

This report was put together by Innovate UK as part of AgriFood Africa Connect, which brings together innovators in the UK and Africa to address African AgriFood challenges.

AgriFood Africa Connect is part of the GCRF AgriFood Africa programme, funded by the Global Challenges Research Fund (GCRF) and delivered by Innovate UK. It aims to develop sustainable management of AgriFood systems in Africa, in a way that reduces poverty, increases economic prosperity and improves wellbeing in Africa.



Francesca Hodges and Joanna Scales, Innovate UK Business Connect

Contributors and acknowledgements

Ghana: Mr Evans Agbemafle, CSIR Food Research Institute

Kenya: Dr Angela Makumi, International Livestock Research Institute

Ms Ivy Mutai, Institute of Primate Research

Nigeria: Dr Janet Nale, SRUC, UK

Dr Nnaemeka Emmanuel Nnadi, Plateau State University

South Africa: Prof. Pieter Gouws, Stellenbosch University

Uganda: Dr Jesca Nakavuma, **Makerere University**

Dr Ritah Nakayinga, Kyambogo University

The information in this report is accurate as of February 2024

Contents

Introduction	4
Overview	5
Antimicrobial resistance – a global challenge	5
Taking a One Health approach to tackle AMR	6
What are phages and why are they useful?	7
Phage expertise in Africa	8
Opportunities for the use of PBTs within the African AgriFood sector	9
Application of phages to reduce crop loss	10
Application of phages as biocontrol agents in aquaculture	11
Application of phages in livestock farming	12
Application of phages to reduce food loss and improve food safety	13
Emerging applications for phages	14
Barriers to use of phages in African AgriFood	15
Technical barriers	15
Systematic barriers	17
Summary	19
Case studies	20
References	25



Bacteriophages (phages), are bacteria-specific viruses that can be used in targeted therapy against pathogens. Phage-based technologies and therapies can be used to treat human pathogens, as well as those in livestock and crops, and to improve food and environmental safety. Phages could be used to support efforts to address antimicrobial resistance (AMR). AMR is a global challenge which could result in 10 million deaths globally by 2050. Phages could support in reducing the risk of AMR through improved pathogen control, as well as providing a viable alternative to antibiotics.

In the AgriFood sector the use of phages as biocontrol agents or veterinary medicines aligns with the One Health approach to addressing AMR. The One Health approach recognises the interactions and interdependence between the health of humans, animals, and the environment. There are opportunities to implement phage-based approaches to manage infection or the spread of disease at multiple stages of livestock, crop, and food production.

Through a series of interviews with key experts from African countries, we bring together the ongoing work in this area and highlight opportunities for innovation in livestock, aquaculture, crops and food processing. The barriers to realising the potential of phage-based technologies in the African AgriFood sector are also discussed.



Antimicrobial resistance (AMR) occurs when bacteria, fungi, parasites or viruses evolve new mechanisms that protect them from the action of antimicrobials resulting in treatment failures. This is a natural evolutionary process that allows microorganisms to survive, however the incidence of such resistance developing in pathogenic microorganisms poses a severe threat to global health. The improper or excessive use of antimicrobials and poor management of infections drives AMR in an unnatural and accelerated manner and amplifies its impact.

A systematic analysis of the global burden of AMR carried out in 2019 indicated that out of all the global regions assessed, Western Africa had the highest burden of deaths attributable to or associated with AMR1. Collectively, Eastern, Southern, Central and Western Africa had the highest all-age rate for deaths attributable to or associated with AMR globally. This assessment highlights the disproportionate effect that AMR is having on countries in Africa. This impact is further demonstrated by estimates that AMR could result in 10 million deaths by 2050 globally with 4.1 million across Africa alone^{1,2}. Factors which may aggravate the problem of AMR in Africa include access to sanitation, water quality, healthcare systems, access to quality antibiotics and indiscriminate use of antibiotics.

Taking a One Health approach to tackle AMR

Antimicrobials include antibiotics, antivirals, antifungals and antiparasitics used to treat or prevent infection. Resistance to antimicrobials is an issue for humans, but also affects the environment, plants and other animals, including those used in food production. The One Health3 approach recognises the interaction and interdependence between the health of humans, animals, and the environment4. By considering AMR with a One Health lens, new solutions can be identified to tackle AMR on a global scale and address practices and processes across multiple sectors that impede the sustainable use of antimicrobials. This could include improving healthcare systems and living standards

to reduce the demand for antimicrobials; better management of antimicrobials used in agriculture and controlling their dissemination to the environment; improving global surveillance of drug resistance; and promoting the development and use of vaccines and alternative technologies to treat or prevent infection. One such alternative approach that could play an important role in supporting the sustainable use and availability of antimicrobials targeting bacteria is the implementation of phagebased technologies (PBTs).



