

Science and Technology Committee

Corrected oral evidence: The antimicrobial potential of bacteriophages

Tuesday 14 January 2025

10.20 am

[Watch the meeting](#)

Members present: Baroness Brown of Cambridge (The Chair); Lord Berkeley; Lord Borwick; Lord Drayson; Lord Lucas; Baroness Neuberger; Baroness Neville-Jones; Baroness Northover; Lord Rees of Ludlow; Viscount Stansgate; Lord Wei; Baroness Willis of Summertown; Baroness Young of Old Scone.

Non-committee member also present: Baroness Walmsley.

Evidence Session No. 1

Heard in Public

Questions 1 – 20

Witnesses

[I:](#) Professor Michael Brockhurst, Professor and Chair of Evolutionary Biology, University of Manchester; Professor Joanne Santini, Professor of Microbiology, University College London; Professor Martha Clokie, Professor of Microbiology, University of Leicester.

[II:](#) Dr Jason Clark, Director and CSO at NexaBiome; Dr Clare Trippett, Principal Strategic Opportunities Manager at CPI (Centre for Process Innovation)

USE OF THE TRANSCRIPT

1. This is a corrected transcript of evidence taken in public and webcast on www.parliamentlive.tv.

Examination of Witnesses

Professor Michael Brockhurst, Professor Joanne Santini and Professor Martha Clokie.

Q1 **The Chair:** I would like to welcome our witnesses this morning to the committee's evidence session on bacteriophages and their use. We would like to welcome Professor Michael Brockhurst, professor and chair of evolutionary biology at the University of Manchester; Professor Joanne Santini, professor of microbiology at University College London; and, joining us from Chile, Professor Martha Clokie, professor of microbiology from the University of Leicester. Thank you all very much for coming.

As a kick-off, I would like one of you—and I do not know which one it is going to be—to explain for a generalist audience what phages are and why we are seeing renewed interest in them, remembering that we have a mixture of skills and interests around this panel. I am an engineer, so for me this is all new stuff. Ah, it is going to be Professor Brockhurst.

Professor Michael Brockhurst: Phages are viruses. They infect bacteria. They do not infect other cells. They do not infect human cells, for example. They infect and replicate within bacterial cells and they kill the cell by bursting the cell to release viral progeny. Those viruses then go on and infect other bacterial cells. They infect very specific strains of bacteria, so they are potentially a very good treatment, because they can be targeted towards a particular pathogen and not have the collateral effect that antibiotics have on microbiomes in general.

The renewed interest in recent years is due to the rise in antimicrobial resistance. We are running out of clinical options of traditional antibiotics to treat some infections and bacteriophages are a potential alternative to traditional antibiotics.

The Chair: Thank you very much. That was very helpful. I would now like you all, just very briefly, to give us an introductory statement, setting out your roles, how you became interested in phages and what particular applications you are interested in seeing them being used in. Professor Santini, shall we start with you?

Professor Joanne Santini: I used phages as diagnostic tools during my PhD. That was a long time ago, in the late 1990s. I then had a bit of a gap. It was discovering the first megaphages. Normally, you think of phages as much smaller than bacteria, but we discovered some that are actually bigger than bacteria that are present in the guts of humans and animals.

There was a case at Great Ormond Street Hospital, where someone reached out to me asking if I had phages against one particular pathogen, because a child at the hospital had this pathogen in her gut and they wanted to get rid of it before she was going to have a stem cell transplant. That is what really made me interested in their therapeutic use.

This was a few years ago now and, since then, we have been looking at, rather than more personalised approaches, developing phage cocktails, which target bacteria that cause bloodstream infections. Initially, we started in Malawi, because neonatal sepsis is a huge problem across the world, but now we are looking more widely in the UK at using phages to target bloodstream infection pathogens.

The Chair: What do these megaphages sitting in our guts do?

Professor Joanne Santini: That is a good question. We do not know. We have sequenced the genome. These are big and we do not know what most of the genes do. They are targeting a particular bacterium in the gut that is, in some situations, good for your gut and, in other situations, not so good, if it is found in other parts of the body. These are different strains of the same organism. What they are doing is a really good question. Apart from killing the bacteria, that is one thing we want to find out.

Professor Michael Brockhurst: I am an evolutionary biologist and I was initially interested in phages because they are the most numerous biological entity on earth. We were interested in their ecology and evolution to begin with. In subsequent years, we became interested in using ecological and evolutionary principles to design phage therapies. How can you make phage therapies better able to negate resistance evolution or target particular organisms? What order should you use phages in?

Most recently, we have been interested in using engineering biology approaches to creating synthetic phage therapies. That is our main focus at the moment, with respect to phage therapy.

The Chair: That gives me the opportunity to advertise the fact that we published our report on engineering biology today. I advertise that for people who are listening to read. Thank you.

Professor Martha Clokie: I am a professor of microbiology at the University of Leicester and I am the founder and co-director of the first UK phage centre. We established this in 2023. So far, we have attracted over £6 million worth of investment. We run a team of about 30 academics, doctors and researchers, and we are largely

focusing on work to produce a national phage bank, collecting all of these numerous phages.

We already have a bank of perhaps 3,000 phages and we are trying to acquire and understand that key, fundamental resource and do the underpinning science that is needed to help translate phages into products. I am also the editor-in-chief of the journal *Phage*, which is the only journal to publish about phages, and am on the board of the Phage Innovation Network. I work closely with Jason Clark and Clare Trippett, who will be on the next panel.

The Chair: Thank you very much. That all sounds really fascinating. We are all intrigued that they are used much more widely in some of the eastern Europe countries than they are here. We are all intrigued to know why they are not more widely used in the UK. Indeed, if we are looking at antimicrobial resistance, what are the alternatives? What is the armoury of things we could use for antimicrobial resistance and where do these sit, in terms of the selection of weapons we have?

Professor Martha Clokie: This is really interesting. Essentially, they were discovered very early on in Tbilisi, in Georgia. The research, translation and usage in Tbilisi and the former eastern bloc countries never really stopped. During the Cold War, they did not have access to antibiotics, so phages carried on being used. They developed them and used them quite quickly to treat intestinal, skin and many other diseases.

They never stopped either that work or that translation whereas, in the West, after we discovered antibiotics, the complexity of phages was seen as being quite unnecessary. Why would you develop something complicated that required knowing what you were treating, if you could just use a single compound? Antibiotics were seen as being an easier solution, which really suppressed research in the area of using bacterial phages therapeutically.

Now, as was alluded to in the other answers, the huge issue with antibiotic resistance has motivated a resurgence of trying to work out, in a way, what we need to do to understand this complexity and to get it used within a UK and western context. That is the first part of the question.

The Chair: Does either of you want to add anything to that?

Professor Michael Brockhurst: Conventional phage therapy is quite a promising last resort-type treatment that we should be thinking about implementing in the UK, because we have this wealth of knowledge from other countries. We are not just talking

former eastern bloc countries. We are talking the US, Australia and lots of places with very similar health systems to us. Evidence is building up that phage therapy can be quite effective in various settings.

Taking a longer-term perspective, synthetic phage therapies are part of a broader set of treatments—we could call them engineered biotherapeutics—where we can leverage the knowledge from synthetic biology to create treatments that do things such as target particular pathogens, but also target resistance genes, for example, or plasmids carrying resistance genes.

There are two phases of this. Conventional phage therapy is ready today. If we were allowed to implement it, we could implement it broadly today. Then, in the longer term, we have a whole wealth of very innovative treatments that will come on stream as the fruits of the engineering biology investment come through.

Professor Joanne Santini: Can I just add one point to that? Even though phage therapy in Georgia has been going on for over 100 years, it is only really now that there are people around the world collecting the clinical data that we need to know the nitty-gritty of what is efficacious. How do you get the phage to the site of infection without the immune system clearing it?

We knew that phages worked, from the eastern European data, but I do not think we had the data we needed to be able to more widely use them and use them well, so they work. A lot of that data is now being collected across the world. We know they are safe and now we just need to know the best way to use them, just like any medicinal product.

The Chair: Are they the only alternative that we have for antimicrobial resistance to antibiotics or are there other approaches for antimicrobial resistance?

Professor Joanne Santini: If you asked me, “What do you want: an antibiotic or a phage against your pathogen?”, I would take the phage. We know what antibiotics do to our gut microbiome. Those effects are irreversible. The fact that phages are very specific is a great thing, because we know that they are safe and specific, and kill that pathogen.

There are other alternatives. Of course, people are looking at vaccines as well. One of the pathogens we work on, called *Klebsiella pneumoniae*, has a slimy capsule, like an armour. It has over 100 types of armours. There are issues with developing vaccines against pathogens like that, so we need something else,

apart from vaccines and monoclonal antibodies, as part of the arsenal to tackle antimicrobial resistance.

Professor Martha Clokie: There was a report commissioned by the Wellcome Trust and the Department of Health a number of years ago, and, of the 10 most likely alternatives to antibiotics, bacteriophages were considered among the top three.

I should make the point to follow on from the last question. Although we have this history of natural bacteriophages, we can now understand the genetic diversity and the genomes of phages, which we never have before. Understanding natural phages was one of the top three and then engineering phages. There are also products from phages. If we understand the molecular biology of phages, the genetics, we can just sometimes find the way that they kill pathogens, so you could use that one thing.

These are the top three of the 10. The other seven were, as Jo mentioned, vaccines, but also there are other antimicrobial peptides and immune modulators among the other main categories. There are other approaches but, as there are 10 phages naturally attacking each bacteria, there is nothing of the scale and scope that phages have as an alternative.

Lord Borwick: Could we have a link to that report that was mentioned?

Professor Martha Clokie: Yes. I will send it through.

Lord Borwick: Thank you very much.

Q2 **Baroness Willis of Summertown:** I want to move on to the current state of play for phages. A lot of this came about from a discussion I had with Professor Brockhurst in Brussels a couple of months ago. I want to start on the point that you made there. Can we use phages right now as a last resort? For someone who is dying of a bacterial infection, will a hospital be able to use a phage?

