

Science, Innovation and Technology Committee

Oral evidence: The antimicrobial potential of bacteriophages, HC 886

Wednesday 26 April 2023

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[Watch the meeting](#)

Members present: Greg Clark (Chair); Aaron Bell; Tracey Crouch; Rebecca Long Bailey; Stephen Metcalfe; Carol Monaghan.

Questions 182 - 249

Witnesses

I: Dr Tim Jinks, Head of Infectious Disease Interventions, Wellcome Trust; Richard Hebdon, Director Health and Life Sciences, Innovate UK; Dr Jonathan Pearce, Director of Strategy and Planning at Medical Research Council.

II: Professor Isabel Oliver, Scientific Officer, UK Health Security Agency; Dr Marc Bailey, Chief Science, Research & Innovation Officer at Medicines and Healthcare products Regulatory Agency; Professor Mark Sutton, Scientific Leader in Healthcare Biotechnology at UK Health Security Agency.

III: Dr Morwenna Carrington, Deputy Director for UK Health Security, Department for Health and Social Care.

Written evidence from witnesses:

- [Wellcome Trust](#)
- [Department of Health and Social Care \(DHSC\), UK Health Security Agency \(UKHSA\), and Medicines and Healthcare products Regulatory Agency \(MHRA\)](#)

Examination of witnesses

Witnesses: Dr Tim Jinks, Richard Hebdon and Dr Jonathan Pearce.

Q182 **Chair:** This is the first meeting of the Science, Innovation and Technology Committee. We took on responsibility for scrutinising the new Department as of last night. In addition to that scrutiny, including of the Department's digital responsibilities, I am pleased that the Committee will continue its long-standing role of inquiring into and scrutinising the application of science, innovation and technology across Government and beyond—something that has been important to the Committee over the years. It is good to have that dual mandate.

I would like to welcome the witnesses to our final session on the antimicrobial potential of bacteriophages. This is an inquiry that was the winner of a competition between pitchers from different institutions as to which inquiry the Committee should undertake. It has been a fascinating inquiry, and so we are concluding it with some questions to some of the funding bodies, some of the regulatory bodies and some of the public sector bodies.

To start our session this morning, I am very pleased to welcome Dr Tim Jinks, who has been the Wellcome Trust's head of interventions for infectious diseases since 2021. He leads Wellcome's work finding solutions to antimicrobial resistance. Previously he designed and led Wellcome's strategic priority area for combating drug-resistant infections, deploying a budget of over a quarter of a billion pounds, so welcome Dr Jinks.

We also have with us Dr Jonathan Pearce, who has been director of strategy and planning at the Medical Research Council—the MRC—since February of last year. Dr Pearce has chaired the UKRI antimicrobial resistance initiative and the UK AMR Funders Forum. Welcome, Dr Pearce.

And Richard Hebdon, who is the director of health and life sciences at Innovate UK, the Government's innovation agency. Mr Hebdon leads the health and care team, which provides funding and support for industry-led innovation across a range of healthcare areas.

Thank you, all three, for joining us today. All of you have a common denominator of being funders. Part of the evidence that we have received is that there is some concern that the degree of funding that is available for research and development of phages is not what it should be and could be better. Dr Pearce, you might reflect on that.

Dr Pearce: One point of reflection is that we need to consider phage as a part of both a portfolio of opportunity within the therapeutic space and that we need to consider it alongside alternatives, including small molecule drugs and other breakthrough innovations that can include host factors in the microbiome. We also need to recognise that, unless we also tackle some of the drivers of resistance—so both the emergence and



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spread of resistance—we are at risk of just burning through any new interventions that we bring forward.

For the MRC—and indeed within UKRI—we have taken a perspective to consider all of the drivers of resistance that have multifaceted particular components, which can be both technical, cultural, economic and social in driving the emergence and spread. This Committee may well recognise that that spread can move between the environment, animals and humans and across borders. Therefore, UKRI has taken and has the ability to convene across disciplines and sectors and across boundaries, countries, to develop a balanced portfolio that considers phage in the context of a therapeutic but also in the wider context of the drivers and spread of resistance.

Q183 Chair: We heard evidence from the Cystic Fibrosis syndicate in AMR—antimicrobial resistance—who said that the phage therapy in the UK is poorly funded, and that there have been no phage-specific funding calls. Is that an accurate description of the MRC's—

Dr Pearce: From the MRC we have two primary routes for supporting phage activities. We have our research boards, which can provide support for both basic and fundamental bacterial and phage investigations if they are relevant to human health, and our Developmental Pathway Funding Scheme, which supports the development of pre-clinical and early clinical investigations of interventions, phage and otherwise.

We tend not to ringfence funding within these schemes because we believe that it is better that we support a portfolio of strong proposals to come forward, so that we are managing public funding and directing it to the highest quality applications because supporting low quality science is not going to have the health impacts that we all seek.

If one looks at those schemes, it is interesting. I know that the Committee has considered the lack of clinical trial activity in the UK since 2009. I have looked back from our Developmental Pathway Funding Scheme, which was established in 2008. It has received 1,600 applications across its entire life, and we have only had two phage proposals, both of which were in the pre-clinical space. I think that talks something about the capacity and the pipeline for phage activity in the UK.

Q184 Chair: Have there been any funded phage research projects through the MRC?

Dr Pearce: Yes. We have a portfolio of phage funded activity that stems both from studentships through active programmes within those research board activities, and are also working in partnership with European colleagues as part of the Joint programming Initiative on AMR. I think this Committee has also heard about strengths that exist within Europe, and those kinds of vehicles provide an opportunity for our community to



collaborate with the strengths that are found within the European environment.

Q185 **Chair:** I think what you are saying, Dr Pearce, is that there is funding available, but it is at a more general level and is not ringfenced for phage research. You have expressed a concern that you want to avoid funding low-quality science. Is the implication of that, that the great majority of the research proposals you have had in the phage area are low quality compared to other high quality science?

Dr Pearce: One of the opportunities we have—and actually stimulated in part by this Committee's inquiry but also by the establishment of the new networks, which we might come on to—is to develop a shared agenda for research and innovation, to understand collectively what the key challenges are that we face in order to really develop phage as a clinical tool. I think that that will help to develop the quality that we would all want to have to be able to fund it. The funding is there. I think it is just ensuring that we are working with the community to bring forward that rich pipeline of opportunities.

Q186 **Chair:** Isn't this a little paradoxical? You said that it should not be ringfenced because there is a danger that the quality of the science might be impaired by that, but you have stated an ambition—perhaps inspired by our discussions in recent weeks—to do something more deliberately in the field of phages. Would you consider changing the approach to, if not ringfence, establish the possibility of funding specifically for phages? If the proposals that you have were not adequate you should not fund them, but would you consider identifying phages as an area of research priority?

Dr Pearce: As I said, they have great potential in looking at some of the challenges of spread. They are currently used in managing foodborne pathogen spread. They could have opportunities in diagnostics and in therapeutics, both in animals and in humans. One of the things that we work closely with our colleagues in BBSRC is to ensure that we are considering the opportunity that crosses both between the human and animal health areas.

Q187 **Chair:** Will you establish a specific programme for funding for phages?

Dr Pearce: One of the opportunities that emerges is that we are re-engaging our flagship AMR programme as part of the UKRI tackling infections theme. I think that could be a good opportunity to engage with the community to look at what the opportunities could be within that scheme to provide more focused approaches.

One of the roles that that scheme will play is to build into disciplinary research teams addressing AMR challenges. I think that, as we have heard, the opportunity to network and bring the community together on a shared agenda could provide a good opportunity for that conversation to be had with the community.



Q188 **Chair:** I still do not understand the answer to the question. We want to make recommendations and so I would like your view, from the purview of the MRC: should there be specific identified funding streams for phage research?

Dr Pearce: As I say, I think our preferred route is that we do not ringfence specifically, but we are very happy to work with the community to identify where those shared challenges are, so that we can collectively identify the opportunity and the way forward.

Q189 **Chair:** Just describe what that means in practice.

Dr Pearce: I think that we might hear about the new phage innovation network and the opportunity to work both with the research community and the academic community to identify the key research questions that need to be addressed in order to prosecute successful clinical investigations. By having that shared vision, it will enable the quality that we are very keen to bring forward to be successful through the schemes that we have in place.

Q190 **Chair:** Correct me if I am wrong, but you seem to be saying that you would like to see more research being conducted here but so far you don't think it is of sufficient quality to justify public funding compared to other uses of these funds. Is that correct?

Dr Pearce: Thus far, we have not had the opportunity of the grants that we have seen to have met that threshold. I do think that the opportunity is strong, and that we should be working constructively with the research community to understand what those challenges have been in the past and what it is that we need to collectively address to overcome them.