Phages are naturally occurring viruses that exclusively target and infect bacteria. They accomplish this by attaching to specific receptors on the surface of bacterial cells, injecting their genetic material, then utilising the bacterial cell machinery to replicate and produce new phage virions. This ultimately leads to the lysis, or bursting, of the infected bacterial cell, releasing a multitude of new phage virions ready to infect new bacterial host cells.

The natural ability of phages to specifically target and kill bacteria forms the basis of their potential as antimicrobial agents. Unlike broad-spectrum antibiotics, which can affect a wide range of bacteria (including beneficial ones), phages are highly specific. This specificity offers the advantage of precision in targeting pathogenic bacteria while minimising disruption to the wider microbiota of the environment the phage is introduced to. Maintaining the health of a microbiome is important; the specificity of phages in targeting bacteria can support in maintaining this whilst eliminating infection.

In addition, phages have shown promise in penetrating and disrupting bacterial biofilms. Biofilms are natural but complex communities of bacteria that can be highly resistant to traditional antibiotics. Phages, however, have demonstrated an ability to

penetrate these protective structures, making them a potential option for treating chronic or persistent infections associated with biofilm formation^{5,6}. Within AgriFood this could be relevant within many different contexts, for example, within food processing plants, livestock health and crop infections.

A further advantage of phages lies in their adaptability. They can evolve alongside their bacterial hosts, which means that even if bacteria develop some level of resistance to a particular phage, it is possible to modify or develop new phages that can effectively target the resistant strains^{7,8,9}. Finally, phages are generally considered to be safe to use in food products, and clinical trials of phage products have consistently demonstrated their safety and low toxicity when used in humans¹⁰.

What are phages¹¹?

- Phages are viruses that target and infect bacteria and are abundant in the environment.
- Phages are highly specific, offering the advantage of precision in targeting pathogenic bacteria while minimising disruption to the wider microbiota.
- As the natural predators of bacteria, phages can evolve alongside their bacterial hosts.

