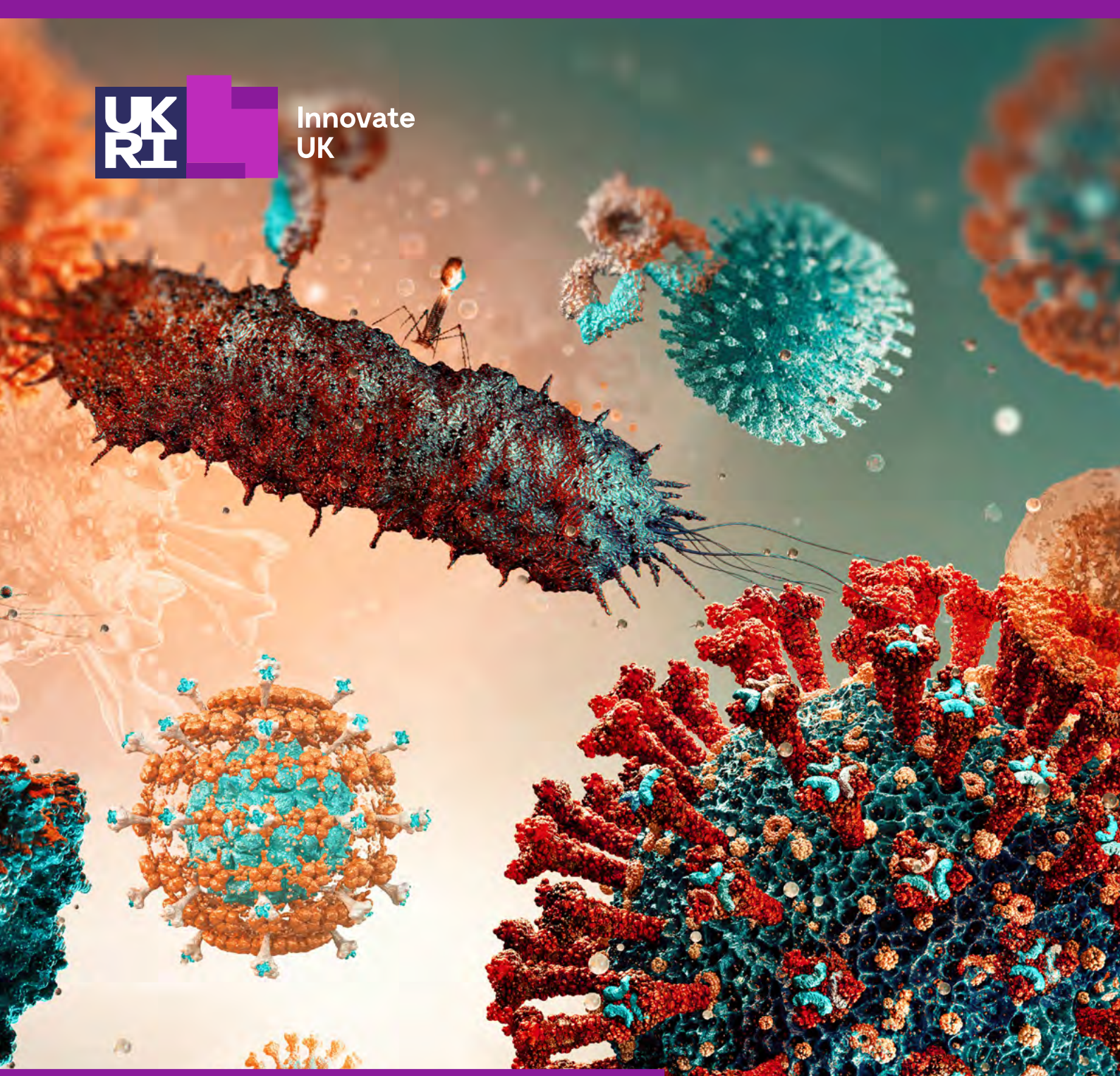

Innovate UK

Developing and delivering phage-based technologies in the UK

August 2024

Contents

Produced by Innovate UK Phage Innovation Network

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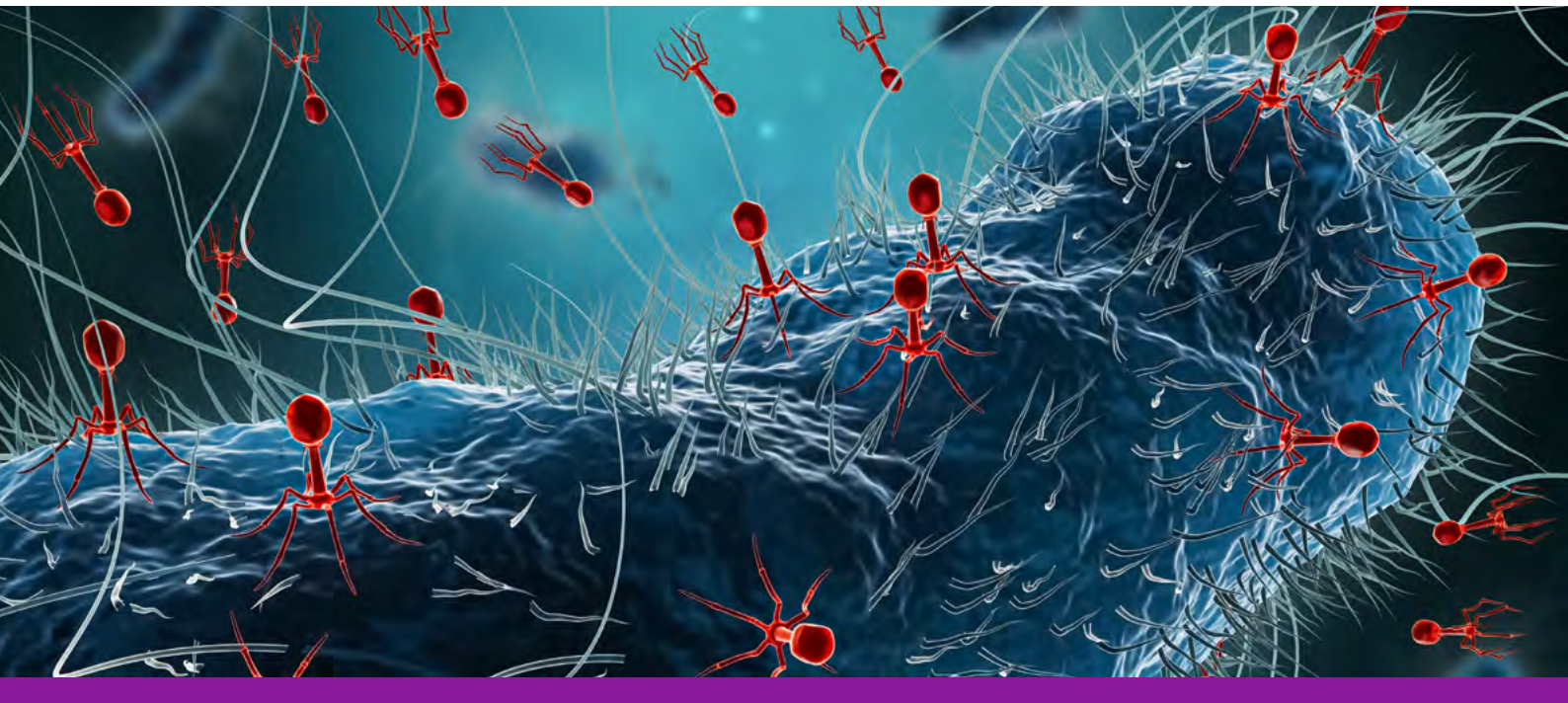
Overview

Bacteriophages, or phages, are viruses that infect bacteria. Phages have gained significant attention in recent years as potential alternatives to traditional antimicrobial approaches across multiple sectors. The UK is rich in talented, accomplished, and world-renowned phage researchers and scientists, and is also home to a variety of companies of varying sizes developing phage-based technologies (PBTs) for use across a variety of sectors including health and agriculture. However, despite this extensive resource there is limited translation of this knowledge into real-world solutions that can be applied across different sectors in the UK.

The Phage Innovation Network was launched in February 2023 with the aim of raising the visibility of UK phage research and development and improving access to PBTs in the UK. The focus of the Phage Innovation Network has been to understand the necessary requirements for growing the phage sector and increasing UK capabilities and capacities.

This work has been informed by phage experts, the wider microbiology and antimicrobial resistance (AMR) communities, specialists from different industries interested in the use of phages, regulators, policy makers, and funders. In addition, this work has also been informed by visits to phage research centres, treatment centres, and companies in the USA, Australia, and Belgium.

In order to understand the requirements for supporting growth and development of the phage sector in the UK, this work has considered the current capacity in different areas in the UK that could be utilised to support growth, the current limitations for the development and use of PBTs in the UK, and a realistic future position for the UK to aim for.



