the best use of the diagnostic tests that are available.

Q40 **Chris Green:** With more standardisation, more consistency, across the UK.

Professor Cosford: I agree absolutely with that. From my perspective, I support absolutely Lord O'Neill's recommendation that diagnostic tests should be made available when there is good evidence behind them, and they should be used routinely. However, we have to be sure that they are used in the appropriate context and they do not take away from the professional judgment of the clinician with their patient.

For example, we are interested in a test called CRP, which I am sure you are aware of. If patients with bronchitis go to their GP, at the moment standard interactions lead to just under 70% of them getting an antibiotic. A detailed explanation, with information and communication skills between the GP and the patient, brings that down to just over about 33% or so, only a third. Use of the CRP test brings it down to nearly 40%, so it stays higher than if you use good diagnostic skills between the GP and the patient and put in place some training programmes. If you use both, it may bring it down still further, which would be the ideal, but there is some early evaluation that suggests that, when GPs use it, they do not necessarily follow the clinical algorithms that are most appropriate. There are some concerns that patients will be dependent on a test, and rather than having that discussion they will come back to the GP and say something like, "I just want that test to tell me if I need an antibiotic again, Doc." That is not where we want to end up. We want to end up with really good diagnostic tests that support the diagnosis once the GP and the patient have come to a conclusion about what appears to be going on, and the diagnostic test to help confirm that.

Q41 **Chris Green:** In the NHS there is the so-called CQUINs—the commissioning for quality and innovation incentive scheme—for rewarding innovation in particular areas of healthcare. What response have you received from clinical commissioning groups on the new AMR CQUIN launched earlier this year?

Professor Cosford: To clarify, the clinical commissioning groups are subject to the quality premium, and hospitals are subject to the CQUIN. Last year we had just a quality premium, where we saw the significant reduction in antibiotic prescribing that we discussed before. This year, we have the two together. The hospital CQUIN is based on both accurate identification of sepsis, and getting antibiotics in quickly when they are needed, and overall reduction in the use of antibiotics, obviously, when they are not needed. So far, 85% of trusts in the first quarter have signed up for the CQUIN, and we expect that to go up during the year. A significant proportion of them, around 40%, have already met some parts of that CQUIN. It is encouraging progress so far.

In terms of the quality premium last year, all the CCGs signed up, and all but one met at least one of the two areas of the quality premium that was in it last year. It was based on total reduction in antibiotics and reduction in broad spectrum antibiotics, the ones that we are particularly concerned about; 185 of them met both of those. Again, they seem to be an effective way of creating an incentive, but also some momentum behind people in CCGs and trusts taking action across the board for antimicrobial resistance. I am particularly keen to emphasise that it is about appropriate use, so that we do not see people with serious infections not getting antibiotics when they need them rapidly.

Q42 **Chris Green:** Thinking about the actual prescribing that GPs do, could CCG restrictions on GP prescribing put them in breach of General Medical Council duty of care obligations to patients?

Professor Cosford: They certainly should not do so. This is partly why all our guidance and support for GPs to make the right decision is there, to support the clinical interaction between them and the individual who has come to them for advice and help. Of course, we have to be very clear that the different incentives and work that we do to improve quality are there to make that a better interaction, with a better outcome, rather than one that is going to cause harm or lead to them being in danger of being in breach of GMC requirements. I do not believe that is the case. It is not something that has come to me as a problem. Now you have mentioned it, I will check, but I really have no evidence that that is the case.

Q43 **Chris Green:** In terms of changing behaviours and administering or prescribing antibiotics, what training is in place?

Professor Cosford: Obviously, there is the basic training for all healthcare professionals, where we have worked with Health Education England to review that higher education institutions have appropriate skills for antimicrobial resistance and antimicrobial stewardship. The last figure I saw was that around two thirds of them have all that in place, and we are working with Health Education England to improve that position further. A lot of our emphasis is on further training and education tools for doctors, nurses and other clinicians who are already in practice. We work with the royal colleges and we have the TARGET system, as I mentioned, which has educational tools for GPs.