Q191 **Chair:** To review and consider the evidence that we have had, one of the aspects of frustration is that there has not been a clear forward view, a kind of road map, as to how we go from potential to testing in a rigorous way whether phages can be of use as an alternative to of those drugs that would not cause microbial resistance. I am not getting a clear view as to whether there is an intention to provide some clarity so that people can decide to make commitments.

Dr Pearce: As I say, I think that we have a very strong opportunity now with the establishment of the new networks to bring that clarity forward, working with the community to take that collective view of what the steps are—the evidence that we would wish to see—in order to be able to build that clinical evidence. I think that the Committee has heard of the lack of clinical trial evidence, both in the UK and internationally, and I think that is a key focus for the field, and what are the steps that we need to have in place in order to be able to prosecute that programme.

Q192 **Chair:** Just briefly, Mr Hebdon, UKRI funds the MRC. I know you are from the Innovate side of it and obviously the development aspect is important. Should UKRI be establishing greater clarity as to whether or not this is an important area of future research? Is it unfair to expect



clarity from the MRC? Does it need a steer from UKRI?

Richard Hebdon: First off, we characterise phages as an emerging technology area in the field of complex biological medicines. Typically, how UKRI and Innovate UK would approach this kind of area would be exactly the kind of work that Jonathan mentioned earlier concerning the phage innovation network. For example, if we look at related emerging technologies areas in the life sciences, like the biofilms and microbiomes area, we would begin with this network and stakeholder and community-building activity, which would bring in together all of the different parties.

If you look at the specific area of biofilms, we started on a journey there probably going about 10 years ago before I joined innovate UK. We began in a very similar fashion. We started with networking, bringing together the various stakeholders, industry, academia and so forth, understanding the obstacles and challenges. From that we were able to build a business case for feasibility study funding in the biofilms space in the 2015-16 financial year. That eventually led to the establishment of the National Biofilms Innovation Centre, an innovation and knowledge centre that is jointly funded and supported by BBSRC and Innovate UK.

Therefore, we do work both bilaterally and across UKRI, but going forward this is potentially an area that we could definitely explore.

Q193 **Rebecca Long Bailey:** Moving to Dr Jinks, your organisation has identified antimicrobial resistance as a key challenge. What role do you see phages playing in meeting those challenges?

Dr Jinks: Thank you. I will be almost repeating and emphasising what Dr Pearce has said. We see that the role as a diverse, alternative approach as an antimicrobial treatment is a key importance in what phage does bring to the space. With AMR we have a critical problem that the pipeline of antibacterial agents, in particular, is inadequate for current and particularly future needs. Therefore, our priority is to address that issue, to bring forward innovative approaches so that there can be safe and effective treatments, and particularly those that can overcome the increasing drug resistance that is driven by AMR.

Phage presents an alternative approach in terms of that treatment base. We think that that is important, but we view this as a portfolio approach. We are not seeing sufficient evidence to prioritise one particular type of modality over another. Instead, we want to see a breadth of approaches that are investigated and developed with the most promising types brought forward, and phage is one among several modalities that we believe is important.

Q194 **Rebecca Long Bailey:** Have you assigned funding to phage research and the development of phage therapies and, if so, at what scale?

Dr Jinks: We have done that. Over a long period of time, Wellcome has supported phage-related research for product development, though very little has been targeted to natural phage. I know that the evidence that



has been brought to this Committee has been focused around natural phage, and Wellcome has predominantly funded genetically engineered, genetically modified phage as innovative approaches to this space.

More recently, we do specifically instruct we have two funding vehicles that we support. The first one is CARB-X. That is a multi-funder international funding platform to support early or R&D product development for AMR priority pathogens. In that, there is agreement among all funders that there should be support for alternatives as well as small molecule treatment types, and specifically including among the biologicals, phage. Phage is one of a set of options.

In the CARB-X vehicle there has always been the opportunity and the open funding calls for phage-based innovations to submit their applications to be considered for funding investment and support. In 2019 there was a specific funding call that was ringfenced for biologics but not narrowly for phage and, certainly, not so narrowly as for natural phage.

The other funding vehicle, which Wellcome is a partner in supporting with industry, is the AMR Action Fund. I believe you received evidence from the AMR Action Fund. The fund has made a direct investment into Adaptive Phage Therapeutics, which has also submitted evidence here.

In Wellcome's joining into the limited liability partnership of the AMR Action Fund, we ensured that the diverse approaches, including phage, would be included as things to be specifically considered but not necessarily prioritised. In both cases, competitive approaches are how funding decisions should be made and not giving an absolute preference just on the basis of the modality.

Q195 Rebecca Long Bailey: Thank you. That is helpful. In terms of what is holding back phage funding, we know that there are countries in other parts of the world that have prioritised phage funding. If you can be as clear as possible as to what you think would specifically hold back phage development funding, and what challenges need to be overcome to ensure that there is a priority pathway for phage funding.

Dr Jinks: I don't think of it as there being some great resistance or holding back of funding for phage. It is about whether or not the opportunities as presented are competitive against other approaches. For us, ultimately what we are concerned about is whether or not innovation is delivered to healthcare systems that are safe, effective, is sustainably available, useful and can be used.

Whether it is phage or a small molecule, at the end of the day, is rather less important. We do not want to create a particular distortion in the innovation ecosystem in one direction or another, because that risks cutting off other spaces.



The issue is around how competitive are the ideas and approaches around phage as potential therapeutics. While it is well-described as an emerging technology, it is one with a very long history. That long history in some ways is not serving things very well because it creates a certain bias in the understanding of the situation, the opportunities and the way forward.

What I see is that for phage to be developed as therapeutics they need to consider better how product development needs to happen, how you can have a product that is one that can be produced at appropriate quality and is something that can be used in a way that is relevant to healthcare systems. For example, one of the big challenges remains: what is an appropriate dose of treating with a phage?

This is the sort of thing that undermines the opportunity and the potential to bring things forward, because it is not built on a sufficient base of evidence about what a treatment should really look like in real world medical care.

Q196 Rebecca Long Bailey: You mentioned the word “competitive”. As a Committee, it would be good for us to understand what you mean by that. For example, in previous sessions we have heard from researchers who have suggested that phage therapy is a very individualised approach.

Would that pose an issue towards your challenge of competitiveness when it comes to getting a return on investment? Is that the key hurdle that we are trying to overcome here. Is it a question of profit that could be made from phages versus the amount of investment that is required in them?

Dr Jinks: That is an excellent set of questions, and it brings in some of the overarching complexity in this space that impacts not only phage but all other antibiotic-type treatments. There is the market failure and the issues that relate to that, but I will start first with your question as it relates to individualised therapy.

Indeed, it does create something of a higher hurdle to overcome in terms of competitiveness against a therapeutic candidate that may be more widely used and, therefore, provide broader benefit in terms of reducing the burden of disease and illness. However, that is not an absolute cut-off point. We certainly have approaches where we think about things in terms of being rare diseases and individualised medicine. Individualised medicine is now a burgeoning approach in how things are done.

If it is clear that an individualised approach is one that is practical, I think the issue of the competitiveness is somewhat reduced. However, if it is not clear how that can be achieved in a real setting, that does increase the barrier for things to be able to go forward.



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At the moment, we have a situation where, particularly for natural phage-based therapies, the lead time for generating what would be that treatment is too long for those patients who are critically ill and, at the end of the day, it is totally impractical. Therefore, how can that be brought forward in a way that can be sustainable and cost effective?

The business case, overall, is a very important one and it is not just about phage. It is much more far reaching. The fact is there is an absolute market failure as relates to antibiotic-type treatment and antimicrobial treatments for bacterial infections. This is holding everything back. We have a situation that is restricting the availability of funding, more broadly, particularly private sector funding. Something that we need to see are changes in the environment, so that there can be more sustainably paid for drugs to have a sustainable pipeline and one that invites in private sector investment.

I think it is a very difficult ask to say that the full costs of research development deployment and use should be covered by public sector and charities. In a way, that is one of the major issues that is hampering phage and other antimicrobial-type treatments for bacteria.

Q197 **Rebecca Long Bailey:** Do you agree, Dr Pearce?

Dr Pearce: As to the hurdle of the market access?

Rebecca Long Bailey: Yes.

Dr Pearce: Yes. We have been talking often here about push factors and research funding, but we need the pull of the market to also be in play. Otherwise, as Dr Jinks was outlining, the public and charitable purse needs to take much more of the burden down into the market area.

I don't think it is necessarily a lack of profitability. It is around return on the required investment to undertake what can be sustained, rigorous trialling to ensure that we are actually meeting both safety and efficacy thresholds that we would expect through treatment modality.

Q198 **Rebecca Long Bailey:** Mr Hebdon, is there anything that you would add to those comments?