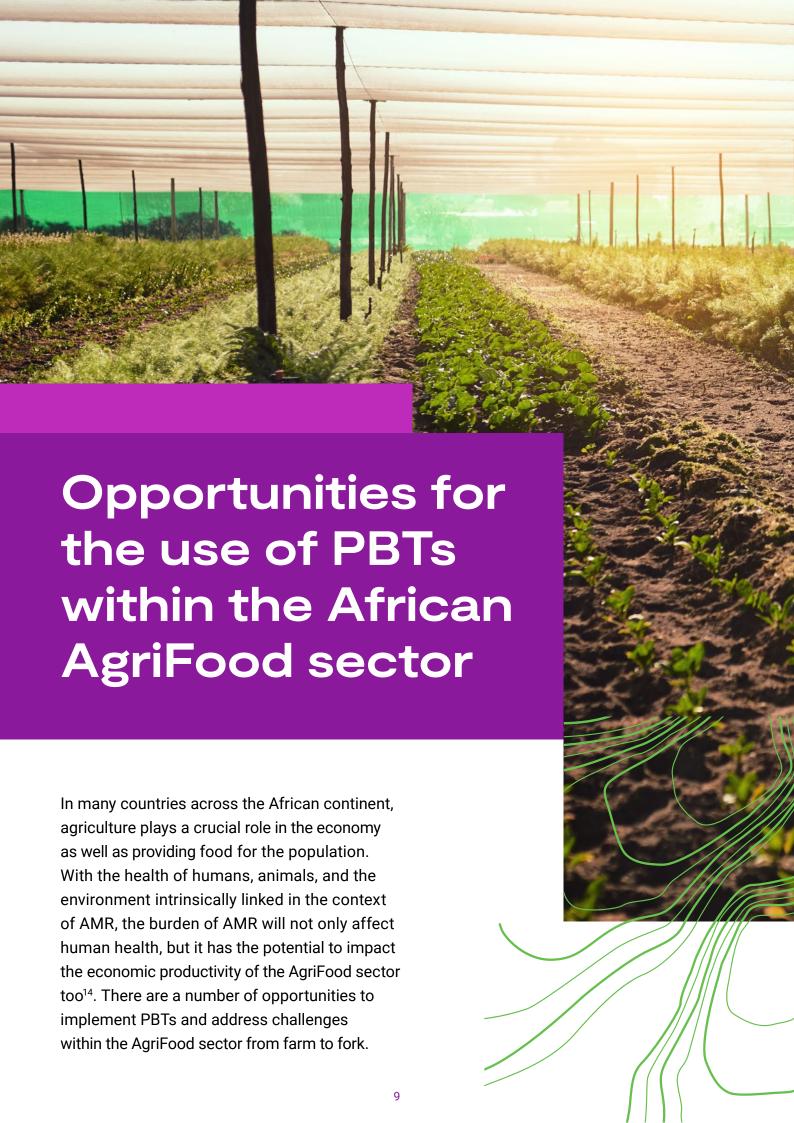


Phage scientists in Africa have made significant strides in the field, achieving milestones which reflect a growing expertise in phage biology. Over the last six years or so, a number of projects developing phage-based products for use in the AgriFood sector have been carried out in Africa. These projects have studied the use of phages for a variety of applications and bacterial targets including *Campylobacter jejunii* and *Salmonella* in poultry meat, *Ralstonia solanacearum* causing bacterial wilt, and *Edwardsiella*, *Aeromonas*, and *Streptococcus*in aquaculture.

The Africa Phage Forum (APF) was established in 2021 with the purpose of promoting scholarship, collaboration and mentorship among researchers for the advancement of phage research in Africa. The APF community includes undergraduates, postgraduates and established researchers at various stages

of their career who are all united through APF activities, stimulating knowledge exchange and collaboration. Other initiatives include Phage Kenya which is a collaborative programme uniting phage researchers based in Kenya working to progress phage research through spreading awareness and community building¹².

To support the growth of phage expertise in Africa, since 2017 the non-profit organisation Phages for Global Health, has delivered four two-week laboratory training courses in Uganda, Kenya, Ghana, and Tanzania. In addition to this, over 50 institutions in Central, East, West, and Southern Africa have been involved in phage research and there are several collaborative networks across the continent that exist to connect researchers, enhance scientific capacity, and further the development and use of phages in Africa¹³.



Application of phages to reduce crop loss

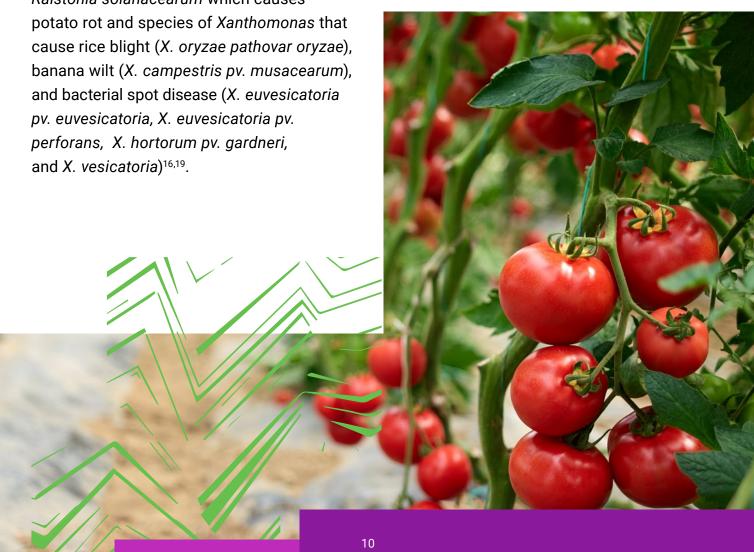
Challenge

Estimates suggest that 10% of global food production is lost due to plant diseases, with there being over 200 pathogenic bacterial species¹⁵. Those considered to be the most important globally belong to the genera Pseudomonas, Ralstonia, Agrobacterium, Xanthomonas, Erwinia, Xylella, Pectobacterium, and Dickeya^{16,17,18}.

In Africa, key bacterial diseases include Ralstonia solanacearum which causes

Opportunity

Phage-based biocontrols have been used as an alternative treatment for bacterial agricultural disease in both greenhouse and field conditions²⁰. This includes applications in soft rot infections by Pectobacterium in potato and Xanthomonas infections causing bacterial spot in tomatoes^{21,22}.



Application of phages as biocontrol agents in aquaculture

Challenge

According to the Food and Agriculture Organization (FAO), aquaculture production is at a record high (and growing further) with 178 million tonnes of aquatic animals produced in 2020²³. Top producing countries in Africa include Ghana, Nigeria, Uganda, Kenya, and South Africa with indigenous tilapia and catfish species being most abundantly produced on inland freshwater systems²⁴. Aquaculture provides a controlled and sustainable means of producing protein as well as a source of income, so bacterial infections in fish that lead to disease outbreaks are of significant concern to those working in this sector. Key pathogens include species of Aeromonas, Yersinia, Edwardsiella and Vibrio25. Use of antibiotics to control outbreaks can catalyse the development of resistance in bacteria. Alternative approaches to disease management which reduce the impact on AMR are needed.