I have mentioned the importance of the information-giving, the leaflets and the conversation between a doctor and their patient. The system has some educational packages to help GPs reflect on how they have the conversation with their patient that leads to the end result being not a prescription, if it is not appropriate, but without losing the doctor-patient relationship, which is, of course, very important in making sure that the individual will come back if they have symptoms that are of particular concern. That bit we call safety-netting, and that is in there as well.

There is a similar system called "Start Smart – then Focus," which we are working on with the secondary care system. That is in place. Then we have some wider education resources. There is something called e-Bug, which is an electronic training education system for use in schools, to teach about infection and the problems of resistance, and obviously there are our public awareness campaigns, which are slightly different. There is a panoply of things. There is always more that we need to do, and we evaluate as we go.

Q44 **Chris Green:** Finally, in terms of farmers and vets, what training programme is there for them?

Simon Hall: For new vets, the Veterinary Medicines Directorate lectures at all the British veterinary schools, and talks about all matters of responsible use of medicines, including AMR. Of course, we do not have a national health service for animals. Vets are independent businesses, so we have to approach them in a different way. The chief veterinary officer speaks whenever he gets an audience at conferences, and is out there on social media. Most significantly, the British Veterinary Association has a seven-point plan that is heavily promoted across its membership; it is really in the lead on this, encouraging the profession to behave responsibly.

Q45 **Chair:** Thank you very much. Very briefly, because I am conscious of the time, Lord O'Neill, you seemed to disagree slightly with Professor Cosford when he was talking about the use of diagnostic tests. Do you want to give an alternative, briefly?

Lord O'Neill: Of all the interventions to solve this problem globally, the role of diagnostics, in my view, is the biggest. I joked with Sally Davies soon after I started the review about why I was needed when all the scientific world knew what the problem was. Before she answered me, I had quickly concluded that you need to drag everybody out of their comfort zone. One does not need to take away the trained, wonderful qualification of medical practitioners, but they are still behaving in the way of decades ago in having a very educated guess in many cases. You guys are all looking at your phones, and I have been too—we live in a world where these damn things completely dominate our lives. By incentivising the right artificial intelligence and others, you can make enormous progress with these things and we need to do it.

Q46 **Graham Stringer:** If I can take you back to a previous answer, Lord O'Neill, you said this Government have less passion for dealing with antimicrobial resistance. Is that represented in any way in numbers? Is there less investment, less money, less commitment? It is difficult to measure passion.

Lord O'Neill: Maybe less passion was the wrong phrase—less public voice. The Prime Minister himself and the Chancellor played an active role in international engagement on the issue. That is what I was referring to.

Q47 **Graham Stringer:** So you think this Government are less engaged

internationally.

Lord O'Neill: I have not seen them talk about it anything like as much as the previous leadership did.

Q48 **Graham Stringer:** Can we put some figures on the commitment? Do you have figures for the amount of resource, in cash terms, that is going into this strategy?

Lord O'Neill: Are you asking me again?

Graham Stringer: Yes.

Lord O'Neill: These guys are probably better qualified on that.

Q49 **Graham Stringer:** I was asking you as an economist.

Lord O'Neill: What I would say in that regard is that the British Government backed beforehand a number of initiatives that we were suggesting before we completed our review. The Fleming Fund was a response to one of our ideas about the need for greater surveillance. I think the number is currently standing at £265 million.

Helen Shirley-Quirk: It is £265 million for the Fleming Fund.

Lord O'Neill: That is a new commitment that the British Government made, and I am not aware of any other Government in the world having done that. That is of significance. The UK, jointly with China, announced a commitment to the beginnings of a global innovation fund. There have been some announcements about that overnight. The US has been quite strong on that, but, again, no other European country has made, as of yet, a commitment to that kind of size of money. On those two kinds of measures, the UK has done a pretty good job. It is not enough.

Q50 **Graham Stringer:** In terms of the way you described the problem, compared with how we are tackling other problems that need resources put in—for instance, climate change—that is a lot of money, but in terms of the size of the problem, it is relatively trivial, isn't it? If you are talking about $10 trillion loss of world product in 30-odd years' time—

Lord O'Neill: It is 100.