Richard Hebdon: No. I think Dr Pearce and Dr Jinks have put it very admirably. It is a very important point that we have a serious market failure with respect to novel antibiotics. That makes the whole challenge around bringing forward novel antimicrobial technologies, like phages, doubly difficult.

Q199 **Chair:** Dr Jinks, I was interested in your response to Rebecca on the environment: that there need to be changes in the environment if there are to be more opportunities for commercial development. Could you elaborate on what you mean by the changes to the environment?

Dr Jinks: Yes. Dr Pearce mentioned push and pull, as the kind of jargon that we use in this space. Typically, for medical products the pull is how



drugs are procured and paid for. For antibacterial-type agents, in particular, the system for procurement and payment for the drugs is one that does not support commercial sustainability in this space. It particularly does not address what should happen to support innovation and innovative products.

Q200 Chair: Who are the bodies that need to change the practice to correct that?

Dr Jinks: This is an area that does create quite a lot of political sensitivity. It is the players and ultimately Governments. It certainly is worth highlighting that there have been very significant efforts in leading the way from the UK, and work that was done by NICE to come up with a mechanism to negotiate a price that creates a form of a pull mechanism for antibiotics for NHS England.

That has been deployed as a pilot and we hope that the evidence about the effectiveness of that instrument, in providing an appropriate level of funding to support the sustainable supply of the drugs, as well as to create that pull around the innovation piece, so that we can have a pull that is oriented around mobilising the private sector that complements the push that can come from classical earlier stage funding.

Q201 Stephen Metcalfe: Good morning, everybody. Welcome. I want to go back to the principles of why we are looking at this. Dame Sally Davies came before this Committee some years ago—quite a few years ago—and stated on the record that she was less concerned about the impact of climate change and more concerned that, during a routine hip operation at some point in the future, they would not have the antibiotics available to ensure that she came out of that operation safe and well. I have misquoted that, and I accept that, put it on the record, but that was the fundamentals of it.

We have been looking at the solution to that for probably a decade. One of the solutions that came up at the time when we did an inquiry, and why we are looking at this, was about phages. What I am not getting the sense from you—and we have had lots of proponents of the technology coming before the Committee—that you think that this is the silver bullet, the all-encompassing solution to the problems that we have with AMR. You stated right at the beginning, Dr Pearce, that we need to tackle the emergence and spread factor.

Could all of you just give us a brief summary of what you think the technology can bring, and whether you are waiting to see if it emerges and does something more? Because I am just not getting the sense that we are really supporting this.

Dr Pearce: I am happy to pick that up. I fully recognise the nature of the opportunity to target very precisely a bacteria without causing damage to the wider microbiome. These features have great attraction. Clearly, to look at that diversity and to consider all the approaches that we can bring to bear against this challenge is important.



You might have also heard evidence around the critical need to match a target bacteria with a phage to ensure that you deliver the right phage to the right site with the right amount. All those steps require careful unpicking. While there is a great opportunity to bring in other expertise in formulation and delivery to help with that, by the very nature of a phage, it poses specific challenges. It is self-replicating. Unlike a drug, where you put it in and you can have a predicted outcome as to how it will flow through the body to a site, this phage is a self-replicating entity. This poses a challenge because you may need only one, but how many do you need to hit this site? Some of those sites are deeply seated. If you have a bone infection, you now need to get the phage through the bloodstream to the right site.

These are significant challenges. I am not saying they are not unsurmountable, but there is a good opportunity to bring a collective view to those challenges and how we should collectively go about addressing them, which comes back to the point that Rich was making about how we are in an emergent phase, and we need to have that open discussion about those barriers and how we can circumvent them.

Q202 Stephen Metcalfe: Does anyone want to add to that? I can see you describing specific uses and there is more work to be done and so on. Fast-forwarding, will it make a significant contribution to the problem with AMR or do we need to look somewhere else for that significant contribution to AMR?

Dr Pearce: As we have highlighted, it provides one of the portfolio of options that we should look at because of the scale of the challenge that AMR poses.

Q203 Stephen Metcalfe: It would not keep you awake at night if this technology was not emerging?

Dr Pearce: It is one of a number of approaches that we need to prosecute.

Q204 Stephen Metcalfe: Thank you. Unless anyone wants to add anything, I will move on.

Taking the fact that phage has significant potential benefits, not necessarily resolving all our issues around AMR but it would be able to do some things, Mr Hebdon, you have set up or have been working on the Knowledge Transfer Network. You mentioned that earlier. Can you give us a broad update on who you have been talking to, the progress and any specific weaknesses you have identified that we could make recommendations to try to help fill?

Richard Hebdon: Yes, certainly. Thank you for that question. Through the Innovate UK Knowledge Transfer Network, the KTN, we launched the Phage Innovation Network in January 2023. That is a forum to bring together the different stakeholders in the phage space, broadly, not just



in human health but also animal health, crop protection and other areas where phages are being looked at for potential commercial applications.

That brings together that group and creates a forum to look at some of the obstacles and challenges that my colleagues have been talking about today, particularly things around the development and manufacture of phages and phage products because there will be some common challenges to that whether you are developing something to be used for human health, animal health, crop protection and so forth.

Essentially, it is quite early days. The work is led by my colleague Francesca Hodges, whom I believe is in the public seating area behind me. She has been leading on this for Innovate UK. We had a first meeting in March, which brought together a lot of the key stakeholders. Some of the outputs from that were incorporated in the written evidence to this Committee.

Essentially, through the Phage Innovation Network, we seek to do a number of things. One is to understand this emerging innovation area so that we can understand in the future how we can help to design the right kind of public interventions, how we improve cross-sector access to phage-based therapies—we can look at how these might play a role, for example, in reducing antibiotic use in future—creating the business community around innovations in phage research for sector growth, and also for changing perceptions of anti-infectives and their role in society. It has some broad aims.

On 16 May next month, there will be an event at the University of Leicester, which will coincide with the University of Leicester's Centre for Phage Research opening. All the various experts from industry, from SMEs in this space, from academia, clinicians and regulators will come together to discuss how we define the infrastructure and other things that we need to take this area forward.

Q205 Stephen Metcalfe: Are there any particular weaknesses? You said there is a lot of activity now.

Richard Hebdon: To build on that, by “weaknesses” do you mean weaknesses in terms of where the UK is lacking or generally there is a lack of capability or infrastructure?

Stephen Metcalfe: Yes. Perhaps infrastructure particularly or where you do not see any progress made where there needs to be some to make sure that the infrastructure and the ecosystem grows at an even pace.

Richard Hebdon: Yes. This was highlighted in our written evidence to the Committee. Certainly, through the Phage Innovation Network, we have identified a requirement for production facilities and other infrastructure—for example, biobanking facilities—analytical characterisation and formulation capabilities. Formulation of phage products will be important in the future if we are designing new products.



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Also, the need for specific regulations governing the use of phage-based therapies, which I believe you will talk about with our colleague Marc Bailey from MHRA later.

We also want to understand the economic disincentives specific to the phage, how that links to the wider market failures we have talked about in the antibiotics space, also, how we can get around some of the challenges with respect to clinical trials. As Jonathan and Tim have already highlighted, we do not have strong clinical trial evidence that demonstrates efficacy of phages as yet. These are the main weaknesses that have been identified so far.

Q206 **Stephen Metcalfe:** Thank you. You said that we do not have strong clinical trial evidence. Agreed. Do you have a sense that there is benefit for this? You said we do not have the evidence, but is there a general sense that this is useful?

Richard Hebdon: As a former microbiologist, I get excited by phages and other life science technologies in this space. Simply, we are not at a stage yet where we can make that determination.

Q207 **Stephen Metcalfe:** There seems to be a lot of activity. You have this meeting on 16 May. You met for the first time as a network in March. Do you get the feeling that you are playing catch-up with this or—bearing in mind that we have been talking about this in some form or another for 10 years—is now the right time to scale up activity?

Richard Hebdon: That is a good question. There is not necessarily a timing aspect. There is a sense of a critical mass of interest building. It is clear from our engagement through the Phage Innovation Network and more broadly that there is a lot of interest in this space.

There has been added impetus because of the whole piece around antimicrobial resistance more generally and, thus, people take more interest in some of the specific innovative technologies in this space. It is a convergence of different elements.

Q208 **Stephen Metcalfe:** I would like you to get your crystal balls out, have a little gaze into them and tell me where you think we will be in another 10 years with this, whether that will be a useful place to be. Are there any barriers you would like to highlight to us, as a Committee making recommendations to the Government, that we should address at this point to get to your vision of the future? Just a few words from each of you, if I may.

Dr Pearce: Securing that clinical evidence base is absolutely critical if we are to see this move through into wide-scale application and be of benefit. We should have a laser-like look at that and what that requires in terms of steps.