Professor Michael Brockhurst: In theory, yes. In practice, it is very challenging. Those challenges are around regulation. They are around willingness of clinicians to take the risk that they would have to take, being responsible for that treatment. If you have an infection that cannot be treated through traditional antibiotic routes, there is an option and it is under special regulation from the MHRA. You can procure phages produced under GMP and use those as a treatment today.

That regulatory framework exists, but it is very challenging to implement, in reality. There have been a handful of cases. Martha

would know better than I the number of treatments there have actually been in the UK in the last 10 years or so, but it is very low. It is a handful of cases.

Professor Martha Clokie: Yes. So far, 14 patients have been treated and there are 10 currently in progress.

Baroness Willis of Summertown: What timescale are we talking?

Professor Martha Clokie: I think that is within the last five years, approximately. Recently, UKHSA launched a clinical phage service. It is aiming to expediate this progress. There are 10 phages now going through the clinical phage service it has launched, to try to treat this next set of phages. Largely, these phages have come from Belgium, by the way.

Professor Joanne Santini: I do not know of any cases where phages are being used in this country for acute infections. Martha might know, but I do not know of any for acute infections, where there has been no alternative. There are a lot of acute cases. Just look at the number of people in the country dying of bloodstream infections, where antibiotics do not work.

Baroness Willis of Summertown: You made a comment that you would take a phage rather than an antibiotic. Would you treat yourself?

Professor Joanne Santini: I think I legally can. I might not tell—anyway. Yes, absolutely. When I went to Georgia, I brought back all their phages as well, as many as I could get.

Baroness Willis of Summertown: There was a Commons report on this, which I think all of you probably contributed to. What did you make of the Government's response to that? Would you like to comment on that?

Professor Michael Brockhurst: I would say it was very measured. There were not many real commitments. The input they got from, for example, some of the funders and other bodies was similarly slightly non-committal.

To really get this off the ground, we would need a bigger push. I do not know how far you want me to go down that road but, for example, to open up the funding landscape for this, this needs a push, in the same way that antibiotic resistance needed a push. It was very hard, 10 years ago, to get funding to do antibiotic resistance research. When the Government made a push, led by the Chief Medical Officer, suddenly everything opened up and it

was possible. A similar push and prioritisation of this area needs to happen.

The reason for that is simple: funding committees are made up of scientists and getting new areas of science funded through those committees is challenging, because you need somebody on the committee to advocate for that area of science. If there is no one doing that, because the committee is drawn from people who, say, the MRC has funded over the last decade, which does not include many people working on phage therapy, it is going to be really challenging to get phage therapy funded through traditional committees or the standard funding routes.

That was the disappointing thing about the government response. There was a lack of recognition that, without a push and a prioritisation of this, it is going to be challenging to get it funded through standard routes. That is not to say that, within the UK, we are not funding phage research. The BBSRC is funding large amounts of fundamental phage research. The UK is world leading in fundamental phage research. The translational research is missing and that piece is not happening. There was not sufficient backing or interest in that in the government response.

Professor Joanne Santini: The report was very good. The Government's response was weak. The report was excellent in highlighting the need for more funding and benchmarking funding towards phage research, the need for GMP production and the need for regulatory guidelines on the use of phages. That was all in the report, but what you do with the report is the important thing. The report was very good, but nothing has yet been done. We are all very hopeful.

Baroness Willis of Summertown: Professor Clokie, do you want to add anything to that?

Professor Martha Clokie: Some very useful things have happened since that report came out. For example, there has been a lot more engagement with the MHRA, which is now writing a guidance document as to how phages should be regulated. That will come out in January. There has also been a cross-party committee spearheaded by DHSC, which has been looking at the role of phages across the one health space. At Leicester, we have been working with the MHRA to develop a set of bacteriophage standards, which will be key to both the GMP production and the translation of phages.

There have been these really useful, tangible things that have come out of this so far, as well as UKHSA launching that clinical

phage service that I mentioned, which will help with the translation.

Baroness Willis of Summertown: Is there anyone overseeing this, though, and pulling this together? Is there a particular body?

Professor Martha Clokie: Yes. The most useful body is the Phage Innovation Network, which is part of Innovate UK and led by Fran Hodges, who I believe is in the audience here today. She has been really useful at co-ordinating many of these activities.

Q3 **Baroness Northover:** I had not realised how limited the use of this was at the moment and what its potential was. Looking at the translation and commercialisation of phage research, what more needs to be done? You have started to address this. You have made reference to that Select Committee report and to the Phage Innovation Network; it is very good to have Fran here. I wondered whether you could go into that more and say what you think needs to happen now to move this forward. Should there be phage banks, for example?

Professor Michael Brockhurst: Fundamental to commercialisation is establishing a domestic GMP production facility. Even at a small scale, that would be extremely helpful and it would unblock a lot of challenges that we have. Martha would be better placed to talk about phage banks but, from my perspective, there would be two phases of phage therapy.

The first is a public goods argument. It is public health. We should implement this because it will save lives. That is conventional phage therapy for compassionate use and potentially other cases. That is not necessarily able to be hugely commercialised, but it is justified under public health need.

The second phase for me is synthetic phage therapy, where we can engineer phages readily. They have small, modular genomes. That makes them very engineerable. That opens up commercialisation and enables you to protect IP. That enables companies to have some confidence that their products can return their investment. It also opens up new modalities of treatment, so you end up with entirely new sectors of treatment. Not only can it make traditional phage therapy more effective, but it can also open up treatments that, for example, target and remove antibiotic resistance genes or virulence genes. We have a whole new biotech sector if we do that.

The other great benefit, for me, of synthetics is that you can engineer in biocontainment and you can engineer in safety. If we take these approaches that we have been developing in terms of engineering biology, we can solve a lot of the challenges around

commercialisation of traditional phage therapy by using more innovative approaches around synthetic production hosts, synthetic phages, with modularised genomes, where we have swappable parts. Those can be very flexible and responsive treatment systems.

I am not saying that is going to happen tomorrow, but that is the sort of longer-term perspective we could take on phage therapy if we were to solve some of the “very easy to solve” problems today, which are GMP manufacturing and clear regulatory guidance. In terms of clear regulatory guidance, I am aware that the MHRA is having lots of discussions with people, but nothing has been made public yet. I have not been invited to any of those sessions, which is not to say I should be, but it does show that certain parts of the field are not involved.

The other part of that is that this needs to be a cross-regulator discussion, because synthetics will be genetically modified. That opens up different kinds of challenges. Those are challenges that we can work towards, in terms of biocontainment and making sure that engineered phages can never grow outside of the treatment context, for example, but those discussions need to be happening now. These technologies are coming. They are being developed and they are being well funded at the moment. We need to make sure they can be translated.

For me, that is where the commercialisation of phage therapy happens. It is in five to 10 years. It is a huge sector; it is worth billions. The UK should be positioning itself to make use of that and make best use.

Baroness Northover: This committee is very concerned to go into those areas where there is not only a public good, as you say, but also a potential benefit to the economy in being able to build this here, develop it, take it forward and get the commercial benefit from it. You see those as well.

Professor Michael Brockhurst: They are enormous but, without domestic manufacture, we are going to struggle. Imagine that you develop a synthetic phage. All your IP is tied up in that phage. Do we really want to send that abroad, to be produced somewhere else, and all these things? On some level, domestic manufacturing brings it closer to the clinic, but it also enables us to have these treatments to hand in the UK, under UK law and all of those sorts of things. To me, it is a no-brainer. We need to solve it and it would not take a huge amount of money. It is a relatively straightforward solution. We know how to do it. It just needs a bit of a push.

Professor Joanne Santini: I totally agree with everything that Mike said. I agree that we need to have an NHS-funded, personalised medicine approach, like we have for stem cell therapy, for compassionate use of phages. We need the GMP facilities for production and for safety. We also need to be able to collect more data that will feed into programmes such as machine learning, so we can then determine what phages we can use in particular cocktails to treat not just one bacterial pathogen specifically, but a whole disease.

We need the data for that. You need data to feed into the machine learning, in order to be able to then come up with new approaches or new cocktails for a particular pathogen. That will also help with the engineering of phages because, at the moment, we are lacking a lot of host range data.

The Chair: Apologies, we are going to have to move on to the next question, because otherwise we are not going to get through this session.

Baroness Northover: I was just going to say that GMP stands for good manufacturing practice, given that that is the first time it has been mentioned.

The Chair: Thank you. Lord Borwick is going to pick up on regulatory issues.

Q4 **Lord Borwick:** What are the main regulatory issues holding back phage therapy? What are the regulators concentrating on at present? Are there any correlations with the work on Covid that was being done in China, to avoid regulation?

Professor Joanne Santini: We are passing this over to Martha, because she probably has more intel.

Professor Martha Clokie: The regulations are largely that you need to produce bacteriophages using good manufacturing practice. We should be producing medicines at the highest possible standard. The regulatory framework that phages could be produced under does exist and we also probably do have capacity in the UK to manufacture bacteriophages, but we do not have the expertise to be able to run it or to repurpose our facility programmes that produce biologicals to bacteriophages. We need that to be more joined up.

The regulators, within human medicine, food safety and animal safety, are talking to each other to work out what the sets of criteria should be to manufacture. Essentially, you need to make bacteriophages that are separated from any bacterial contaminants

and that are high-purity products. Something we have been doing to push that is to work with the MHRA to produce a genomic set of standards. That will mean that companies wanting to work in this area can validate their end product against this set of standards, which will allow and help with that translation.

The regulators are engaged and we potentially have the resource within the UK, but it needs to be joined up and it needs to be fed. It needs to be input into a lot by bacteriophage expertise, to allow it to be joined up and to allow that translation. At the moment, it is being done in a very isolated way.

Lord Borwick: It is the MHRA that has the leading people on this.

Professor Martha Clokier: Yes, that is right.

The Chair: What would you like to see them do? What do they need to do to join this up?