Q51 **Graham Stringer:** It is a small amount, isn't it?

Lord O'Neill: I will take it right back to something I think your Chair said at the start. The dilemma is that throughout post-war life, if not earlier, global policy makers have typically responded to scary outbreaks of a crisis. They are very bad at trying to pre-empt them and, as we showed, if you take all our interventions globally for a decade they cost $40 billion. It is less than 0.25% of global GDP. In the world I come from, that translates into a return of 2,500%. The amount of money to solve this problem on a global basis is not that big, but it requires policy makers to behave with more pre-emptive action than is typically the case that one observes.

Helen Shirley-Quirk: Can I complement what Lord O'Neill said? There has been no reduction whatsoever of the funding that the UK is putting in. There is substantial funding. Some £200 million has been committed to targeted AMR research over the last couple of years, and that is in addition to the core investment in research and development through the medical research councils, much of which also goes to research that is relevant to AMR. There is, as we have talked about, significant investment in terms of supporting or tackling the problem at a global level through our overseas development projects.

We have already talked about the specific incentive schemes that have been put in place in the UK. In terms of tackling AMR, a lot of what we are spending on AMR, as Paul was talking about, is through education initiatives, through reach-out like that. It is not really just about special pots of money; it is around how everyone is targeting their actions. I feel that I can speak positively about what we are doing in terms of setting a lead internationally, but, as Lord O'Neill said, it is a global problem. The UK is playing a very significant part in putting its money where its mouth is—is that what you say?—but we are equally encouraging and prompting other countries to contribute as well.

Q52 **Graham Stringer:** When the Committee looked at the issue initially, two and a half years ago, there was disagreement between, for want of a better word, the farming lobby and the alliance to save our antibiotics about the scientific basis for the problems caused by overuse of antibiotics in animals. What is the latest research on that? Lord O'Neill is smiling.

Lord O'Neill: One of the things we highlighted, I think, is possibly the most detailed literature survey ever of evidence about that in agriculture. You will find, not surprisingly, that the few people who question the evidence are usually those who have a vested interest. If I remember correctly, 85% of those who independently analyse it conclude the opposite. In our review, in the final review and in our special report on agriculture, we have detailed reference to all those things.

Q53 **Graham Stringer:** You think the transmission of antimicrobial resistance via the overuse of antibiotics is a major problem.

Lord O'Neill: I bow to the weight of scientific evidence. I would add one other thing, which is why the Danish example needs to be thought about much more seriously by people in farming all over the world: they took the challenge head on and reduced inappropriate usage to the scale that I think you yourself referred to, but, very importantly, they have grown their share of the global bacon market. Their productivity has actually risen. It has not gone down.

Q54 **Graham Stringer:** I have two final questions. What does 50 milligrams per kilogram represent in terms of current practice? How much of a reduction would it be?

Simon Hall: The baseline was 2014, and it was 62, so it has dropped from 62 to 56. We are halfway there.

Q55 **Graham Stringer:** This is my final question. Do you think in terms of worldwide action that we need a structure similar to what is used on climate change, such that, like the international Committee on Climate Change, there should be an international committee on antimicrobial resistance?

Lord O'Neill: It depends on how the UN deals with what the co-ordinating committee feeds back in two years' time. I hope not, because the evidence of such committees in past life is not necessarily spectacular, but the scale of the challenge is so big that, if there is no evidence of serious efforts by each of the three key bodies at the centre of the co-ordination, there may need to be one.

Helen Shirley-Quirk: I was going to make exactly the same point. There is the co-ordination group, or there will be, to follow up the declaration. We want to see where that gets to. We want to see, as the UK, and the Government want to see, action driving ahead with momentum on this, but we would hesitate to set up yet more international bodies if they are not necessary. Let's see where we get to with the mechanism that has been put in place.

Graham Stringer: Thank you. My apologies. I have to leave.