There is an element around capacity development. The field is exciting, but it is small in terms of the number of people directly active within it.



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Part of the management of that is to ensure that we link it to those other fields—formulation, immunology, clinical trial capability—so that, rather than having to necessarily build it out, we pull it in. These networking activities could be valuable for that.

I will come back to the point I made earlier about having a clear road map for the scientific challenges that, as a field, we need to overcome so that we have that as a shared vision. Then I come back to the funding. We have the vehicles to fund that work if we have that shared vision and are moving forward with it.

Dr Jinks: I am similar. I hope that we find in 10 years' time that we have an assessable evidence base that gives an indication of the real benefit and start to inform the value and how phage would be used in healthcare.

Alongside that, we should have a stronger regulatory science to support the clinical evaluation of phage and similar innovative approaches. A particular weakness right now, which I want to call out, is that the regulatory science does not enable the generation of the evidence that is necessary to evaluate. In 10 years' time we could see stronger regulatory science.

I expect that we will see a diversity of approaches that might be phage-based. While the discussions here have been more narrowly focused on natural phages, we should see how there can be different ways of using phage and what offers the most potential benefit, overall, in the human health space.

Alongside that, there should be a prioritisation of how phage can be used in other areas. Dr Pearce highlighted something that is critically important here: this as a one health issue cutting across to animals, plants and the environment. There are significant opportunities in these other spaces where phage might deliver real benefit much sooner. That would change the impact in the human health space as well.

In 10 years I expect to see much greater use of phage as a way of controlling bacteria and reducing the impact of AMR in other spaces and therefore taking pressure out of the human healthcare system.

Richard Hebdon: Tim and Jonathan have articulated this very well. Assuming that the science base points towards clinical efficacy and safety of these phages, in the next 10 years it would be good to see progress on the development of production and bioprocessing, appropriate regulation standards, analytical measurements and so forth, to enable the commercial development of phages.

First, I suspect that we will see real-world applications more likely in the animal health and agriculture space. For example, we are seeing already phages being used to control crop diseases. Lessons will be learned in



terms of how we develop, regulate and produce at scale those kinds of products.

Tim's point on the wider phage piece was interesting. It is not necessarily about natural phages either. The potential for engineered phages would then of course see them classified as advanced therapy medicinal products and, also, phage components. Phage lytic enzymes, for example, offer some interesting avenues in terms of specifically targeted antimicrobial technologies.

It is hard to predict the future. We try. We help to try to make it. It is the start of an exciting journey and, potentially, going forward, if the scientific challenges can be met, it could be an exciting industrial area for us in the future as well.

Q209 Chair: Thank you very much indeed. Your answers to Stephen were helpful and illuminating, but is there a chicken-and-egg problem here? You are the funders. You have all said that, in one way or another, we need the evidence base to be able to make progress on this. You have also each said, diplomatically, that the proposals that you get are not competitive at the moment, which is to say—and this is in some ways a good thing—you have so many high-quality research proposals in the field of AMR that they do not make the cut.

The dilemma is this: if you need to establish an evidence base but organically the process is not producing fundable proposals—and Dr Pearce said earlier that you do not want to ringfence funding for phages—how can you make this breakthrough? How can you have a strategy to get this evidence base in place without breaching what I understand to be your preferred approach of not ringfencing?

Dr Pearce: Yes. By ringfencing, it does not mean we do not have a proactive role to play. The opportunity of setting out this road map where we have that shared vision. As funders, we have a privileged position to have seen numbers of applications in the area and to understand where they were weak, collectively and independently. The opportunity to have an open discussion with the community to set out those features, how we collectively address them and, indeed, whether there are structural elements.

We have funding mechanisms that can provide support to build on the network and to provide funding for biobanking and other features. Looking at it as a collective whole, it is a shared problem. It is not that we are waiting for the community to come back with a higher-quality application. Because of the nature of the challenge and the nature of the opportunity, we are committed to working with the community to finding those shared solutions.

Chair: We are grateful. That was a very enlightening session. Thank you very much indeed for your written evidence and your appearance today.

Examination of witnesses

Witnesses: Professor Isabel Oliver, Dr Marc Bailey, and Professor Mark Sutton.

Chair: Can I invite our next panel of witnesses to join us at the table? As they take their seats, I will introduce them. Dr Jinks referred to regulation as one of the conditions that was necessary to have right for the development of the sector, so we will look at some aspects of regulation.

I am pleased to welcome Dr Marc Bailey, who was referred to earlier. Dr Bailey is the chief scientific officer at the Medicines and Healthcare Products Regulatory Agency. With him, and joining us at the table, are Professor Isabel Oliver, who is the chief scientific adviser and transition lead at the relatively new UK Health Security Agency, and I think is still the director of the National Infection Service. Is that right, Professor?

Professor Oliver: I was previously director of the National Infection Service at Public Health England, yes.

Q210 **Chair:** Thank you. Also joining us at the table is Professor Mark Sutton, who is the scientific leader in healthcare biotechnology at the UK Health Security Agency. He is also a professor for antimicrobial therapy at the Institute for Pharmaceutical Sciences at King's College London. Thank you very much indeed, all of you, for joining us.

We have discussed the funding challenges and opportunities. We are interested in the regulatory aspect of it. In the evidence that we have taken so far before the Committee, it has been put to us that the lack or the underdevelopment of a regulatory framework for phages is holding back the development of the intellectual property and the technology here. Perhaps I could have your response to that, starting with Dr Bailey.

Dr Bailey: Thank you very much for the question. The MHRA basically regulates any medicine or medical device on the basis of whether it is safe, effective and can be produced at sufficient quality for use in humans. We have a number of different regulatory frameworks, as it is said, which effectively enables us to make those decisions through what we call a process of benefit risk: what is the benefit for the patient of having the medicine versus the risk to their safety and their health of having the medicine? It is getting that balance right for every single one.

The regulatory frameworks are actually very flexible. We tend to develop regulatory frameworks in response to innovations in medicines and medical devices. If we see a framework coming through that is becoming increasingly common, we will develop a conceptual framework that may then become enforced in either guidance documents or even in legislation.



For phages, there has been an insufficient number of applications of consistency for us to have an absolutely rigorous framework. Instead, we are looking to develop our other existing regulatory frameworks to fit. The Committee has received written evidence where we have talked about some of the existing legislation in the Human Medicines Regulations. I will be happy to discuss those in detail but, perhaps in terms of an emerging regulation framework, at this stage we have a patient-specific or case-by-case regulation.

We see at the moment anecdotal evidence where people have identified a patient and they wish to try a phage therapy. That would fit, typically, at the moment, under what we call the specials or extemporaneous model, which is effectively only partly regulated by the MHRA and is controlled by others. If we see what the earlier people have been talking about, which is effectively that push-pull mechanism increasing frequency, we will then start to develop a particular regulatory framework reflecting the specifics of what is coming through. It is hard to make a ubiquitous framework. It is tailored by the medical condition, the delivery mechanism, the therapeutic mechanism of action and other parameters.

Q211 Chair: Based on the work that has been done so far in these individual cases and applications, what is the MHRA's current assessment of the safety and effectiveness of phages?

Dr Bailey: Our current assessment is that we have seen encouraging indications that they are safe and effective. There are the anecdotes in the literature where patients have been treated and the cases that have shown good efficacy. We are also encouraged by the fact that phages are ubiquitous in the environment. Humans have been living with them for many years and there are those at an effective safety level. Other regulators have also looked at this and it is of note that the FDA has given them the status of generally regarded as safe—GRAS—which is all encouraging.

However, there is ultimately that lack of clinical data. Clinical data is where you have applied robust scientific methods at scale to reach it. That would hold us back from saying, "Yes, this is absolutely safe". We do not have the evidence to reach that conclusion.

Chair: That is clear. Thank you very much indeed. I will turn to my colleagues, starting with Tracey Crouch.

Q212 Tracey Crouch: Dr Bailey, the overwhelming evidence we received is that GMP remains a major obstacle to both the medical and commercial use of domestically produced phages. What support are you currently offering to SMEs and clinicians to meet the criteria for GMP?

Chair: For those who may be tuning in and do not know the initials, GMP is good manufacturing practice. Perhaps you might give a brief definition or explanation of that term.



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Dr Bailey: Absolutely. Thank you very much for the question. Good manufacturing practice is a regulatory system for ensuring the quality of a therapeutic medicine or medical device in comparison to appropriate standards to ensure that quality. At its heart, it is a risk evaluation system. For each step in making a therapy, what is the risk that it has introduced something damaging to the patient or has been mishandled so that it is inactive?