Professor Martha Clokier: They need resource. Like everyone else, they are underresourced. To develop this programme, we have done it on quite a small scale. We have been borrowing from other resource to at least do this proof of principle: "This is a set of genomic resources". There needs to be a specific call, where you bring in phage expertise; you bring in the MHRA and UKHSA; you develop a programme to focus on those next steps. At the moment, there is no resource to support this work.

Lord Borwick: It is not that the resource is being spent on other things.

Professor Martha Clokier: It probably is. It does not even have to be new government resource. It just has to be prioritised within our existing funding streams, within the Medical Research Council funding, within the BBSRC. As Mike said at the beginning, if this area was prioritised, we would see both the health and the economic benefits relatively quickly.

Q5 **Baroness Willis of Summertown:** We have heard from other engineering biology applications that one of the problems is lack of knowledge across the Civil Service. Therefore, that is where it comes to freeing up the right resource in the right place. Do you see that in phage?

Professor Michael Brockhurst: Yes, we do see that in phage. There are different ways you can do the synthetic phage approach I am talking about. You can take genes out. You can put genes in. You can give these phages completely different functions. I do not

know how that sits within the current guidelines the MHRA has. I do not know how that interfaces with Defra.

On some level, these things need to be discussed among them and then published. For me, part of the barrier here is that this process is not very open and nothing has been published within 12 months. I understand that things are about to be published, so that is very good, but it does not feel like the regulators are very open to the field. It feels like they are used to talking to large pharmaceutical companies, particularly the MHRA, and are less used to talking to people like us. They are trying, but it is challenging.

As a field, we need to engage with them. I am an editor for *Microbiology*, the Microbiology Society's journal, and we have commissioned people at the MHRA to write some reviews for us around perceived and real regulatory barriers to phage therapy. We hope that those will be quite user friendly. They will be published this year, we hope in the spring.

We are doing our bit. We are trying to engage with them, but it is challenging. It is challenging for them, too. This is not an easy problem. I do not know that they are always so used to working across boundaries, but we do need to talk to them, because there are things to do with genetic engineering that they potentially will not be aware of with phages. We probably should be having those conversations now, as I said earlier.

Q6 Lord Lucas: If we engineer a phage to knock out a particular bacterium, what is the potential for that moving geographically, so that it knocks out the same bacterium in places where it is actually useful to us or, indeed, migrates to a beneficial bacterium? Are there dangers that we should be aware of?

Professor Michael Brockhurst: Natural phages are everywhere anyway. That probably is not such a concern for the use of natural phages. You would just be increasing the local abundance of that phage within that human as you treat them. For synthetic phages, it is definitely something we need to think about.

We have an engineering biology Mission Award, which is around biocontainment and biosafety of phages. You can build biocontainment into engineered phages from scratch. By having orthogonal, multiple modes of biocontainment within the genome, you can prevent it escaping from the treatment context and you can completely limit it to growing there, so it can never grow outside.

There is risk we need to consider, but one great advantage of synthetic phage therapy is that you can build in those safety

switches, those biocontainment measures, from day one. We are actively thinking about that and doing it today whereas, for conventional phage therapy, it is much less of a concern. Martha looks like she wants to chip in.

Professor Martha Clokie: Natural bacteriophages are just everywhere. Anywhere you find those bacterial species, you will find those phages. In terms of safety when phages are being used, they have an incredibly high safety record. We do not need to worry so much about using bacteriophages in terms of gene shunting around in a natural context.

The Chair: Professor Santini, was there anything you wanted to add?

Professor Joanne Santini: I have nothing to add on that, but could I briefly go back to the regulations? My suggestion is that we follow countries that already have good regulations in place. The FDA in the US can approve compassionate use of a particular phage that does not necessarily need to be produced to GMP within a couple of hours. That means that we can potentially save people who have an acute infection.

In Australia, they have a very good protocol where they are doing this across the whole country. They are collecting clinical data from phage therapy and it is essentially a one-arm clinical trial, which will then feed into further investigations. Belgium's phages are being used to treat patients in the UK and all around the world. They are not GMP either. They are produced under the magistral. Portugal has just approved phage therapy using the magistral treatment.

I am sure that the regulator is looking at these countries, but I would really like us to follow suit and improve on what they are doing, and not necessarily try something different.

Professor Martha Clokie: What Jo is saying is that many countries are making bacteriophage therapy work and we can look to those countries to get the best bits from them and make them work within our own regulatory system. The problem is that the architecture of bacteriophages, the ecosystem that surrounds going from phage to product, is different for a phage than it is for a conventional antibiotic. This is the stumbling block. Whether you use a natural phage or a genetically modified phage, the ecosystem needs to be understood and clarified. We need to get that clarity within that.

Q7 **Lord Rees of Ludlow:** We have heard something about funding,

but I wonder whether you could say a bit more about why it has been rather hard, it seems, historically, to get very much funding through the MHRA or the research councils, given that this is a hugely extensive and possibly very important field. I wonder whether you have any comment on that and on the possibility of more investment by pharmaceutical companies. Are they currently investing and, if not, why not? Can we do something about that?

Professor Joanne Santini: There has been quite a lot of funding for different aspects of basic phage research. I am not going to give you a number, but Martha has been quite successful and so has Mike in getting funding for basic phage research. That is great. For more applied phage research, Martha has had some money regarding agricultural use of phages to treat chickens; she will tell you about that.

It is much more difficult in humans. If it is basic discovery, that is one thing; you apply to certain people. If you have phages and you have an idea for a therapeutic, it is not so clear where to get that money from. For preclinical funding for phages, it is also not clear where to go.

Professor Martha Clokier: It has been easier to get resource and funding for the agricultural space. This is really important for humans as well, because about 70% of all the antibiotics that are made and manufactured are used in animal production. That means that, within our agricultural systems, we drive antibiotic resistance and those bacteria end up in humans.

If you can use phages to support clean, healthy, sustainable agriculture and food sources, right from the start you reduce the amount of antibiotic-level resistance. It has been seen as easier to have a regulatory pathway within that sphere. That has meant that more money has been funnelled into that space.

Regarding the human space, another piece that has contributed to the lack of funding is that phages have bad press. There is this perception: "They've been around for ages, so why aren't we using them? Why don't they work?" Also, it is seen as something a little bit Russian. These are not overly helpful connotations, surrounding the culture.

What is different now is that we have had this great revolution in terms of our understanding of molecular biology and genetics. We can now develop bacteriophages within a much more informed method, both for natural and for the engineered bacteriophages. In a way, that acknowledgement and the fact that we are looking at phages in a completely new way has not been translated though to

funding initiatives. Phages are blighted in every way. They are blighted by the complex issues surrounding their biology, the procedure, their translation, as well as the cultural narrative.

Lord Rees of Ludlow: Do you think it might be easier to get them to be used instead of antibiotics in cattle and things like that, than in humans?

Professor Martha Clokie: Certainly at the moment, yes.

Lord Rees of Ludlow: Is the situation improving? Can our committee make any recommendations to improve the funding situation and the perception, emphasising that this is not old-fashioned but a really modern technique with potential?

Professor Michael Brockhurst: The recommendation I would like to see is a prioritisation of translational phage research, because the UK has been very good at supporting fundamental phage research and synthetic biology phage research. What we really need now is a push around translation of that research into the clinic and applications such as agritech.

As I alluded to at the beginning, that is not going to happen on its own. The panels at MRC and at NIHR are not likely to have strong advocates for this research area, just because, historically, it has not been funded by those agencies. For example, if MRC or NIHR had a call around translational phage research, it would not even need to be huge amounts of money, but that would really kick-start the field and allow us to do the things we have been talking about: consolidate the field and enable new collaborations among people who are already working in this field, but cannot at the moment work together because there is a lack of translational funding.

The Chair: Somebody mentioned Innovate UK funding for this area.

Professor Michael Brockhurst: I do not know much about Innovate UK.

Professor Joanne Santini: You need to be a company to get money from Innovate UK.

Professor Michael Brockhurst: I was going to talk about pharma. I have engaged and tried to engage with large pharmaceutical companies to get them to come on board our Safe Phage project, which is our Mission Award. We could not get them interested. We did get a small SME from Paris interested to use our technology.

The message from large pharmaceutical companies was that they kind of know they are going to have to do this eventually, but they do not want to do it yet. They want all the problems to be solved and then they will come along and do it later. That is damaging and unhelpful.

It is similar to the problems we have around antimicrobials: a lack of enthusiasm in this space for large pharma to invest its money. The way we solved that with antimicrobials was through funding that was directed towards companies. Again, prioritisation and some encouragement for them to get involved in the sector would be massively helpful.

Professor Martha Clokie: Innovate UK is a government-funded research council, which aims to put academics together with businesses. It is a mechanism. This area could be prioritised within that. Another area that could be prioritised is for NICE to have funding for an economic analysis, because, when you look at all the economic benefits that could occur for this country, that would motivate the funding needed to make it happen.

The Chair: Innovate UK has a programme in this area already.

Professor Martha Clokie: It does, but it comes within its antimicrobial programme. This area is not being prioritised. It could be prioritised further.

Q8 **Baroness Young of Old Scone:** We talked earlier a little bit about what can be learned in terms of regulation from other countries that are currently using phages. Are there other things that you would like to steal from other countries that have a good track record?

Professor Joanne Santini: Other countries such as the US and Switzerland are setting up small-scale GMP facilities. Individual labs in the US, in universities, have funding—I do not know where from—to set up small-scale GMP facilities. In Switzerland, they have set up the first small-scale GMP facility.

We do not necessarily need to just have one big one. We could look to have several small ones, which would be good. If you wanted to then set up such facilities that would cost less, say, in Africa, to treat a lot of infections there, it is much more achievable than a large-scale facility. That is one thing.

Professor Michael Brockhurst: Jo has really covered it. We can do a lot more in terms of learning from the solutions of other countries. There are very pragmatic solutions out there to some of these challenges around regulation and GMP. We could adopt

those, even in the short term, and that would catalyse use of phage therapy in the clinic much more rapidly.

Baroness Young of Old Scone: Professor Clokie, do you think that the work that is being done on regulatory frameworks at the moment takes enough account of international experience? We are not trying to invent it from scratch, are we?