Summary of phage-specific strengths in the UK

One key area of focus is the development of phage therapy as an alternative or supplemental antibacterial therapy in human medicine. Phage therapy involves using specific phages to target and kill bacterial pathogens. Globally, clinical and safety trials have been conducted to evaluate the efficacy and safety of phage therapy in treating infections caused by bacteria. These trials consistently show that phage therapy is safe, by a variety of routes of administration. Although the efficacy of phage therapy has not been consistently demonstrated by clinical trials, this is considered to reflect methodological rather than mechanistic shortcomings and where the right amount of the right phage, or combination of phages, has been delivered to susceptible bacterial cells, efficacy signals have been observed [1].

In February 2023, Healthcare Improvement Scotland (HIS) published a report conducted by the Scottish Health Technologies Group (SHTG) which presented analyses of the published evidence on phage therapy and randomised controlled clinical trial outcomes [2]. This assessment included a formal recommendation for NHS Scotland which indicated that the use of phage therapy is effective for patients with difficult to treat bacterial infections and the inclusion of phage therapy alongside the standard of care is cost effective for the treatment of patients with difficult to treat infections [2].

In addition to their use in human medicine, phages have shown great potential for applications in the agrifood sector. Their ability to specifically target and kill harmful bacteria makes them valuable tools for improving food safety and agricultural practices. In the UK there is ongoing research into the identification and characterisation of phages that effectively target bacterial species of concern both nationally and internationally within agriculture and food production and to formulate them into products suitable for application in different contexts.

Within the agrifood sector PBTs can be utlised in a variety of ways including as a natural alternative to chemical pesticides in the biocontrol of plant pathogens; in food safety and preservation to control bacterial contamination and target pathogens associated with foodborne illnesses such as *E. coli*, *Salmonella*, and *Listeria*; for livestock production to combat bacterial infections and reduce the need for antibiotics in animal farming, which is crucial in the context of antimicrobial resistance; in food processing to target spoilage organisms, such as lactic acid bacteria, which can affect the quality and shelf-life of food products and cause waste; and in aquaculture where phages can be employed to combat bacterial diseases in farmed fish that can lead to significant economic losses. Phage research in the UK encompasses the study of phage biology and evolution as well as research that focusses on translating this biology into useful and relevant applications. World-class researchers in universities and institutes across the UK are actively working to understand phage genomes, how phages interact with their bacterial hosts, and how they evolve over time. This research directly informs how phages can be manipulated for practical purposes and helps in identifying and characterising phages that are suitable for different applications.

Furthermore, work is being done to develop phage-based diagnostic tools for the rapid detection and identification of bacterial pathogens. These tools aim to provide quicker and more accurate diagnosis for bacterial infections, allowing for timely and targeted treatment [3]. Phage-based diagnostics have potential for use in the field of clinical microbiology in both human and veterinary healthcare settings by providing a faster and more specific alternative to conventional diagnostic methods.

In terms of industry, UK-based companies are actively involved in the development and commercialisation of phage-based products. These include phage-based antimicrobial agents, plant-protection products, surface disinfectants, and food safety solutions. Overall, their goal is to provide effective alternatives to traditional antimicrobial approaches and chemical disinfectants, which face challenges such as antimicrobial resistance and environmental concerns [3,4,5,6,7,8].

UK Research and Innovation (UKRI) funding for phage R&D

The following is a summary of funding provided by UKRI organisations for projects that encompass research into or development of PBTs. From 2015 to 2021, the Medical Research Council invested £2.3 million in funding phage-related research projects. This includes three international collaborations funded through the Joint Programming Initiative on Antimicrobial Resistance [9]. The Biotechnology and Biological Sciences Research Council (BBSRC) supports the phage research community by building capacity and capability for phage research, including human health applications. From 2017 to 2022, BBSRC invested £4.7 million in research exploring the use of phages as alternative antimicrobials and to advance the fundamental understanding of phage biology [9]. Based on information accessed through Gateway to Research, Innovate UK has funded approximately 23 phage-related projects since 2011, totalling £7.4 million of investment. This funding has been provided through Smart Grants, collaborative R&D projects, and other feasibility studies and a large portion has been applied within the agri-tech sector with results from Innovate UK-funded work currently being utilised within the European Union's plant-protection product regulatory system.

Wider strengths in the UK

Listed below are existing strengths in the UK that can be utilised to support the growth and development of the phage sector in the UK. These strengths have been highlighted through engagement and consultation with phage experts, the wider microbiology and AMR communities, specialists from different industries interested in the use of phages, regulators, policy makers, and funders.

1. The UK has world class academic foundations in microbiology, genomics, computing, phage, and AMR research which shows that we are well equipped and have the necessary expertise to support the development of PBTs and translation of basic phage biology into real world applications.