For something like GMP, we understand why people are concerned. It is a regulation with a lot of steps and a very high quality. That high quality comes from the fact that these are used in people, and we expect the quality to be the highest. However, we tend to take a pragmatic approach to risk. We encourage early engagement with anybody working on this to understand their risk profile and where the particular damage is.

This is part of what we offer as an agency. If you are an innovator approaching for the first time and you believe that your product will be effective as a medicine, we offer an advice service and we encourage everybody to engage early with the advice service. It is free and easily accessed and will enable everybody to put down their thinking and our thinking without it being a regulatory decision. It is just a discussion. That will, we hope, give useful guidance.

That is then followed by a scientific advice process, which is designed to start getting into the real technical details. This is when you hope that the innovator has some evidence that can be discussed as opposed to an advice meeting. A subset of that is the innovative licensing and access pathway we are developing, which is where we work in combination with the health technology advisers, such as NICE, not only to look at our remit of safety, quality and efficacy but their remit of economic drive. NICE has been mentioned earlier as looking to help this area.

Finally, when you have strong clinical evidence, we will also give regulatory advice, but these are all case-by-case mechanisms. It very much depends on what the innovators come to us with as to what will come out of it.

Q213 Tracey Crouch: Thank you. That is very helpful, and people will take some comfort from your response. I think it is also important for the record to say that, while we did receive a majority of evidence saying that there was an issue, UK Phage Therapy argued that it was appropriate for medicines to be manufactured in accordance with GMP, which, although costly, is a surmountable obstacle. People who have had an alternative experience of the process may take some comfort from your reply there.

That said, the USA permits domestic non-GMP phage production for compassionate cases and Belgium allows such production to prescribe specific phages to individual patients. You talked about some of the regulatory reforms earlier on in your response to the Chair. Is the MHRA considering perhaps drawing from the experience of Belgium and the USA



regulatory models, as a basis for allowing UK non-commercial production of phages for individual patients?

Dr Bailey: We would absolutely consider it. It would come down, again, to the application. It is difficult to do a generic process. We also deliver in terms of a particular innovator. As I said earlier, it depends on what they are attempting. There is the element—as has been mentioned by Mr Hebdon—around formulation: how the phage is prepared, how it is manufactured and how it is administered to the patient, all of which would have to be considered. This is what usually drives it into a case-by-case evaluation.

Q214 **Chair:** You say that the experience of other countries could be used on a case-by-case basis, but is it not the case that what Tracey has described is a generic set of approvals not to be compliant with good manufacturing practice in the USA? If they can have a generic approach, why should we not?

Dr Bailey: It is difficult to understand. We see that people approach this, effectively, under special or extemporaneous productions—and this is in the written evidence—where, in the case of an individual patient, they decide that phage therapy is most appropriate. That lies outside our immediate regulations. It lies with other bodies. Our advice would still be to understand the quality and the safety of what is being driven there in that case, but we cannot actually manufacture it.

What we can do is learn from these other partners. If you look at the magistral method, we can consider whether we need to develop guidance to enable it more clearly and publicise that guidance. Similarly, the work in Australia—

Q215 **Chair:** Just on that, Dr Bailey—sorry to interrupt—the magistral method is the method employed in Belgium, I understand. Is it possible to summarise that briefly for those who may not be familiar with it?

Dr Bailey: Certainly. The magistral method is—if you do not mind me checking my notes to be absolutely sure—for, basically, unlicensed medical products. They are supplied to a bona fide, unsolicited order and formulated in accordance with the specifications of an authorised healthcare professional for use on an individual patient.

In effect, the patient care team takes the decision to work with the pharmacist to develop a preparation and administer it to the patient. That is in line with what we call the specials in the case, but would need to be developed case-by-case. It lies outside our immediate remit, so it would be a discussion with our other regulatory bodies to ensure it happens.

Q216 **Chair:** If there was a desire to do that here, what other bodies would be required to change their rules to accommodate it?

Dr Bailey: I could not give you an absolute answer to that today. I will certainly look to make sure we come up with a complete list. We know



that various of the pharmacy bodies would be involved but, as I say, I am happy to provide that as a written answer.

Chair: Thank you, Dr Bailey. That would be very helpful.

Q217 **Carol Monaghan:** To follow on from that, in one of your earlier responses, Dr Bailey, you talked about the lack of clinical data being problematic. Is clinical data from other countries considered evidential whenever we are considering phage use here?

Dr Bailey: In general practice when developing a medicine, yes, we accept clinical data from other countries, as long as the people providing those data show that it has been done in compliance with our own requirements. Effectively, that is a robust method that fits in with clinical practice and making sure that the data have been collected at a sufficient level of quality for us to make a decision. If we cannot make a decision, we would always go back to the applicant and explore what the holes are.

The issue here is that we have not seen very much around phages at all, even from other countries. That data has not been submitted to the agency, and if it is not submitted, we cannot draw an opinion on it.

Q218 **Carol Monaghan:** There is also some evidence of the effectiveness of phage use within food and agriculture, and their use among animals for treatment of animals. Could that be used as evidence when talking about use of phages with compassionate cases?

Dr Bailey: We would absolutely look at that case in terms of understanding the details. The regulations around a human medication or therapeutic product are very highly demanding, because of their use in humans and the requirement for the highest levels of safety. There are differences between the regulatory framework for that and for, say, food or an agricultural product. We would definitely look at the evidence that is available, but it would be case-to-case about how applicable it is and what the gaps are between the agricultural practice and the human practice.

Q219 **Carol Monaghan:** We have also heard that phages could be treated like flu vaccines, where individual phages could be stored in biobanks, assessed for safety and then combined as required for specific bacterial infections. Could you tell us something about the merits of that approach?

Dr Bailey: It would be very much a merit approach because that would mean that the phage has been characterised, and some of the issues about making it at scale—which is what you need to treat a patient—must have been addressed. It is of note that other countries, particularly through the STAMP system, have looked at some of those tests that would be required.

Yes, we would welcome applications if they were using phages from an appropriately curated biobank. I am aware that funders in particular are



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addressing that phrase, “appropriate curation”. It is something that we are developing, and we would look at the evidence.

Q220 **Carol Monaghan:** Appropriate curation. That brings us back to GMP again, does it?

Dr Bailey: Not necessarily for a biobank, no. GMP is a good manufacturing process. This would be GMP as it relates to the source material. Of course, with a bacteriophage you have a very specialised growth criteria. That is where it heads into GMP, but it is not an exclusion under GMP; it is part of the controlled risk we would consider under GMP.

Q221 **Rebecca Long Bailey:** Professor Oliver, what assessment has the UK Health Security Agency made of the potential for phages to address antimicrobial resistance?

Professor Oliver: Thank you very much and good morning. Our assessment is that bacteriophage therapies offer a very interesting alternative treatment for resistant infections, used either instead of antibiotics or in combination with antibiotics. They provide some hope and exciting opportunities, in what is obviously a very complex and challenging situation in relation to antimicrobial resistance.

The UK Health Security Agency works to support the Government mission to contain and control antimicrobial resistance by 2040. As you know, in that vision there is a description of the need to develop new diagnostics, new treatments, new vaccines and interventions to tackle AMR, and we do need multiple tools to do this effectively.

We also contribute to the delivery of our five-year AMR action plan. The five-year AMR action plan has a commitment to explore new and alternative treatments, including phage therapies but also immune modulators, monoclonal antibodies, biofilm inhibitor materials and others. In that context, we have a number of deliverables in our own contribution to the AMR action plan. That includes supporting research and training in alternative treatments, including bacteriophages. We have a number of research studies under way. We also support training of PhD students, we have had significant numbers of visits, and we have good collaboration with academia.

We also have a deliverable around the development of standardised methods for the evaluation of new therapies, and we have work under way to evaluate a cocktail of synthetic phages for the eradication of *Pseudomonas* biofilms.

Importantly, we also have a deliverable around rapid antibiotic susceptibility testing because diagnostics are a key component. It is not just about the development of safe and effective treatments in the context of bacteriophages but also thinking about how we might be able to deploy them and use them in practice, including in the NHS, and the development of rapid diagnostic tests is critical to that.



Q222 Rebecca Long Bailey: You mentioned the five-year AMR action plan and that you had the ability to explore new treatments, and you mentioned deliverables specifically a few times. Can you just elaborate on the deliverables that relate to phages, what funding you have allocated, and how far those particular projects or areas have developed so far?

Professor Oliver: The UK Health Security Agency is not a research funder, as you know. In the area of bacteriophages at the moment we have several pieces of work. One is funded through NIHR infrastructure funding, through a programme called Open Innovation in AMR. It is a project to help us develop the infrastructure that we need to develop and evaluate new treatments, including bacteriophages. We have used that infrastructure that we have developed to collaborate with academia, including the universities of Southampton, Exeter and others, to help develop the evidence base that you have been hearing this morning is so needed.