Professor Martha Clokie: I think it does. The MHRA is actually quite linked in with the European Medicines Agency—EMA—for example. It tries to take into account best practice in other countries. That is being taken account of. That will come out in the thing that the MHRA is going to publish. Certainly, it was interesting that there was a small phage workshop in Brussels just before Christmas, which had many countries talking about what they are doing to get phages used in their clinics. An overview of that being fed directly into our regulatory bodies, for example, would be very useful.

Baroness Young of Old Scone: The Chair talked about this perhaps being a precursor to us looking at personalised medicines generally in the NHS. What are the lessons from what is happening in phages for personalised medicine generally in the NHS? Do you have any thoughts on that?

Professor Michael Brockhurst: Personalised medicines are a great idea. Phage therapy is a very promising personalised medicine, but they all face the same sorts of challenges. You need a really detailed and thorough diagnosis. You need to be able to integrate a lot of different information to get you your personalised medicine. It is almost a machine learning problem.

In the case of phage therapy, you would want to take a genome sequence, integrate that information with symptoms, with all the clinical data you would have, and pop out a personalised phage cocktail or something like that. That is a challenge. That requires pretty good IT. It requires standardised data frames, which you would input that data into.

As we have seen through discussions with the regulator, flexibility is required for some of these personalised medications. GMP is a challenge. How do you flexibly manufacture phages that are different for every single patient within that framework? There are frameworks, but we need to make them work for phages. I see the challenges around integrating data, improving diagnosis and having the IT infrastructure and data standards you can use to actually inform personalised medicines. These are big challenges that we have not solved.

Professor Martha Clokie: There are similarities with, for example, personalised cancer treatments. If you have good diagnostics, phages and bacterial infections could even be a simpler framework to learn to improve personalised medicines in other places. It goes both ways. We can learn a lot from existing personalised treatments and then, if we can get it right with phages, we should therefore be able to inform other personalised treatments across the spectrum.

Professor Michael Brockhurst: I totally agree with that.

Professor Joanne Santini: It is very similar to where stem cell therapy was five or 10 years ago. Even now, when you are looking at treatments for inflammatory bowel disease, it is very personalised. It is very similar to that and we can learn, once again, a lot from what has been done in those areas and how they have been funded.

Q9 **Viscount Stansgate:** This session is going to inform a letter that we may well send to the Government with conclusions and recommendations. In conclusion, could you summarise what you think are the main recommendations you would like to make for the way in which phage therapies, and research and development of them, can be improved for the benefit of all?

Professor Michael Brockhurst: My recommendation would be to take a longer-term view of phage therapy. This technology, or phage biotechnology in general, has huge commercial and health benefits. Those, in my view, derive from next-generation synthetic phage therapies. That needs investment now in solving the basic infrastructure needs for rollout.

I would like to see a focus on solving immediate problems for conventional phage therapy, but with a longer-term view that there is this large biotech sector we can create through solving those problems.

Professor Joanne Santini: I agree with everything Mike said. I know we talked about regulation and regulatory guidelines at the last committee hearing. I would like to reiterate that an approach like the FDA for compassionate use of phages might be useful, where we are putting the patient first. Of course, using unlicensed medicines is always a risk, but we should be taking each case on its own merits and making decisions based on the individual patient.

Professor Martha Clokie: I would say that we already have a lot of expertise. Since the last inquiry, there has been increased willingness, but not the resource to allow that willingness to be translated into action. I suggest that the very next steps need to

be identified, to be able to join up those existing structures, so that that translation can happen.

Q10 Lord Drayson: Is there any data that you already have, or that you could get and send to us, on the actual clinical use of phages today in different countries in the world, such that we could accurately get a handle on where the UK stands relative to these other countries? You have mentioned several examples where we have been behind. Are there some hard numbers?

Professor Martha Clokie: Yes, there are. Even since the last inquiry, there has been a very nice paper published by the Belgium team. They just presented data from the last 100 patients they treated on a compassionate basis, showing clinical efficacy across the spectrum. There was also a recent phase II clinical trial led by BiomX, an Israeli company, looking at phages and pseudomonas in lung diseases and showing, again, clinical efficacy. I would be happy to collate that information and send it to you.

Lord Drayson: That would be great, so that we can see how many UK patients have received such a treatment, how many in the US, et cetera. Then we can see where we stand.

Professor Martha Clokie: We are very behind. There has been a massive increase in the last decade in clinical trials, but none of those has happened in the UK, even though we have the capacity to do that. We are ahead in the fundamental research, but we are very behind in being able to translate it. We could expediate our presence in that field with a bit of reorganisation.

Professor Michael Brockhurst: May I add one more recommendation for the letter? It would be having a prioritised funding push around translation of phage biotechnologies. That is essential for this field and for us to really be able to deliver clinical benefits.

The Chair: For these compassionate uses that you talk about, these individual cases, are the outcomes generally good?

Professor Michael Brockhurst: Yes.

Professor Martha Clokie: Yes. Within the UK, they were used to treat diabetic foot ulcers. Literally, if someone's leg was about to be removed, phages were deployed. The NHS trust that was doing that, up in Dundee and in Edinburgh, was able to save most of the patients that it could give bacteriophages to.

In general, globally, people see clinical efficacy in over 70% of the cases, even though, often, phages are being used when patients

have been infected for many, many years. They generally have a very good record of efficacy, often when combined with antibiotics. We have not really had the time to go into that but, often, phages can be used to preserve and extend our antibiotic use.

Professor Michael Brockhurst: To contextualise this, most of the data we have for use of phage therapy is in patients that are extremely sick, have chronic infections that have been treated with antibiotics for decades and cannot be treated with anything else. That is the most difficult patient in the world to treat and that is where phage therapy is working.

Imagine if we were able to use phage therapy in simpler cases and more traditional infections such as UTIs. If a drug company was proposing a new antibiotic, there is no way it would try that out in a CF patient who has an infection that has been in their lung for 20 years being treated with antibiotics every single year. The fact is that phage therapy is working in these cases, the most difficult arena in which a new therapeutic could work, and it does work. That is just to contextualise the kind of data that we could provide for you.

The Chair: It is effective in roughly 70% of those difficult cases.

Professor Michael Brockhurst: Yes, precisely. There have been recent clinical trials. BiomX did a phase 2 clinical trial last year, where the phage treatment was more effective than standard treatment and antibiotic treatment. That is on its website and has been publicly released.

Professor Joanne Santini: Most of these cases, as I have probably said already, are chronic cases. We do not have the data for non-chronic cases. The only other thing I wanted to add is about being able to adapt. The trials happening in the US at the moment are adaptive trials, where they can make tweaks to the trial as it goes along, to make sure that they are successful in the end. To be able to make those tweaks is going to be really important, so that it works.

The Chair: Having an adaptive trial is not the normal way you would run a trial.

Professor Joanne Santini: Typically, no.

The Chair: Are we able to do that, under UK regulations?

Professor Joanne Santini: I do not know. Martha might know.

Professor Martha Clokie: It is something we need to look at.

The Chair: If you can find that out easily and tell us, that would be very helpful. At that point, we are going to have to draw this session to an end. It has been absolutely fascinating. Thank you all very much. You have agreed to send us various bits of information. We would be delighted to receive that and we will take that as formal evidence. If there is anything else you think of that you think we would be interested to see, we would be very interested to have that from you as well.

There has been a transcript taken of this session. That will be sent to you shortly for any minor corrections that you need to make. At that point, thank you, all three of you, very much indeed. Apologies that we had to keep cutting people off, but we have managed to get through it and get a lot of information in a short time. That has been extremely helpful. Thank you very much.

Examination of Witnesses

Dr Jason Clark and Dr Clare Trippett.

Q11 The Chair: I would like to welcome our witnesses to this second session of our inquiry into bacteriophages. In this session, we are going to focus on the wider use and commercialisation of bacteriophages. Our witnesses are Dr Clare Trippett, principal strategic opportunities manager for health and life sciences at the Centre for Process Innovation; and Dr Jason Clark, director and CSO of NexaBiome. The session is being broadcast on parliamentlive.tv and a full transcript will be made available to you shortly after the meeting to make any minor corrections. I am going to ask Baroness Willis to kick off this session.

Baroness Willis of Summertown: You were both in on the previous session, which I found absolutely fascinating. It is generally a completely unknown area for most people. Maybe you could both make an introductory statement setting out your roles, but also how you became interested in phages and this whole question of translational science. If we want to translate it, it absolutely comes back to where both of you are based. Dr Clark, would you like to start?

Dr Jason Clark: I am currently CSO and acting CEO of NexaBiome. We are a phage company developing licensed phage therapeutics. Unlike the compassionate use piece that was covered quite a lot earlier, we are looking to take them through full clinical trials. I usually would describe myself very much as a phage person. I have worked in phage for 25 years and a bit, originally at a research institute. This is my third phage company.

At the first company I was at, we were using phages to deliver DNA vaccines. Those were synthetic phages, actually, to some extent. Then, at the second company I was at, we were looking to develop phage for decolonisation of *Staphylococcus aureus* before elective surgery. We did some really good stuff there. As far as I know, we were the first company in the world to produce phages to GMP. That was in the UK.

We had a full clinical trial planned. We had some really good interactions with MHRA but, unfortunately, at the time, phages were not as cool and trendy as they are now, so we were not able to raise the funds to actually do the clinical trial.

Then this company that I am at just now, NexaBiome, is phage therapy, but we have a formulation method for stabilising phage delivery. That is our IP and that is how we commercially protect what we are doing.

Baroness Willis of Summertown: Can I just have one question before we move on to Dr Trippett? This has been going on for 25 years, which is an awful long time. Why has it not taken off?

Dr Jason Clark: Quite a lot of this was touched on in the previous session. If there was no problem with antimicrobial resistance, we would probably still be talking about phages, but in a very limited sense for treating very specific infections. The need to find alternatives to traditional antimicrobials has definitely helped.