Q56 **Carol Monaghan:** I would like to pick up on some of the things that Graham has already mentioned. Lord O'Neill, can I take you back to the figure of 50 milligrams per kilogram? Your report talked about the Danish situation. What evidence is there that reducing that figure caused the expansion of the industry? I am a scientist. Lots of factors can affect something.

Lord O'Neill: Yes, of course. One has to not confuse correlation with causations, as you imply with your question. I am no scientist. I have no scientific answer to any of the issues, but the core genuine concern that the farming community may have in any country in the world—that if we adopt these principles, it will result in us not being able to produce as effectively—is what we highlight. It may well be, almost definitely, as a result of having to do it, that they had to undertake other things that contributed to the improvement in productivity, but that is neither here nor there as far as I am concerned. In terms of saving 10 million lives, they took that step, and possibly others, and they are in a much better place as a result.

Q57 **Carol Monaghan:** Is 50 milligrams per kilogram considered a safe level or is it simply an initial target? Should we be more ambitious with the targets we are setting?

Lord O'Neill: The way we specifically suggested it was our best guess for the right sort of framework, and it was up to those with expert knowledge to take it further if need be, so I have no idea. It is a much more sensible

thing to do than something like a blunt supposed ban for growth promotion, which is very easy to circumnavigate, as is topical in the United States almost every day in this debate.

Q58 **Carol Monaghan:** This is generally to whichever panel member feels able to answer. We know that antibiotics have led to growth enhancement, so how can the Government work to ensure that they do not continue to be used simply for growth enhancement?

Simon Hall: In 2006 there was a Europe-wide ban on the use of antimicrobials for growth promotion. That has already been discussed. That is something that is easy to say but harder to deliver, but it does mean that the approvals for all the relevant medicines were changed to say that they are really only eligible for therapeutic use. Then, realistically, it is what Lord O'Neill said earlier. On any given occasion you might have a discussion as to whether the group of animals were ill at the time, or whether they were at risk of becoming ill or not ill at all and the drugs were being used just to improve productivity. The 50 milligrams per kilogram target sidesteps that; it says we need to see the overall consumption of antimicrobials going down, and then there is a separate discussion around the critically important ones. That drives the behaviour.

Q59 **Carol Monaghan:** Do you think there is a change in behaviour or opinion on the use of these for disease prevention within agriculture?

Simon Hall: Yes. The discussion earlier was quite reasonably about misuse of antimicrobials in agriculture, and how it feeds through into resistance problems for people. Of course, farmers are equally concerned about resistance problems in their own animals, so yes, everybody—farmers are citizens too—wants these important medicines available for people, but they are equally concerned that they have use of them when required in their herds and flocks.

Lord O'Neill: We used to talk more and more during our review about what we called the Shake Shack factor. I do not know if any of you have ever been to Shake Shack; it originated in the States where they started to threaten the market share of big US food producers. I do not think it was for this reason, but they sell themselves as using antibiotic-free meat. It has led to the same approach from McDonald's with chicken and so on. That has not yet moved over here, but in my judgment it is a rather encouraging sign and at some point, if it does not flow to Europe, policy makers should consider doing something about it.

Q60 **Carol Monaghan:** We should be looking at what is in vogue with the public, and we might actually make more progress.

Lord O'Neill: Yes.

Simon Hall: I spoke before about antibiotic-free being quite a crude and potentially misleading label, but our retailers are definitely interested. The British Retail Consortium has been invited to and attended various

summit meetings, and although it is commercially confidential, we know that some individual retailers are looking to strengthen requirements for antimicrobial usage on their assurance scheme. Food—meat, milk, or whatever—produced on British farms going into the supermarket supply chain is almost always subject to farm assurance, so farms are inspected to make sure they are observing various standards. Strengthening the AMR component of those standards will have the effect that we are describing, although perhaps in a more sophisticated way than simply saying something is antibiotic free.

Q61 **Carol Monaghan:** Mr Hall, could I stay with you? The National Office of Animal Health have responded to Lord O'Neill's report and stressed the importance of antibiotics to the country's food supply production. What evidence is there really on the balance between the requirement to supply food and the requirement to tackle AMR?