We use our own skills and expertise to address the priorities of the organisation, obviously including AMR. At the moment, we have scientific teams led by Professor Sutton—who you will hear from—doing work to identify phages for future treatment and to help us understand the mechanisms and impact of resistance, because there is still much that we need to learn and understand about the pharmacodynamics and pharmacokinetics of bacteriophages. As I said earlier, they provide an exciting opportunity and hope for the future, but the science required to develop them into a treatment that is safe and effective is still under development.

As I mentioned, we have a programme of work to develop rapid diagnostic methods to enable the use of bacteriophages in clinical practice. There is a third programme or third deliverable where we are also receiving funding from the National Institute for Health Research, through a programme called Invention for Innovation, which links specifically to that diagnostics component. Professor Sutton is the lead investigator for some of this work and he can explain in more detail.

Q223 Rebecca Long Bailey: Thank you. Is there any plan to increase the resources that you currently have targeted at phage development and research?

Professor Oliver: At the moment, we are supporting the Department of Health and Social Care on the development of the next five-year AMR action plan. Within that, we are seeking to understand the research needs and priorities and the key gaps in evidence to allow us to maximise the opportunities that exist from alternative treatments.

At the moment, in terms of developing areas for the UK Health Security Agency, we have a PhD programme that we fund, and we are just in the process of allocating the next round of PhD projects. We have two specific projects that we are considering in this area.



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As the UK Health Security Agency, we are also keen to explore opportunities to support the manufacturing of bacteriophages. In our scientific teams at Porton Down, we have people with skills, expertise and experience of working to GMP standards who could work with academia, SMEs and industry to enable the manufacturing of bacteriophages. We are keen to explore that but that would be subject to a business case for external funding.

We have a number of new research applications for funding in collaboration with partners because we have some unique skills, expertise and capabilities but they are best deployed working in partnership with industry and academia.

Q224 Stephen Metcalfe: Good morning, everyone. Professor Sutton, we heard earlier from Mr Hebdon about the work of the phage Knowledge Transfer Network. Could you say what interaction the UKHSA has had with the phage community and with the network?

Professor Sutton: Certainly. Good morning. We have had academic collaborations in the phage area for over 10 years, particularly with Dr Anne Turner at the University of the West of England. We have always taken a route that is very collaborative. We work still with a lot of academic groups—we do not try to do everything in-house—because we think that is the most effective way forward.

I am delighted to say I was asked to chair the Phage Innovation Network. As explained earlier, it is a very new entity, but I am very excited to see that programme of work develop. The initial meetings have been really encouraging, looking at the engagement from the community. In that broader phage area, I am also on the advisory board of Antibiotic Research UK and the CF AMR Syndicate. We have made written submissions to the Committee.

Q225 Stephen Metcalfe: That is in your capacity as representing UKHSA?

Professor Sutton: Indeed.

Q226 Stephen Metcalfe: You feel that you are fully embedded in this, that the community is now coalescing around—

Professor Sutton: Yes. As Professor Oliver explained, we have unique capabilities within UKHSA. This open innovation concept is about leveraging those to help the community to move forward more quickly, particularly in the translational science base where we think we have particular skills.

Q227 Stephen Metcalfe: Excellent. We have heard quite a lot that there is a lack of evidence or of an evidence base. When you are looking at the effectiveness of phages obviously you draw on evidence that is available in the UK, but do you also look at evidence that is published abroad?

Professor Sutton: Yes, absolutely. Organisations like Phage Australia have made enormous gains in a very short time. We have also had



interactions with the defence community in the US. There is a company called Adaptive Phage Therapeutics, which came out of the United States Department of Defence funding. We have had some interactions through US colleagues as well.

I guess our role is understanding that applied translational story. We are very mindful of the evidence gap in terms of clinical studies. It is also thinking about models of how phage therapy would be applied in practice, whether it is a series of single phage or a cocktail of phage—as I am aware you have had evidence around—and thinking about what sort of constraints it might place on NHS or UKHSA microbiology labs, if they were asked to support that sort of technology roll-out; and where the gaps might be and where we would need to work with others to support that translational application in the clinic.

Q228 Stephen Metcalfe: A wider, more general question is: do you all believe that phages will play a significant role in the future in tackling antimicrobial resistance? Is there a question of getting there or is there—

Professor Sutton: Echoing the comments earlier from the first panel of witnesses, we also take a portfolio approach. We don't just look at phage, we also look at microbiome modulation, biofilm disruptors. There is a very strong likelihood that we will need a range of different therapeutic entities. You could argue that our current arsenal is too narrow and, therefore, we need a range of different approaches in the future.

To your 10-year question from earlier, I would hope that the framework is in place where things, like phage or maybe some of these other biologics, can come into the market and play a full role within a 10-year window. Maybe they are not in the clinic in 10 years, but certainly that framework and understanding of the evidence base should be in place by then.

Professor Oliver: From my perspective, and maybe just to expand a little bit on that, the emerging evidence is very encouraging and so I think it is likely that they will play a role. How big a role is difficult to say at the moment. As well as needing a portfolio of therapeutic options, we must not forget that to really tackle AMR we need a broad range of interventions, from improvements in infection prevention and control, to increased awareness and behavioural aspects. We also need to explore the potential role of vaccines.

There are enormous developments in the area of vaccines that might help us reduce the burden of infection and consequently reduce the burden of AMR. It is a very big problem and, therefore, it needs a full range of solutions, not just therapeutic solutions.

Stephen Metcalfe: It has a role to play?

Professor Oliver: The evidence suggests that it will have a role to play. How big is still to be understood better.



Dr Bailey: A similar answer, ultimately, which is that the AMR therapy is absolutely required. We welcome a portfolio approach of innovators attempting a whole range of different methods, and we seek to make sure our regulation is flexible enough to reach that safety and efficacy decision promptly so that patients can benefit.

Phages have strong anecdotal evidence of use, but what we tend to find is that people are very creative with their uses of them. We welcome creative uses or maybe combinations with other parts of the portfolio to achieve the end result. We would absolutely work to support any such step forward.

Q229 **Stephen Metcalfe:** This is an opportunity to put something on the record. Are there any particular areas of development you would like to see that would make this happen and make it easier to assess their efficacy? Is there something we should be recommending to Government?

Professor Sutton: I could take a run at that. The Chair mentioned a chicken-and-egg situation earlier. Arguably, we are in the same situation when we were thinking about that clinical evidence base. Without GMP manufacture, you cannot generate the products that the regulators can address and that then go into clinical trial to generate the evidence that they are effective. I think—and it is a personal view rather than a UKHSA view—that there needs to be strategic investment in some of those components to allow us to unblock that cycle and potentially be able to move forward.

Stephen Metcalfe: Very helpful, thank you.

Professor Oliver: You were exploring this issue with the funders this morning. We do need targeted funding for phage infrastructure and translational research. We probably also need to invest in national manufacturing capacity. We will certainly continue to monitor this as part of our progress with our AMR action plan. It is one of our reportable indicators and we do monitor this.

Stephen Metcalfe: Mark, a final word?

Dr Bailey: From our perspective, it is understanding the regulatory need: what kind of research, as regulators, we need to perform in order to adapt quickly and to understand where the risks are for the patient from any of these therapies.

Chair: I would like to thank Professor Sutton, Professor Oliver and Dr Bailey for your very clear evidence to us on the regulatory aspects.

Examination of witness

Witness: Dr Morwenna Carrington



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Q230 Chair: I would like to introduce Dr Morwenna Carrington, who is the deputy director for UK health security at the Department of Health and Social Care. Dr Carrington has responsibility for managing the risk of antimicrobial resistance, as set out in the National Risk Register for civil emergencies, and also oversees delivery of the current UK AMR national action plan. Thank you very much indeed for joining us today.

The Government's five-year plan to tackle antimicrobial resistance noted that the Government are exploring what role phages could play in this. Perhaps, Dr Carrington, you could set out what progress you feel has been made and what the next steps are.

Dr Carrington: Thank you. I would like to start off by saying how very much we welcomed the inquiry looking at this issue. We look forward to the recommendations coming out of this inquiry. Thank you very much. It is a very interesting area for us.

As you have set out, the Department for Health and Social Care is the lead Department for responsibility for tackling the risk of antimicrobial resistance, but it is important to note that our approach to tackling antimicrobial resistance covers the broad spectrum of the risk of AMR across the whole of the One Health spectrum—that is not just human health but also animal health, food, the environment, plant health and so on—and also across all four UK nations and with partners internationally as well. It is not just domestic efforts.

We regularly monitor progress against all of the commitments in the national action plan. We have an annual review process. The last one was in the summer of 2022, and we will be doing another one this year as we enter the final 12 to 18 months of this five-year action plan period.