The reason it has not developed so much in the past is related to IP. You cannot patent phages. It is to do somewhat with the manufacture and regulations. A lack of clarity around the regulations did not help in the past. That is starting to change, with the new guidance that is coming out, but all those things essentially combined and, ultimately, no one has figured out how they can make money by developing phage products. That is the key. If someone thought they could make money doing this, they would be doing it already. Maybe once the first person does it, all of a sudden it will open up, but getting the first thing over the line is the difficult bit sometimes.

Dr Clare Trippett: Good morning. Thank you very much for inviting me here today to input into this discussion. I am here to represent CPI, which is part of the high-value manufacturing catapult that was set up to transform industry in the UK and to anchor innovation in the UK, to support economic growth and societal impact.

CPI is a deep tech innovation centre and our job is to facilitate the translation of technologies from the research and invention stage, through to the commercial market. We do not invent and we do not sell, but we help companies to develop and scale up their products and processes. We do that bit in the middle that is typically quite difficult and is often where companies can fail, hence why it has been termed the valley of death.

CPI has national assets to support innovation across a range of sectors, many of which are relevant to phage. We work across healthcare, future food production systems, agritech, sustainable materials and national security. In healthcare, we work closely with the pharmaceutical sector. CPI is quite unique in the breadth of medicine modalities that we work with, everything from monoclonal antibodies, viral vectors for delivering therapeutic genes, messenger RNA vaccines and therapeutics to oligonucleotide medicines.

We also work with microbiome therapeutics, a newer class of medicines that includes bacterial products, such as live biotherapeutic products. These are things like postbiotics and microbiome-derived novel antimicrobials, such as bacteriophage. We have extensive bioprocessing capabilities and expertise at CPI and we work with companies to develop and scale up the manufacturing processes for producing biological products. This includes developing the cell culture processes for growing of the cells that act as the factories to produce biological products, such as phage.

We can develop the purification processes for purifying the product from the cellular debris and components of the manufacturing process, and the analytical tools for characterising the quality and efficacy of the product, as well as the formulation, developing products with a long shelf life. We also support the manufacture of certain types of medicine to GMP grade, so that they can be used in clinical trials. Our RNA centre of excellence is an example of that. CPI is interested in supporting phage product development and commercialisation across the One Health spectrum, including human and animal health and the agrifood sector.

Baroness Willis of Summertown: Just looking at phages in particular in healthcare, have you seen a large increase in people coming to you in the last five years or so? What numbers are we talking about in terms of people attempting to start to move this firmly into the healthcare translational aspect of the work?

Dr Clare Trippett: That is a good question. We have definitely seen an increase over the past couple of years in companies coming to us that have phage candidates they want to take into clinical trials. These are not only companies, but also academics who have candidate products. In terms of numbers, it is probably still under 10 companies, but it is an emerging area and it is gaining traction.

Baroness Willis of Summertown: Just to give us an idea, 10 compares to how many other people coming to you with these sorts of translational issues? What is 10, percentage-wise, of the work that you do?

Dr Clare Trippett: Looking at just the biopharmaceutical sector, I do not have the precise numbers but it is starting to become a significant proportion of the types of therapies that we work on.

Baroness Willis of Summertown: Some sort of understanding of where it sits would be really helpful, if you could feed that back.

Dr Clare Trippett: Of course, I will need to revert back to you with the actual figures.

The Chair: Is your production to this good manufacturing practice standard?

Dr Clare Trippett: Not with bacteriophage, no. We can produce certain medicine modalities, such as RNA, to GMP and we are also developing the capabilities for oligonucleotide medicines, but not for bacteriophage at the moment.

The Chair: What is stopping you from doing it to GMP standards?

Dr Clare Trippett: I would say it is funding, currently.

Q12 **Baroness Neville-Jones:** This is a question we asked the previous witnesses and it would be very helpful to have your assessment. Could you summarise for us the current state of phage research in the UK since the report of the Commons was published last year? What do you think of the quality of the Government's reply? Can you give us your view of where things stand at the moment? As a result of that phase of activity, have there been any advances that you could identify, which have pushed things forward? I do not know who would like to start.

Dr Clare Trippett: I can start with that one. There was a lot of momentum and interest at the time of the Commons inquiry. That has definitely continued to grow since the report was published. Since the report, there have been some very exciting initiatives related to phage funded in the UK.

An example that CPI is involved with is the cystic fibrosis translational innovation hub. This is an initiative funded by LifeArc and the CF Trust. They funded a network of innovation hubs, including a hub that is led by Liverpool University, which aims to progress phage candidates for treating lung infections for people with cystic fibrosis through to the clinic. It is accelerating the commercialisation and clinical application of those phages.

A microbiome and infectious diseases innovation hub has also received investment zone funding from Liverpool City Region Combined Authority. This has been set up to drive development and commercialisation of microbiome therapies and novel antimicrobials, such as phage. There is also the PACE programme, which is a fantastic joint initiative between Innovate UK, LifeArc and the Medicines Discovery Catapult, which will drive the development of new treatments for tackling antimicrobial resistance.

We are definitely seeing growing interest and demand for phage from clinicians. An example of this is the UK's clinical network for the use of phage therapy in bone and joint infections. That is a fairly recent network. It was set up back in 2023, I think, and it now has over 100 members, which is a testament to the growing interest in the clinical application of phage in the NHS.

There is growing public awareness of phage. We see success stories in the media of phage being used to treat people, where it has turned around a situation in which antibiotics were not working. There are also case studies of phage being used to treat people's pet cats and dogs, which particularly captures the interest of the public.

I will maybe touch on some less positive developments. We saw a promising UK-based phage company, which was developing novel therapies for treating resistant infections, go into liquidation. That was unfortunate. To my knowledge, the UK is still absent from the phage clinical trial space. It would be great to see some clinical trials initiated in the UK for phage therapies.

Dr Jason Clark: I would agree with all of that. There were a few things happening even before the STC report, which have been made easier to bring to fruition with the STC report being there. For example, the Phage Innovation Network has helped push a lot of this. It has been instrumental in moving the field forward in the UK in the last couple of years. That started in November 2022.

Then, out of that, combined with the STC report, you have the new MHRA guidelines. This is the first time in the world that we have had a regulatory agency produce a specific set of regulations or guidance for phage therapies. Certainly, it is not something the MHRA regularly does. This may be the first time that it has done something similar. When we talk about phages being at the forefront of personal medicine, that is an example of the kind of thing, producing specific guidelines, it would like to do more often. The phage piece is right out in front there.

Other people have discussed a lot of this, but there is a new phage service hosted at UKHSA. That has come out of the original work that was done up in Edinburgh and Glasgow, where the diabetic foot patients were treated. The guy who ran that is Dr Josh Jones and part of the reason that this service is continuing is because he kept it running while essentially unemployed for a year.

I helped him write the grant that did the original piece of work. Then he was at the NHS for a year. Then he moved away from there and he spent a year just keeping it going, and now he is

based at UKHSA, with Mark Sutton. Again, that may be the first government-hosted compassionate phage service in the world. That links up clinicians with phage, initially from other countries but, as has been touched on a couple of times already, one of the gaps is on-site, in-country manufacturing. That would really help them get going.

Overall, there is a huge amount of momentum and a lot of good things have been facilitated by the STC report, but there are gaps to do with the translational funding and manufacture, as other people have touched on.

Baroness Neville-Jones: How much do you put down to individual institutions taking the initiative and how much of it is a result of Government actually doing something positive?

Dr Jason Clark: I have always had really good interactions with MHRA. It has been quite responsive. I know that is a controversial opinion, but genuinely, whether I have been to see it about our licensed phage products or unlicensed medicines, it has been on the whole pretty helpful and responsive.

The Phage Innovation Network, funded by Innovate UK, has helped a lot as well, but a lot of it has been driven by the phage community. The Phage Innovation Network brought them together, but then researchers, people, companies and regulatory bodies have all worked together to make this happen. It has been a large community push to make a lot of this happen as well.

Baroness Neville-Jones: It would take a large community push. You think there is something that could be regarded as being a community pushing this area forward.

Dr Jason Clark: Yes, for sure. If you want to call it the phage community, it is a fairly small world. Most of them know each other pretty well and, on the whole, we speak fairly regularly and try to work together where possible. Our company has really good links with most of the researchers in the UK, the clinicians and people running the phage service. It is quite well linked up, but part of that is fairly recent. Part of that is through the Phage Innovation Network. I know I have mentioned it a couple of times, but that or something like it needs to keep going, to keep the momentum up.

Baroness Neville-Jones: Are you happy with the pace of development?

Dr Jason Clark: Pragmatically, yes, but I have worked in phage for 25 years. I have seen that exponential increase in momentum from not very much to a bit. It is really good, but it would be very

easy to slip back to where we were before. We were behind a lot of other countries and, in some ways, we have caught them up. We could be in a position to overtake them, because there is a lot of good stuff happening, but it does require the support and funding in some of the areas that have been highlighted already to make it happen.

My company is at the stage of preclinical work, so I can speak to the funding gap—the valley of death, which is a phrase that I have used before. In the gap between the interesting science and the interesting clinical trials, we have to do boring stuff that is not interesting. If it is interesting, something is wrong. That is making the same thing five, 10, 15 times, to show that it works. That is where it is difficult to get funding.

- Q13 Baroness Neuberger:** You have already heard that the committee has published a report today on engineering biology. That mostly focused on industrial biotechnology applications, but it did focus on the life sciences quite a lot. We would like to know from you what role genetic engineering plays in phage therapy. Are we seeing scientific developments from CRISPR and machine learning that can make this a more viable therapy for antimicrobial resistance? In other words, is this really on the up?

Dr Clare Trippett: Genetic engineering is absolutely a key area of innovation in phage therapy. As was mentioned in the previous session, it is going to enable us to produce the next generation of phage therapeutics. Engineering phage can help to overcome some of the limitations that natural phages can have. We can use synthetic biology tools, such as CRISPR-Cas9, to help phages to become more effective at doing their job of targeting and killing bacteria.