2. The genomics infrastructure and capability in the UK is world leading and critical for the sustainable development and effective use of PBTs.

3. The UK has a deep, extensive understanding of the bacterial targets against which PBTs can be used through UK Health Security Agency (UKHSA) surveillance data and sequencing of bacterial pathogens.

4. The growing strengths in artificial intelligence (AI) and machine learning within the UK are key to accessing the capacity to connect data for predictive modelling and effective utilisation of PBTs.

5. Innovate UK Phage Innovation Network is a vital resource and enhances the existing knowledge base by bringing together a fragmented sector to work collaboratively towards growth and development.

6. The report recently published by Health Improvement Scotland supports the use of phage therapy for difficult to treat bacterial infections, which highlights the importance of developing treatment and implementation strategies for phage-based therapies in the UK [2].

Barriers

Listed below are current barriers limiting the development and use of PBTs in the UK. These barriers have been highlighted through engagement and consultation with phage experts, the wider microbiology and AMR communities, specialists from different industries interested in the use of phages, regulators, policy makers, and funders.

1. There is a lack of production/manufacturing facilities in the UK that have the capacity and technical capability to manufacture phage products to meet Good Manufacturing Practice (GMP) guidelines, but also for non-GMP products. This severely hinders the progression of translational work being carried out to develop PBTs across all sectors as phage products cannot be produced in large enough quantities to high enough standards to conduct the studies and gather data required to inform licensing and use. This is not a UK-only issue as researchers and developers in Europe also have limited access to phage manufacturing facilities.

2. Regulators in the UK support innovation and the development of new products, but in some cases there is a lack of clarity regarding the regulatory classifications for PBTs intended for different applications. This, combined with insufficient manufacturing infrastructure, makes it challenging for developers to gather the necessary data for licensing as they are often unable to confirm how a product will be classified.

3. Though there is some existing infrastructure that can be utilised for phage development, in addition to the lack of manufacturing capacity the UK is lacking in further specific national infrastructure such as a comprehensive phage biobank/collection or standards for PBTs that would catalyse development and use of PBTs.

4. There is a lack of sustainable central focus for phage research and development innovation. However, there is active cross sector engagement in the development of PBTs. Though this is currently a barrier, the Phage Innovation Network was highlighted by the wider community as a central point for providing focus, coordinating engagement and establishing strategic priorities for the phage sector.

5. As increasing bacterial resistance continues to reduce the efficacy of exisitng antimicrobial products and therapies, a need is anticipated to increase funding across relevant agencies for the development of novel, non-traditional antimicrobial products. Historically, phage-focused projects and work on other non-traditional antimicrobial products has had to compete with more established topics, such as novel antibiotics or vaccines.

6. There is little constructive, responsible communication to wider communities about the potential benefits of PBTs. This has resulted in a perception that phages do not work, and we do not understand them, when in fact there is an extensive and expanding knowledge base, in the UK alone, that is continuing to build the evidence base for the use of PBTs.

Key actions

Listed below are key actions that have been suggested for ensuring the development and use of PBTs in the UK. These actions have been put together following engagement and consultation with phage experts, the wider microbiology and AMR communities, specialists from different industries interested in the use of phages, regulators, policy makers, and funders.

1. A need for GMP manufacturing capability for PBTs has been identified by the community in the UK to support cross sector development and use. Establishing this capacity in the UK de-risks investment in PBTs, which in turn promotes their development and enables necessary activities including advancement in demonstrating efficacy of PBTs through clinical trials. It was suggested that funding for a manufacturing facility could come from both public and private sources. Groups and existing expertise in the UK, such as CPI, will be key for delivering manufacturing capacity.

2. Formulation and publication of a national strategy regarding support of development and use of PBTs in the UK is crucial for the sector. This should include approaches for responsible communication about PBTs to the public.

3. Key infrastructure, in addition to manufacturing capability, needs to be established to support the sustained use of PBTs e.g., national phage biobank/collection. The foundations for resources like this already exist within the knowledge base, but funding is required to support growth and development, and maximise impact. It was suggested that a joint programme of activity could be initiated between public funding bodies and industry to deliver this.

4. Where the sector pull demands, longer term support for translational projects focusing on building interdisciplinary partnerships between academic groups, and with industry to bring novel, non-traditional antimicrobial products to the market should be sought and utilised by those active in this area.

5. Cost-benefit analyses of the use of PBTs in different sectors should be carried out following the initial analysis published by Health Improvement Scotland.

6. Regulatory guidance that provides clarity on the appropriate regulatory approach for different applications of PBTs and the associated data required for licensing to facilitate development and elucidate clear routes to market should be developed and made publicly available.

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