You will also be aware that we did a comprehensive midterm review of all of the commitments in the national action plan in 2021 and, as a result, published an addendum to the national action plan. The commitment review was stimulated by three primary issues: first, to make some of the commitments SMARTer, so more specific, measurable, achievable, realistic and timely, but also picking up on some of the lessons learned from Covid and noting some of the significant progress that had been made in the animal health sphere against some of the commitments there.

As a result of that mid-term review, we made some changes to some of the commitments. One of the changes we made was to make a more explicit reference to the need to look at alternative therapies, including bacteriophages. Whereas before it had been mentioned in the national action plan, this was now specifically bringing into one of the commitments. That was published last year.

Obviously, in terms of how much progress we have made against the specific commitment on bacteriophages, we are at a relatively early stage despite now entering year four of the five-year national action plan.



We are still at an early stage in terms of monitoring progress, but we are really interested to see an increasing groundswell of work domestically but also internationally on bacteriophages, which I think has been evidenced by some of the work that Mark Sutton set out—the work that the UK Health Security Agency is leading on—but also this establishment of Innovate UK's Knowledge Transfer Network on phage therapy. It is going to be really interesting to see how this gets taken forward.

Q231 Chair: From the previous sessions, you will have heard that there has been some frustration among practitioners and researchers in the field of phage. That things have not been progressing as quickly or as decisively as they might hope. Are there moves afoot to be able to achieve a breakthrough here or are we doomed to a cycle of them not quite breaking through into the mainstream?

Dr Carrington: I would say two things. First, referencing again the broad spectrum in terms of our approach to tackling antimicrobial resistance as a threat, we are very keen that we look not just at the potential uses in relation to human health but at some of the other use cases, such as in agriculture. We have heard examples of animal health and in the plant health sphere, and there are some specific projects where I think bacteriophages have proven to be efficacious, in tackling bacterial infections in poultry flocks, for example. In terms of progress, I think we would want to look across the broad range of potential use cases.

I would draw out not just the animal health and the agricultural sphere but, also, I think that there is some difference of opinion about where bacteriophages might best be deployed in human health: whether we continue to use them more in relation to compassionate use, in bespoke, named cases where perhaps traditional treatments might have failed, or whether we pursue bacteriophages as being more of a first-line treatment, perhaps in combination with antibiotics, for specific conditions on more of a population level. Those three different, broad use case categories will all need to be explored in parallel.

The second point is that obviously we have a very large number of commitments in the current national action plan that cover the breadth of the different types of ways that we want to tackle the risk of antimicrobial resistance. The national action plan is currently divided into three pillars.

The first pillar looks at reducing need for and unintentional exposure to antimicrobials. That really is about reducing the infection burden in the first place. That, again, is where one of the use cases of bacteriophages might come in, particularly in the agricultural sphere, reducing the bacterial load in poultry or pig populations, for example.

The second is about optimising the use of antimicrobials, and I will come back to that because the third pillar is about investing in innovation, supply and access. Currently, the commitment on the bacteriophages sits in the third pillar but obviously we have a range of commitments—over



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100 different commitments—in the national action plan across all three pillars.

Therefore, we need to take a balanced portfolio approach to the extent to which we invest in each of those different areas. We are very interested to see the potential for bacteriophages as another tool in our armoury to tackle the risk of antimicrobial resistance, but we would not want to overemphasise the potential for bacteriophages to the detriment of some of the other advances that we want to make across the three pillars.

Q232 Chair: In terms of the research aspect, the Government has a strong interest in research being carried out, and part of the action plan and the risk register is antimicrobial resistance. A lot more money is being given to the research community, principally through UKRI. Public-funded research is increasing to about £20 billion a year. To what extent is the Government giving a steer to UKRI that they want and expect funding to be deployed in line with this Government priority?

Dr Carrington: It is important to recognise that, in terms of research funding into antimicrobial resistance, we have three different potential routes, so not just funding through UKRI—although that is extremely important—but also direct funding through the National Institute for Health and Care Research, NIHR. We also have some dedicated health protection research units, which are NIHR-funded but co-delivered with the UK Health Security Agency. There are different ways in which we can support AMR research.

Research also is a dedicated programme within the current five-year national action plan and we have a long list of commitments on AMR research. We have been doing a lot of work under the auspices of our chief scientific adviser, Lucy Chappell, to prioritise those research commitments and match those up with the funders of that research through the Funders Forum, which I think you heard about this morning.

We have been doing a lot of work to prioritise the research to make sure that the research that we need to get funded gets funded and gets delivered, but I would echo the point that I think was made by other witnesses earlier this morning: that while we work very hard to work with funders and the research community to emphasise the importance that Government place on AMR research more generally, we would not want to specify or earmark specific research funding for bacteriophages over and above some of the other research priorities in the national action plan.

Like others have said already, we are very receptive to research applications coming forward, but each would be judged on its own merit through a robust peer review process to determine which ones would be taken forward for funding.

Q233 Chair: Finally from me, what work is taking place between the UK Government, other Governments around the world and international



bodies like the WHO to co-ordinate and join forces in this research and development?

Dr Carrington: I am not aware of any direct work that we are doing with the World Health Organisation but I mentioned some of the specific research projects. We do have a global antimicrobial resistance innovation fund, which is called GAMRIF. GAMRIF's priority is to support research and development for the benefit of lower and middle-income countries primarily, but it works with other funding and delivery partners to jointly and co-fund some research projects.

There are some specific examples of where GAMRIF has supported research on reducing, as I said, bacterial load in poultry flocks in Kenya and in Pakistan, for example. There is another project, I think, about tackling necrotic enteritis in poultry flocks in China. There is a lot of partnership work that we undertake with other partners globally on bacteriophage research.

Q234 **Tracey Crouch:** First of all, I would like to apologise because I will have to leave very quickly to meet a constituent, so I am not being rude.

You mentioned in your opening responses the work that is being done on animal health and plant health. Who is the Government lead for phages? Is it the Department of Health or is it separated among the other Departments as well?

Dr Carrington: Inasmuch as there is probably a Government lead for bacteriophages, I would probably refer to Professor Mark Sutton—who was on the panel just before this—in the UK Health Security Agency. Obviously, we work very closely with the UK Health Security Agency and with all of our delivery partners across Government, including the Department for Environment, Food and Rural Affairs, the Veterinary Medicines Directorate, and the Food Standards Agency. I am aware that Mark Sutton co-ordinates very closely with colleagues in the Animal and Plant Health Agency, VMD, and DEFRA as well, to look at bacteriophage applications across the One Health spectrum.

Q235 **Tracey Crouch:** If there were to be a strategy specifically on phages, you would expect the Department for Health to lead that strategy?

Dr Carrington: Given the Department for Health's role in being lead Department for antimicrobial resistance overall, yes. We would set that out in the national action plan. It is worth noting that we are in the process of developing the content for the next five-year national action plan at the moment.

You will be aware that we published a call for evidence just before Christmas, which closed at the end of January. We received just under 200 responses to that call for evidence to inform the development of the content for the next national action plan, and a handful of those responses referenced bacteriophages and their potential applications in the future.



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Q236 **Tracey Crouch:** I appreciate you may have to write to the Committee with the answer to the following question: are you aware of what the total phage resource is that is deployed against Government, including the UKHSA and the MHRA, in terms of spend, staffing and function?

Dr Carrington: It would be difficult to estimate, and I think it would be difficult to put a precise figure on it, in terms of both funding but also the staff resource being allocated to bacteriophages.

Q237 **Tracey Crouch:** Do you think you would be able to write to the Committee with some form of response, to give us an indication? I appreciate it might be difficult to give a precise—

Dr Carrington: I can certainly take that away as an action.

Q238 **Tracey Crouch:** Thank you. What steer, if any, if the Government giving to UKRI in terms of its funding bodies in terms of phage research? Is it giving any specific direction?

Dr Carrington: Just referring to my previous answer, no specific direction on bacteriophages. However, we work very closely with UKRI through the AMR Funders Forum to ensure that Government's priorities for research on AMR more generally are taken forward. We are very pleased to see the importance that UKRI are placing on antimicrobial resistance within their tackling infections theme.

Q239 **Carol Monaghan:** In one of our earlier sessions in this inquiry we heard about the cost to the NHS from conditions such as diabetic ulcers. The figures were quite staggering. I think something like 1% of the NHS budget was quoted as being spent on that particular condition. Have the Government made any sort of estimate of the savings to the NHS that phage therapy might be able to produce, specifically where antibiotics have failed?

Dr Carrington: The short answer is no, but I would add to that and expand by saying, first of all, that we recognise the huge cost burden that is placed on the NHS as a result of antimicrobial resistance and also, separately, as a result of diabetes. We are really interested in the potential for bacteriophages to deliver cost savings to the NHS.