Phages can be engineered to deliver CRISPR-Cas systems to kill bacteria more effectively. We are effectively equipping them to become more powerful and improve their efficacy. This can also reduce the likelihood of the emergence of phage-tolerant bacteria, because the infection is cleared so quickly, so the bacteria do not have as long to be able to adapt. We are seeing some of those CRISPR phage technologies in clinical trials now, so it is going to be really interesting to see how they progress.

Baroness Neuberger: Not in this country, right?

Dr Clare Trippett: No, not in this country. That is right. As well as for infectious disease, engineering phage can also open up new applications. Professor Brockhurst mentioned this in the previous session, but there is potential to open up this whole new avenue in

the biopharma industry. For example, phage can be engineered to be a novel cancer therapy. It can be engineered so that it triggers an immune response in the body and stimulates the body to produce anti-cancer antibodies.

Phage can also be a fantastic delivery vehicle for a therapeutic payload. Phage can be engineered to deliver, for example, anti-cancer molecules to target cells in the body.

There is also interest in engineered phage lysins as novel therapeutics. Phage lysins are enzymes that can act as precision antimicrobials and can degrade the cell wall of specific bacteria. We can use genetic engineering or protein engineering to further engineer their properties, so that they are more effective.

Professor Brockhurst mentioned this as well, but genetic engineering also opens up exciting intellectual property opportunities for phage. That is obviously going to increase the potential for commercialisation.

I will just touch on AI. Again, this can be a very helpful tool in phage research. Tools within AI, such as machine learning algorithms, can be based on what is now starting to be a very extensive database of phage genome data. This can help us to identify phages. It can help with predicting their life cycle and, really interestingly, it can predict the interactions between a phage and its bacterial host. If we can understand these interactions in silico, it can help with developing more targeted and effective treatments. It can also help with more quickly matching a phage to a pathogen, so it can accelerate treatment.

Baroness Neuberger: How much of this kind of work is happening here in the UK?

Dr Clare Trippett: There is a good proportion that is happening at the research level in the UK, but again—

Baroness Neuberger: No development.

Dr Clare Trippett: —we are not seeing the translation as perhaps we are in countries such as the US.

Baroness Neuberger: Dr Clark, do you have anything to add to that?

Dr Jason Clark: Between Professor Brockhurst and Dr Trippett, we have covered most of it. The only thing I would say is that I agree the potential is huge. As a company, we are initially looking at machine learning for the reason that Dr Trippett said, in terms of

matching phage to bacteria and trying to select the right bacteriophage for the job. Most of what I would say has already been covered.

Baroness Neuberger: We have covered a lot of my final question. What role do you think phages could have in an overall strategy for antimicrobial resistance? We know quite a bit about that. What do we need to do to make that happen?

Dr Jason Clark: The realisation now is that there is no magic cure any more. We cannot say, "Just take penicillin and you are fine". Phages are part of a more holistic approach to treating infections. You might use them with antibiotics or other ways of improving circulation or cleaning wounds. They are very synergistic and can be used with other treatments. Because the mode of action is relatively unique, they have that potential. They fit nicely into our overall antimicrobial resistance strategy.

What needs to happen? It bears repetition that, although we have the new UK clinical service and those other researchers who are working on this, getting phages into patients, having UK-based GMP manufacturing would help with that. The funding for not even necessarily clinical trials but the preclinical piece would help support the movement of clinical trials, which is what you need for the real widespread use of phages. The compassionate use piece is always going to be relatively limited. It needs to be by definition.

That is where we are. Lots of it has been said before, but—

Baroness Neuberger: It bears repeating.

Dr Jason Clark: Yes, it does.

Q14 **The Chair:** We heard the mention of a phage cocktail in the previous session. Do you think that that kind of approach, which slightly depersonalises this, might give commercial companies more interest in doing this? There is potentially a bigger market.

Dr Jason Clark: That was a good point. The product we are developing is for diabetic foot infections. We are trying to build on the work that was done up in Glasgow and Edinburgh. We have a phage cocktail that we would use for that. Ours would be three or four phages.

The Chair: That does not have to be tailored to an individual. That can be used in quite a wide range of patients.

Dr Jason Clark: We get coverage of more than 99% of clinical strains with the phages that we have. Diabetic foot infections are a little bit unusual, in that there is one specific bug that you need to

pick, which is quite susceptible to phage. It works quite well for phage treatment, which is part of the reason that we chose it as our first indication, but other people have used phage cocktails in clinical trials for burn wounds.

Most of the clinical trials that have happened, if not all, have been phage cocktails because, in order to have a licensed medicine, it needs to be relatively static. It needs to have good coverage, because phages are so specific. You need a range of phages in that product.

There was a meeting with MHRA last week where this came up. The only thing that would be useful is more clarity around how you can update your phage cocktail. The flu vaccine is a good example of an analogy there. You will need to change your phage cocktail over time, not because resistance has happened, but because the circulating strains change. Being able to switch phages in and out once a year, for example, is something it would be great to be able to do and still not have to go through the full clinical trial process again. You can probably do that under the existing regulations. It just needs clarification about the best way to do it.

Baroness Willis of Summertown: I have a quick question. Just hearing you talk about all these applications and the different approaches, we have heard in other aspects of engineering biology that there is a real problem in not having the skilled workforce to be able to develop and enhance these sorts of applications. We do not have a next generation of students coming through, because we do not have the DTPs, but also we do not have the technical skills. Are you finding that? Do you find that within your own companies?

Dr Clare Trippett: That is a very good point. A challenge with skilled workers in the engineering biology sector is, because it is so multidisciplinary, we need to bring together not only people who have the skills in the life sciences sector, but also people who may have an understanding of the bioinformatics and the computational biology side of things. It is bringing together a multidisciplinary set of skills, which is quite difficult.

Dr Jason Clark: We have what you would probably call a highly skilled, specialised team, but they have all pretty much been trained by us. We have a very low turnover rate of staff, so that works quite well for us, but it is very, very difficult to find people in the UK who would fit immediately into a phage company without a decent amount of training. It is quite a specialised sector, so we expect that anyway.

Q15 Lord Berkeley: The first question is for Dr Trippett, initially. When you gave evidence to the Commons inquiry in May 2021, you said, “The UK does not currently possess the infrastructure to enable progression of phage therapies into clinical trials” and manufacture. That is nearly four years ago. What has changed since then, if anything, and what is needed? Is it facilities, researchers, finance? Both witnesses have talked about that previously. Are you getting any help from the MRC, NIHR and Innovate, for example, to take this forward?

Dr Clare Trippett: The UK’s translational gap for GMP manufacture for phage therapies, which was identified during the Commons report, is definitely still evident today. In terms of progress, CPI is now supporting process development and scale-up of phage therapies up to the preclinical stage. For example, we are working with the University of Liverpool to develop a manufacturing process for phages against *Pseudomonas aeruginosa*, which, in some people, can cause very serious and life-threatening infections.

This work involves developing, optimising and scaling the manufacturing process, defining the critical quality criteria for the product and developing the analytical methods for assessing the product quality and efficacy. However, we do not currently have the required assets for taking phages through to a GMP-compliant process. Therefore, at the moment, the phages that are made within CPI can go no further than clinical studies and could not be used in people or in clinical trials.

Companies and researchers we are working with would need to go outside the UK to source their phage, to take that into the clinic. This can potentially present logistical issues for companies and, of course, it is a lost opportunity for the UK, from both a financial perspective and a healthcare perspective.

As with phage therapies, there is also a GMP manufacturing gap in the UK for other types of microbiome therapeutics, if we think of that as an umbrella term for a number of modalities, including phage, but also things like life biotherapeutic products. Companies with these other types of microbiome therapeutics, and companies and researchers developing new products, are having to source material outside of the UK to go into clinical trials.

As a catapult centre, our role at CPI is to support researchers with translating their pipeline of products through to the clinic and the commercial market. With appropriate funding, we would be able to address the gap in manufacturing microbiome therapeutics, including bacteriophage, through to GMP. This would build on

existing capabilities that we have already in bioprocessing and in GMP production of biopharmaceuticals. A flexible facility for phage and other types of microbiome therapeutics could help to mitigate any risk associated with the financial viability of manufacturing phage therapies alone, while it is still an emerging market.

Just going back to purely focus on phage, as has been discussed previously, there are two routes for phage to reach patients. There is the compassionate use, on an unlicensed basis, and then we hope, in the future, patients will have access to commercially available, approved, licensed products. CPI is working with the UK Health Security Agency—UKHSA—to explore how together we can provide phage manufacturing at both small scale, for patient-specific treatment, and larger scale, to support the development of commercial phage products. With the right funding, this would address the challenges in accessing phage in the UK.

Lord Berkeley: That is useful progress but, Dr Clark, it is still quite slow, is it not?

Dr Jason Clark: We need to be clear that what is missing in the UK is specialised phage GMP manufacturing. At the company I was at prior to this, we made phages to GMP in the UK and it was not easy, because no one had done it before, but we did manage to do it. It just took us a lot longer than it should have done and it was incredibly risky. Ultimately, that delay caused the company to fail, you could say.

What is missing is having a manufacturer that has in-depth knowledge about the processes, procedures, risks and how you handle phage specifically. For our clinical trials, it would be better to have UK-based manufacturing, but we can source the phage from outside the UK and it is a relatively minor inconvenience.

The Chair: That does not give you IP concerns, in that you have designed this phage and now that is being released somewhere else for others to make it?

Dr Jason Clark: For the people who do this for a living, if there were any IP concerns about what they were doing or if there was any problem with IP, would not be in business very long. We know very well the people we are working with. They are in Slovenia. We know that they do a good job. There are no concerns about that at all for us.

It is better to have UK-based manufacturing, if it is of the same standard as the stuff in Slovenia, because then you can go and inspect it more easily and, being someone from the UK, I would

love to see us have that capacity of building up our skills base and healthcare security. There are definite arguments for having it but, from a clinical trials point of view, we can get phages made to GMP.

To answer your question, it is slow, in terms of getting something set up in the UK. It would have been nice if there had been a bit more progress after the STC report but, to Clare's point, what is missing is specific funding for this particular thing.