Simon Hall: I suppose we would like to be in the Danish situation where it is win-win, so provided we work with the industry sectors and give them time to adapt, and then encourage them to adopt the right behaviours, which are to improve the health of their herds and flocks through good hygiene, biosecurity in general, use of vaccination, use of good feed and good environment, their productivity should improve at the same time as antimicrobial consumption goes down. That is the win-win.

Q62 **Carol Monaghan:** Would you recommend a set of clear standards that goes out industry-wide: "This is what is required"?

Simon Hall: Yes. Those standards already exist. It needs some additional motivation to adopt them across the industries, but better that the standards are set by the farmers themselves than by Government, because they know how to run their businesses.

Q63 **Jim Dowd:** Farmers know how to run their businesses, but they also know how to access large sums of public money; but we will put that to one side. In your review, Lord O'Neill, you highlighted the need to develop further antimicrobial drugs. I do not know if you are necessarily the best person to answer this, but what financial incentives should be developed to encourage industry to produce new drugs?

Lord O'Neill: I was wondering when this topic would come up, if at all. It was the one that generated the most noise around our recommendations, of course. We specifically recommended a set of interventions at the early stage and a set of recommendations at the later stage. The one that focused all the excitement within the industry is what we call a market-entry reward, which is essentially a very large prize—$1.2 billion I think was the central number, but it would be a number around it—for the successful producer, on evidence of success of its being usable, of the right sort of identifiable needed new antibiotic, primarily Gram-negative, as well as subjecting it to very careful stewardship and making it affordable in the emerging world. The controversy was about where the

money comes from, where we suggested that the industry should have more enlightened self-interest to play a role.

Q64 **Jim Dowd:** After the development of penicillin there was considerable development and considerable pressure by the pharmaceutical industry generally to find other antimicrobials. Why does that energy or that commitment not exist today? Clearly, there is a huge commercial prize for new antibiotics.

Lord O'Neill: The pharmaceutical companies?

Jim Dowd: Yes.

Lord O'Neill: From a scientific and a commercial perspective, it is an extremely costly thing to do. You can spend hundreds of millions of dollars and not actually end up with a successful drug. In my experience, having understood all of this a lot more now, pharmaceutical companies, like many other businesses, tend to be organised on product lines. They have a rate of return hurdle that is risk adjusted, and it does not meet the biscuit, so to speak. There are a lot more, on the headline at least, attractive things for a risk-reward to do than invest in antibiotics, unfortunately. The whole reason we devised our intervention, because it is a classic market failure, in economic terms, is to come up with a set of interventions that help change that way of thinking. The industry is quite reluctant to see it in that way. Certainly it was quite reluctant initially, and broadly speaking it is still quite reluctant to see it in the way we suggested.

Professor Cosford: Lord O'Neill will understand all the economic incentives better than I do. From a simple clinician point of view, we need new antibiotics that never get used except in the very rarest circumstances. That does not seem to me to give a profit to an organisation that has to make money out of the process. That seems to me the fundamental problem.

Lord O'Neill: Of course, that is true and it is well-put evidence as to why they find it so unattractive, but what a lot of them also do not seem to understand, in my view, is the power of the importance of antibiotics, and that a lot of other things they make a lot of money out of will not have a market unless we have antibiotics. As somebody who has been in business for 30 years, I think the way they look at their business lines is part of their dilemma, and they need to think differently.

Q65 **Jim Dowd:** There are different models you can adopt in this fashion. Do you think adjusting the patents, for example, so that companies can make more money over a longer period would be a better approach, or simply subsidising the R&D?

Lord O'Neill: No. We looked at virtually every option that has been discussed, that we are aware of, including of course that one, which is very popular among the big US drug producers. We do not think it is a particularly smart thing to do. It might work for the very first one that

received the patent extension, but it would not succeed in getting a whole host of genuine research for the needed Gram-negatives, in my view. It would be a very generous prize for the pharmaceutical company to get an extension over something out of which they are making, in virtually all cases, very large amounts of money.