I would also refer back to the point I made about the fact that there are a range of potential use cases through which bacteriophages could reduce the cost burden on the NHS. Whether that is by reducing the burden of bacterial infections in food-producing animal populations and, therefore, reducing the threat of foodborne infections and also zoonotic infections or, separately, the potential benefit in terms of direct treatment at a population level for specific clinical pathways, for example, perhaps, diabetic foot. The third is the more bespoke, last-resort type of approach used for bacteriophages at the moment.

In addition to all of those potential use cases, there are also the direct savings that bacteriophages have the potential to deliver and the indirect



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savings. We have been focusing very much on the ability of bacteriophages to tackle bacterial infections that have proved to be resistant to antibiotics, but the literature also highlights the potential for bacteriophages to make bacterial populations re-susceptible to those antibiotics. There is a potential for bacteriophages to extend the lifespan of some of our existing antibiotics.

Therefore, trying to do an estimate of the potential savings to the NHS would be quite complex. We would need some more specific use cases to be developed before we could do that analysis. We are aware of the work that has been done in Scotland on that particular topic and it looks very interesting.

The last thing I have to say is that, obviously from a patient safety perspective and a patient outcome perspective, our primary concern is better patient outcomes in terms of being able to tackle antimicrobial resistance.

Q240 Carol Monaghan: I appreciate your answer and that you are not able to commit to a figure. Would it be fair to say that the savings are potentially substantial?

Dr Carrington: I think it would be fair to say that it has potential, but I would also like to highlight the fact that this is just one potential alternative therapeutic to tackle resistant infections.

I don't want to draw too much on the Covid example, but Covid really demonstrated the importance of having robust clinical trial data to demonstrate efficacy. A lot of things can look very promising in the early days that do not then prove to be as efficacious or as safe as people would have hoped. The Covid RECOVERY trial highlighted that. There were some examples of therapeutic substances that were trialled through the RECOVERY trial that then proved not to be as good as hoped. It is really important for us to look at the clinical trial data and determine which are going to be the most useful.

Carol Monaghan: Which we don't have very much of.

Dr Carrington: Which we don't have very much of, no.

Q241 Carol Monaghan: Can I ask you what work the Government are doing with companies who want to manufacture phages to scale and how regulation is being considered, particularly around GMP standards?

Dr Carrington: I don't think I have anything more to add to what the witness from the MHRA said in the earlier session. The regulation of medicines is very much the purview of the MHRA. What our colleague said earlier spells out the work that it has been doing to work with companies on good manufacturing practice, for example.

Q242 Rebecca Long Bailey: Just a very brief question from me. There have not been any phage clinical trials in the UK since 2008. How concerned



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are you that the UK might be falling behind other countries across the world on this research?

Dr Carrington: I am not worried about the UK falling behind generally. As you know, we are a world leader in tackling antimicrobial resistance and our previous chief medical officer, Dame Sally Davies, is now the special envoy for AMR on behalf of the UK. We continue to promote the importance of tackling antimicrobial resistance globally and I think our role in tackling antimicrobial resistance is recognised. We have also been a world leader in the subscription-style model for incentivising the development of new antibiotics. We have a lot we can point to.

I also think we are doing a lot to invest in clinical trial infrastructure more generally. I know NIHR have put a huge amount of funding into strengthening our clinical trial framework in the UK. I think there is a recent review that has been announced, to be led by Lord O'Shaughnessy, to look at our clinical trial infrastructure in the UK as well. Recognising the importance of robust clinical trial data, we are doing a lot to invest in the clinical trial infrastructure and the framework within the UK.

I would just refer back to the other point, that we welcome applications from researchers and companies to conduct clinical trials on bacteriophages because it is evidence that we think we sorely need.

Q243 Aaron Bell: Are there any plans that you are aware of for the UK to develop and fund phage biobanks, as has happened in some other countries, which could then be readily accessed by researchers, clinicians and even SMEs as well?

Dr Carrington: We do not have any plans at the moment to invest in that area. Again, it would rely on there being a robust evidence base to justify the expenditure. Having read the literature and some of the other evidence that has been submitted to the Committee, you can see that it would be a useful part of the toolbox to facilitate bringing bacteriophages forward. It is definitely worth looking at.

Q244 Aaron Bell: My colleague, Carol Monaghan, mentioned regulation and it is one of the things that is holding people back. In terms of foundational research, we have a world-leading base here. What assessment has the Department made of the potential for the UK to build on that, essentially, and for the NHS itself to become a world leader in phage therapies and phage products?

Dr Carrington: We definitely have the potential. As I said, we are already a world leader in antimicrobial resistance more broadly. I think the work that has been referenced already in terms of establishing the Knowledge Transfer Network through Innovate UK is an example. Some of the work that is being taken forward by the UK Health Security Agency and being led by Mark Sutton is really interesting and this is definitely a growing area. I would be confident that the UK could play a leading role.



Q245 **Aaron Bell:** Looking at it from a commercial perspective as well as the clinical-medical perspective, what thoughts do we have about the potential for the UK to become a place for inward investment into phage research and phage production, to get companies based here on that, or would that require the regulatory issues to be addressed first, do you think?

Dr Carrington: Probably, yes. Again, we have a lot of potential. I would also flag that we need to get the regulatory and production bits sorted in the UK. I know that good manufacturing practice has been highlighted as a potential barrier, but it also supports our ability to export production as well. We should not underestimate the importance of good manufacturing practice in terms of mass production of bacteriophages.

Q246 **Aaron Bell:** More generally, do you think we are agile enough to adapt to this with the speed that we may need to, if we get positive results from either studying the literature abroad or any small-scale trials we do in the UK under compassionate use and so on? Are we likely to be agile enough to change our regulations with deliberate speed—if that is what we decide to do—or do you think it would end up taking quite a few years to get there and we would run the risk of being outpaced by the Belgians and Australians of this world?

Dr Carrington: It would depend on the evidence base.

Aaron Bell: Again, evidence base.

Dr Carrington: We can move quickly where a persuasive case can be made for either regulatory change or for continued investment in some areas.

Q247 **Aaron Bell:** If the evidence is there, you think we could move fairly quickly to adjust the regulations and encourage that inward investment?

Dr Carrington: We would have to work with MHRA on what was feasible in terms of the regulatory pathway, but yes.

Chair: Stephen, do you have a final supplementary?

Q248 **Stephen Metcalfe:** Two areas, I suppose. In the light of everything you have said, do you see phage technology as a game changer that needs to be supported to find all this evidence that is missing, to get us to the point where it is a deployable, really important part of our fight against infection, or is it for the sectors and for scientists to prove that to you and then you will provide support as required to make it work? I suppose what I am trying to get to is: what are your hopes for this, versus reality?

Dr Carrington: My hope is that bacteriophages are definitely part of our armoury, part of our toolbox because—as I think Mark Sutton said this morning and some of the other witnesses have said already—there is no single silver bullet that is going to help us solve the problem of antimicrobial resistance. We do need a range of technologies, a range of



alternative therapeutics and a range of different interventions, but bacteriophages could certainly play a part in that.

As I mentioned before, part of the problem is that there are a range of different use cases. The effort is being spread across different potential applications rather than it being focused on solving one particular problem. That is probably right at the moment, because we do want to explore all the potential applications for bacteriophages rather than focus too much on one, which may not deliver the anticipated benefits that we hope.

It is right at the moment, as I say. The most benefit to come from bacteriophages might come from an area that we do not currently think of because there are so many different ways that they could be applied.

Q249 **Stephen Metcalfe:** This a technical question, which I meant to ask earlier and you may not know the answer: are phages subject to the same risk of developing resistance from bugs? I don't know the answer to that.

Dr Carrington: There is the potential for bacteria to develop resistance to phages in the same way that they do to antibiotics at the moment, and that would definitely need to be looked at. The benefit of phages is the fact that there are so many different types, hence the focus on producing cocktails of phages to tackle bacterial infections so that, even if resistance develops against one, you have alternatives that you can try.

The range of potential alternative types of bacteriophage is so vast that there is a lot more confidence that, even if resistance does develop, it will not cause quite the same negative impact as resistance to antibiotics, where we have a very small range of products.

Chair: Thank you, Dr Carrington, for your evidence today. Thank you to all of our witnesses this morning and, indeed, all of the witnesses throughout this inquiry, including those who took the trouble to submit some written evidence to us. I was grateful and pleased that Dr Carrington said that the Government were looking forward to our report and recommendations on this. We will reflect on all of the evidence that we have taken and make some recommendations in the spirit of being helpful to the Government, to the nation, and to the scientific community in this very interesting and, hopefully, important area.