Baroness Young of Old Scone: Are there no controls over phages being brought into the country from abroad, not for clinical trials but for compassionate use or for developmental purposes? What are the rules?

Dr Jason Clark: When you started asking that question, I was not sure this was going to come up. It is one of the peculiarities of the regulatory route that is used for compassionate use just now. If you import phages for use compassionately in the UK, they do not need to be made to GMP in the country that they are made in. The MHRA counts it as an imported medicine and you need MHRA approval before you can import that medicine, so it would do all the checks it would do for any other kind of medicine, but on the phage.

It does not need to be made to GMP, but it does need to be made to a certain standard, which is why it would come from the company in Slovenia, the people in Belgium or maybe the US. You would not get it from a university lab somewhere. It has to be from a recognised manufacturer.

Baroness Young of Old Scone: You would not take from the old Soviet countries.

Dr Jason Clark: There have been some discussions about doing that, but it has not happened yet.

Q16 **Lord Drayson:** I am just a little confused about the history and status of GMP manufacturing for phages. You mentioned a company was trying to do it and it went bust. Is that correct?

Dr Jason Clark: The company that I was at before the one I am at now was planning a clinical trial and, as part of that, we made phages to GMP.

Lord Drayson: In the UK.

Dr Jason Clark: Yes, but the issue that we had was that it was not a specialist manufacturer. We were learning as we were going along as well.

Lord Drayson: What was the name of that company?

Dr Jason Clark: Our company was Novalytics. The company we used to manufacture the phage was a company called Angel Biotech, which is now no longer with us.

Lord Drayson: You are now CSO of NexaBiome. Is NexaBiome building a GMP manufacturing facility?

Dr Jason Clark: No. If there was a UK-based manufacturing facility, we would like to be involved in the consortium that was working on it, because we have skills and experience that could help, but, for us, we are looking to develop licensed products. We need phage for clinical trials. We are looking at one or two batches of GMP phage in three or four years to do our clinical trials and then nothing for a couple of years, while we do our clinical trials. It would not be sustainable if we built our own GMP facility.

Lord Drayson: So no one is building a GMP facility in the UK right now.

Dr Jason Clark: There have been a lot of people talking about it and proposing it, including CPI, but no one is actively doing it, no. Any GMP manufacturer in the UK would make phage, if you paid it enough money. It is just that there would be risks involved, because it would not have done that before.

The Chair: Did the specialist facilities in those companies that have now disappeared exist somewhere that could have been kept going?

Dr Jason Clark: Not in the UK. They were in the US. The company that is now in Slovenia spun out from a phage company. There have been other phage companies with GMP facilities, but it has proven difficult for them to justify the investment.

The Chair: Sorry, I misheard you. I thought you said that previous companies had made phages to GMP in the UK.

Dr Jason Clark: We worked with a contract manufacturing organisation to make phages to GMP. Sorry, I should have made that clearer. Our company paid another company a lot of money to make phages to GMP.

Lord Drayson: Who did the manufacturing of phages to GMP in the UK?

Dr Jason Clark: We used two companies. One was called Angel Biotech. It is no longer with us and it did not do a great job of the manufacturing. The other one was Cobra Biologics, which is still

going, as far as I know. It, for a while, was quite interested in phages, but then it proved quite difficult to bring it all together in a way that was justifiable commercially. I do not think it does that any more.

Dr Clare Trippett: If I might just add to that, there has been a lot of progress made since then. I do not know if you would agree with that, Dr Clark. Now is definitely a much more positive time for bacteriophages than it might have been years ago, when these companies were working in this area.

The Chair: That is probably a perfect time to move on to Lord Wei's question, which is about commercial prospects.

Q17 **Lord Wei:** My question is particularly for Dr Clark but, Dr Trippett, do jump in. You have already started to talk a bit about NexaBiome's own business model. We would love to hear a bit more about how it works. Are you doing the trials, but then it is ultimately licensed to big pharma? Is there consulting or direct product to market or into the NHS? What are the various options and why are you going down the route that you are going down, in terms of your business model? Without sharing too much commercially sensitive information, in broad terms, how do you generate revenue from what you are doing?

Dr Jason Clark: As I mentioned at the start, what is slightly unique about our company is that we have a formulation method for stabilising phages for delivery. Historically, we have explored a number of fields for using that, including food technology, animal health and veterinary health. We had always shied away from the human healthcare piece, because it seemed like too big a gap to cover.

In the last couple of years, thanks partly to the external developments in the UK, we have started to focus on human health and are now exclusively looking at diabetic foot infections. Our business model would be the same as pretty much any new antimicrobial. We are looking to prove the technology through preclinical work and early clinical stages, and then, while it is not impossible that we could find the funding for the later-stage clinical trials, like phase 3 clinical trials, it is more likely that there would be an exit event before that happens.

A large pharmaceutical company usually would come and buy up, once you had developed enough clinical data to show that it works. Then it would take them through the later stages of the clinical trial process.

Lord Wei: I just want to focus a little on this challenge that has

come up in other questions and relates to this whole area of commercialisation. It feels like a lot of the applications right now are quite niche, targeting antimicrobial resistance, where you are competing with other technologies that are established, like antibiotics. That makes it quite hard for, say, the manufacturers to have the demand to keep going.

In the human or non-human space, are there not other, bigger markets—even gut health or people have talked about animal health, almost the supplements market, if you like—that could sustain the demand and build up the market and education, while you work on these more niche areas? Do you think the only way forward is this very targeted biotech approach, developing something clinically and then selling to a big pharma company? Is that the only real route that you see at the moment or are there mixed models, where you can cross-subsidise from one market to another?

Dr Jason Clark: I am sure every company would say this, but one of the issues that we have had is that we have always been underfunded for what we are trying to do. We have looked particularly at animal health, replacing antibiotics in pig feed and these kind of things, but we never quite managed to get anything over the line, partly due to the regulatory issues. Things are definitely better now than they were when we were looking at it, but the regulatory issues and actually raising money to take things to the next level were always difficult.

Part of the reason, which I have alluded to already, that we are focused on diabetic foot infection is that, although it is quite niche, we also need a success, basically, in this clinical trial. By keeping it as focused as possible, we give ourselves the best chance of success and then we can build out from that. It would be bad for us—probably terminal for us, as a company—if we tried a clinical trial in something a bit broader and it did not work.

From our point of view, that is why we are focused on something that is really targeted and that we think we can control and have a really positive effect on. It is a huge problem as well, of course. From that, we would like to build out our platform to be able to address other technologies. For clinical trials, you really do have to be focused on a specific indication, with the aim of broadening things out afterwards.

Lord Wei: Correct me if I am misunderstanding, but are there any phages that are generally considered safe, almost like vitamins, where you could build a market, build public awareness and get VCs more interested in the space before you leap to the clinical

journey? Is it all so new at the moment that you cannot treat some phages as completely safe, like vitamins that you can churn out for the consumer market, as you go on the journey to more specialist uses that you need to prove?

Dr Jason Clark: Part of the issue that we have with the regulation of phages is that, even when you look at the compassionate use frameworks in other countries, these were all pre-existing frameworks that have been adapted for phage. Because of that, phages fit into strange niches in different countries' regulation.

For example, in the US, you can apply phages under the "generally recognised as safe" regulations on foodstuffs. You can spray phages on food, such as cheese and cold meats, to prevent listeria and E. coli, and people can eat those foods and fruits, but for a human medicine it still needs to go through all the clinical trials, show an effect and show it is safe.

There is a strange dichotomy, where you can sometimes apply phages. You can buy acne face creams on Amazon that have phages in them. Whether they work or not is another question, but seven out of 10 people say that it is great. You can get those kind of things, but to actually take it through the process where you have a pivotal, definitive clinical trial, where you show that it has a medicinal effect and is safe for use in the general population, is a big step up from the other treatments you have been describing.

Compassionate use, use in animals, cosmetics and food treatments all help build awareness and make it a little easier for us but, ultimately, there is still quite a big gap to get to the clinical piece.

The Chair: Are we allowed to spray them on food in the UK?

Dr Jason Clark: Yes and no. I believe that it does actually happen in the UK.

Lord Wei: It sounds to me that there is a potential commercial market, where it is not scientifically proven, to use phages where they are generally considered safe. We are not there yet when it comes to targeting it towards real, clinically proven illnesses and conditions. We do not have that regulatory framework and there is a big gap between the two. Is that what you are saying?

Dr Jason Clark: We do have the regulatory framework, but there is a funding gap.

Q18 **Baroness Young of Old Scone:** Can I ask a dim question? I am not a scientist. Is there any risk that the unregulated uses of phages are going to result in phage resistance, like we used to do

with antibiotics?

Dr Jason Clark: Phage resistance is a thing and, in an enclosed environment, it will happen. The bacteria will become resistant to phage but, because phages are biological, they can evolve to overcome that resistance. There is no bacteria that is resistant to all phage. There will always be a phage that can kill that bacteria.

This relates to, as I was talking about, updating our phage cocktail. We would do surveillance of the strains that were circulating in the UK. If we found that one phage was not working as well, because there were resistant bacteria appearing, we would like to be able to switch that out, either by evolving that phage that is already in there or by isolating a new phage that can go in. In a closed environment, you will have a problem with phage resistance but, overall, you can always find a phage that will kill a bacterium.

Baroness Young of Old Scone: “Always” is quite a long time.

Dr Jason Clark: They have been around for many, many millions of years and they have evolved to be very good at killing bacteria.

Baroness Willis of Summertown: This is just for clarification, because I was slightly confused by your reply to Lord Wei’s question. Are phages used in other countries in the same way as a prescription drug? Is it just in the UK that we are not at that point and, therefore, cannot build that business model, or is this also the case in Russia, the US and the other places we have been hearing about?

Dr Jason Clark: There are no licensed phage therapeutics available. They will use them in Georgia and a little bit in the Soviet Union. You can go into a shop and buy a phage preparation for use, but it has not been licensed by the FDA, the EMA or any major regulatory agency. That is a very peculiar Georgian thing. For human medicines, no one has managed to take a phage product through the regulatory pathway yet.

Baroness Willis of Summertown: Even in the US.