Q66 **Jim Dowd:** I am sure they feel they can never make enough money to keep them going.

Lord O'Neill: Of course.

Q67 **Jim Dowd:** If there were to be direct intervention in the R&D of antimicrobials, how could it be so structured as to prevent special pleading from all kinds of other areas of research?

Lord O'Neill: If there was an intervention of the type that we are suggesting, could it lead on to other things? That is a valid case to raise, but there is a lot to be said. The breadth of the scope of the role of antibiotics is so important, and the pharmaceutical industry is given such a lot of support by policy makers in many parts of the developed world and elsewhere that it is a pretty unique case.

Helen Shirley-Quirk: Clearly, it could extend beyond antibiotics to other antimicrobials.

Lord O'Neill: I meant antimicrobials in general. They talk about that: "Well, if we go down this path, what happens next when somebody else dreams up something else?" It is a valid point to argue.

Helen Shirley-Quirk: The way Lord O'Neill's report puts it is to talk about both push and pull. What we are talking about in the market-entry reward mechanisms is around pull, encouraging and creating an environment in which industry is more inclined to invest, and to make the investment through those mechanisms.

There are other things that we are doing, as suggested in Lord O'Neill's report, around looking at reimbursement mechanisms as well, within this country. There is some work under way to look at how to de-link the price you pay from the volume of sales. That is incredibly complex. We are working with industry on it and discussing it with NICE. The modelling and the evaluation mechanisms that you would have to use do not yet exist, so there is some way to go on that, but we are working on it, and I think we are ahead of the game compared with other countries. No country yet has a mechanism for that.

In the meantime, we are still investing in the push mechanisms—putting extra funding into research to encourage the development of new antimicrobials, and indeed diagnostics. We are tackling it from both the push and the pull, but the pull mechanisms very much need to be tackled at a global level, and that is why we pushed to get the G20 to pick this up and run with it. As Lord O'Neill said, it cannot all be driven from the UK.

We think that the G20, with its focus on economic issues, is ideally placed to take that forward.

Lord O'Neill: I am glad Helen said that. I should have said this. Under the German chairing of the G20, the OECD has been asked to play a very specific role in considering all of our recommendations, and others, and to actually come up with their independent expert advice as to exactly what the German G20 should implement.

Jim Dowd: Sure. Thank you very much, Ms Shirley-Quirk; my last question was on de-linking and you have saved me the effort. Thank you.

Q68 **Chair:** Can I go back to that de-linking question, just about the timing? I think originally there was supposed to be some sort of agreement by the end of the year and then potentially a pilot next year. Is that not now the case?

Helen Shirley-Quirk: The work is still under way. I think there was a meeting last week, or maybe it is next week—it is one or the other; it is actively progressing. Actually developing the models will take some time, but my understanding is that it is still on track. I do not have a precise date for you.

Q69 **Chair:** No, but we should see a pilot next year, we hope.

Helen Shirley-Quirk: We should see some progress towards a mechanism that could potentially be used. Having the pilot depends also on having the new antibiotics that you would want to use it for.

Q70 **Chair:** As a very final brief question, are there alternatives to antibiotics? Are there other therapies that can have the same effect and can kill microbes?

Lord O'Neill: Vaccines, especially in agriculture. We were repeatedly surprised, when we were trying to learn, how little the role of vaccines has been explored in agriculture. I nearly brought it up in response to this discussion, because it seems not far off the no-brainer box.

Professor Cosford: I agree with that. The more we prevent through either vaccination or other mechanisms, the better, and the less we create the need for antibiotics. Of course, we need antibiotics when we need them and we must have them available, but to go back to my initial point that this is about reducing the burden of infectious disease, there is a whole range of things we need to do to reduce the burden of infectious disease, in which antibiotics/antimicrobials are an absolutely essential part, but they are a part.

Chair: Fine. Thank you all very much indeed. I am sorry it has been a lengthy session, but we have got an awful lot out of it. Thank you all.