Dr Jason Clark: Even in the US, but that is where the slight dichotomy comes in. Under certain specific food regulations in the US, you can spray the phages on food and people can eat those phages, but a medicine would have to go through the full clinical trials pathway.

Viscount Stansgate: I have one quick factual question. How many compassionate uses of phages are there in the UK a year or, indeed, in other countries? Are there figures that show to what

extent they are used as a last resort?

Dr Jason Clark: I think Martha made the point that in the UK 14 people have been treated and another 10 are in the process of being treated. Some European countries have treated more people, but you are not talking about thousands. The Belgians published a paper on their first 100 cases and they have done maybe 200 now. It is a small number.

The Chair: I think we asked the last panel if they would send us any data they had about that. Thank you for prompting us on that.

Baroness Northover: They did say the 14 and 10 over five years.

The Chair: As you said, I think we heard a figure of 100 or more elsewhere. We will look forward to getting that and we will publish that information when we get it.

Q19 **Baroness Neville-Jones:** Can we revert a moment to the regulatory side of things? Just a moment ago, Dr Clark, you said there was a regulatory framework. The question I have rather suggests that the regulatory scene is not complete or particularly defined. I gather that you are actually working on the regulatory framework with, among other people, Professor Clokie. How is the work going? Do you feel that you are moving towards a regime that has some hope of acceptance and getting strong MHRA support?

Dr Jason Clark: I think the new regulatory guidance is coming out this month. There are no new regulations there, but it points you in the right direction for existing regulations for both licensed therapies—ones that go through clinical trials—and unlicensed medicines, so the compassionate use piece. There are no new regulations there.

While there will be some phage-specific points that come up as you work through those regulations, if you are developing a product, 90% to 95% of the regulations that you need are already there. It is pretty complete, particularly for licensed phage products, because you need to treat them the same as any other medicine. They need to go through the same process as any other medicine.

Baroness Neville-Jones: If there are no new regulations, what is the point of the publication?

Dr Jason Clark: Finding those regulations and understanding them in the context of phage is very difficult. At the meeting we were at last week, someone described—

Baroness Neville-Jones: Is it a consolidation, then, that is taking place?

Dr Jason Clark: Someone described it as being like the *Yellow Pages*. There is lots of MHRA guidance, only some of which is applicable to phage. This document is a relatively short document that will say, “If you are working with phage, look at this webpage. Fill in this form. Do this”. It makes it much simpler for someone who is not a regulatory expert to understand what is required.

Dr Clare Trippett: If I may add to Dr Clark’s comments, I have personally found the MHRA team to be really proactive and collaborative in this area. As Dr Clark has said, the UK does not actually need a new regulatory framework for phage. Existing regulatory frameworks are sufficient to cover phage therapies.

That being said, often people do not know what they do not know. To support innovators who are developing phage therapies, the MHRA is developing this guidance note, which will cover things like the kinds of analytical tests that need to be used to characterise phage. This is due to be published very soon and it is going to be incredibly helpful for innovators who are developing new phage therapies.

Baroness Neville-Jones: When these regulations are shortly published, do you reckon they will achieve a situation in which there is an established regime? Are there more stages to be established?

Dr Jason Clark: There are two parts to this guidance. The first part is the document I have described, where it just points you in the direction of existing regulations in the context of phage. The second part is going to be a publication, largely driven by the community, which covers a lot of what Dr Trippett was talking about there—which assays you use, how you purify them most efficiently—presenting that information in a way that people can understand, but that will also be acceptable to the MHRA.

That will help a lot. It will not be the full picture. Until someone actually goes through the regulations, there are always going to be questions and things that people are not confident about, but it takes us a long way towards formalising what is needed to develop phage products.

Baroness Neville-Jones: When you say it takes us a long way, but not the whole way because there are still questions, is that the result of the state of science, essentially? What is the cause of the gap?

Dr Jason Clark: The gap is that, until you actually go through the process with a product, it is difficult to know what is not quite

there. It gives people the tools they need to start the journey, but then you still have to work through it with the MHRA and it will be a fairly collaborative thing.

Baroness Neville-Jones: It has to do with the maturity of the activity.

Dr Jason Clark: Yes. For example, I was talking about switching phages in and out of our cocktail. That would be relatively novel. We need to work on it as we go through the process, but the groundwork is there and the information that people need to start the process should be there, for sure.

Baroness Neville-Jones: Do you think the MHRA has the capacity to carry this forward? Is it well enough equipped to do that?

Dr Jason Clark: Just now, it is probably a bit understaffed. I know that there are a couple of people working at the MHRA on this specifically, whose funding does not last for ever. We need to keep that phage-specific focus at the MHRA. It does not need a huge team of people. It just needs people who can help direct researchers and companies to the right parts of the MHRA and the right people.

Baroness Neville-Jones: Perhaps that is something we could helpfully draw attention to.

Dr Jason Clark: The progress over the last two years has been great, but it would be very easy to lose the momentum if we do not keep the resource there and do not keep the focus.

The Chair: On that point of what we might recommend, let us move on to Lord Drayson.

Q20 **Lord Drayson:** You and the previous panel have very helpfully, very clearly, made the case for the need for a GMP phage manufacturing facility in the UK. In terms of recommendations that we would be looking to make to Government, do you see that the solution to getting that done has to be publicly funded? There is not, at this stage of phage research, a viable private investment business model that works for an investor to back a company to build a GMP facility for a particular therapeutic application. Therefore, it needs to be a general facility. The business model for funding that can only be funded by Government. Is that the view: that this has to come from Government?

Dr Clare Trippett: It could be a combination of public and private investment. This is something CPI is actively looking at. We are looking at how we could address the—

Lord Drayson: It could be a combination model but, fundamentally, without government funding, there is not a viable investment model for private investment on its own. Is that what you are saying?

Dr Clare Trippett: I believe that there needs to be some public money.

Lord Drayson: How much money is needed to do this? What is the budget for building such a facility?

Dr Clare Trippett: Depending on whether we build something in a facility that exists already or need to set up a new facility, we estimate that it is likely to be in the region of £25 million to £35 million.

Lord Drayson: In addition to Government providing that sort of funding for that facility, what would you say are the top three things that the Government should be doing, and we should recommend to Government, to give phage research, moving into therapeutic development and use, the push that, say, antimicrobial resistance got from Sally Davies back in the day?

Dr Clare Trippett: I would start by highlighting that we have tremendous strengths in phage research and development in the UK. We have all the pieces that we need to be world leading. We have world-class academic research. We have strengths in genomics, the NHS and a network of clinicians who are interested in accessing phage. We also have a strong biotech and biopharma industry presence. With the right strategic investment, we can build on this and become a world-leading location. If we go back to the two routes for patients to receive phage—

Lord Drayson: What do you think Government should do?

Dr Clare Trippett: Sorry, I am just coming on to that. For the compassionate use case, investment in small-scale GMP manufacturing facilities is needed. CPI's role is around helping companies become commercially successful and, for licensed, approved, commercial phage therapies, it is important to have evidence that these products work. This has to come from clinical trials. As we have discussed, there are many case studies now that make us believe that phages have a valuable role in treating infectious disease, but we need the evidence for this.

For this, we need the trials to be done, which requires access to GMP phage. If we had that, it would attract inward investment and interest from big pharma, which will be key to helping to progress the field, with small-scale manufacture and larger-scale commercial

manufacture. We should look at a flexible facility, which could manufacture the full spectrum of microbiome therapeutics.

Also, a national strategy for the development and use of phage in the UK should be considered. This could outline a clear end-to-end pathway for the design, development, manufacture and delivery of phage therapies, both in the UK and internationally.

Lord Drayson: Dr Clark, what are three things that you think Government should do now?

Dr Jason Clark: GMP manufacture is one. As a phage person, I would suggest that the people to speak to are the people running the new phage service about what scale they need. Having spoken to them as well, that would be a very focused phage facility, which can produce phages and gets them out to people as quickly as possible and starts helping people as quickly as possible.

That might be less than the combined facility. It might be £9 million or £10 million, but we need some form of GMP manufacturing, plus an ability to store phages that are manufactured to GMP—a bank of GMP phage—because they can be given to patients in a day instead of a month.

Also needed is some support for the funding gap between the interesting science and interesting clinical trials, the relatively boring manufacture piece, taking it through the preclinical stage. It is really difficult to get from private investors and from public investors, because it is just not interesting.

Lord Drayson: That would have to be grant funding from MRC or something like that.

Dr Jason Clark: Yes, or Innovate UK, which would be more likely to fund that. The third thing, holistically, for the use of phage in the UK, would be to make sure something like the Phage Innovation Network continues. We would need funding for that as well as funding for the MHRA to make sure its phage-specific programmes can continue. They have both helped a lot.

Lord Drayson: The phage bank does sound a good idea. What sort of budget would be needed to set that up? How much is that, broadly?

Dr Jason Clark: That would be included in that £10 million. We have looked at this with UKHSA. I spoke to some private investors with Josh Jones, the guy who is now running that service, and the issue they had with it was that they could see the potential but, because it was totally unproven, it was difficult to fund.

Lord Drayson: What would the annual budget be for maintaining the phage network and maintaining that expertise, to maintain a GMP facility like you described? What sort of money are we talking about to make sure that is sustainable annually?

Dr Jason Clark: It would be the salaries of those at the phage network and at the MHRA, essentially. It is four of five people's salaries to do that. I am going to have to put my finger in the air for the annual running cost for the phage facility, but it would be £1 million, £2 million, £3 million.

Lord Drayson: If you want to, you can write to us with that. The more concrete you can make your asks, the more helpful for us actually having some effect here.

Dr Jason Clark: If we can provide follow-up evidence, that would be really useful, because there is a lot that we have not been able to go through.

The Chair: Thank you very much. It has been another very interesting session, with some very useful prompts for us in your thoughts about what we might say to Government. You have offered to send us some further information. We would be very pleased to receive that as formal evidence.

I will just remind you that you will receive a transcript. If you could make any minor corrections and get that back to us as soon as possible, that would be very helpful.