Opportunity

Phage-based approaches can be utilised to prevent and treat infections. Phages are currently used in Norway to prevent yersiniosis in salmon²⁶ and there is a growing evidence base for the effectiveness of their use against a variety of pathogens within the industry²⁷. With the expansion of the aquaculture industry in Africa there is a significant opportunity to explore the implementation of phage-based approaches for disease management.





Challenge

Misuse and overuse of antibiotics within livestock farming is recognised globally as a driver of AMR. It is estimated that by 2050, livestock production will fall by up to 8% globally due to AMR. Regarding the economic impact of this, it is estimated that there will be an 11% loss in livestock production by 2050, with the highest decline anticipated in low-income countries²⁸. This is a particular challenge in Africa with high misuse of antibiotics due to a lack of diagnostics, training and up-to-date use guidelines, alongside challenges of limited access to quality antibiotics and counterfeiting²⁹.

Opportunity

There is an international effort to reduce the use of antibiotics within livestock production through stewardship and development of novel antimicrobial therapies. Phage-based approaches to treating and managing infections in livestock production offer a potential solution for the limited options available to livestock producers. Phage products are already used in various countries against a variety of different pathogens including *E.coli* and *Salmonella* and the evidence base supporting the efficacy of phage products applied in this context has expanded significantly in recent years³⁰.

Application of phages to reduce food loss and improve food safety

Challenge

In Central, East, West, and Southern Africa, more than 40% of food losses occur after the harvest stage of the food supply chain and before reaching the consumer³¹. Reducing contamination of food during processing is a critical aspect of ensuring food safety and reducing food loss. There are a variety of ways phages can be applied in this context, from preventing the transfer of pathogens into the food chain to improving the longevity or quality of products. The expansion of the formal food sector in sub-Saharan Africa is presenting new food safety risks. Increased commercialisation increases the risk of widespread contamination and challenges within physical infrastructure such as reliable sanitation, power and transport impose constraints on efforts to produce safe food32.

Opportunity

Phage-based approaches are effective at preventing bacterial contamination of food at post-harvest stages of the supply chain to reduce food loss and food waste. For example, spraying or washing vegetables in solutions containing phages to provide a protective film on the surface reduces loss due to contamination after harvest or in storage. Pectobacterium atrosepticum phages were successfully used in preventing the rotting of harvested potato tubers^{33,34}. A similar approach can be used post-slaughter for meat produce to combat the presence of foodborne pathogens such as E. coli and Salmonella. There are a variety of phage products licensed for use in this context in North America and Europe³⁵.



Challenge

Applying the One Health approach to infection control requires the recognition of the interconnectedness of human health, animal health, and environmental health. Addressing bacterial contamination within different areas of the ecosystem is crucial for combating AMR because the spread of resistant microorganisms and resistance genes occurs across these interconnected domains.

Opportunity

Phage-based solutions have the potential to be effective at minimising the prevalence of pathogenic bacteria in different environments. Phages could be applied in the sanitation of equipment used during farming and processing procedures^{36,37}. In addition, they have the potential to be effective agents for environmental decontamination, for example, as a sustainable approach to wastewater treatment^{38,39,40}. Finally, phage-based approaches could be implemented in the management microbiomes to maintain healthy and productive soil for crops⁴¹.



Barriers to use of phages in African AgriFood

Technical barriers

The knowledge base in phage research has grown considerably over the past twenty years or so and with it a deeper understanding of how to apply phages as antimicrobial agents has developed⁴². However, despite this progress there are still technical challenges to overcome globally in the development and implementation of PBTs in the AgriFood sector. These challenges are generally experienced worldwide and are described in more detail elsewhere described in more detail elsewhere that were highlighted during this scoping work regarding implementation of PBTs in Africa.

Maintaining efficacy

Phages are naturally specific to their target bacterial host species. In one sense, this is a distinct benefit of using phages as it means that certain species of bacteria can be precisely removed without affecting the wider microbiome. However, this inherent specificity can make ensuring the sustained efficacy of an off-the-shelf product containing a predetermined combination (or 'cocktail') of phages challenging as the product will not work if the target bacterial species are not susceptible to the phages.

Conscientious cocktail design to create a broad-spectrum product is a practical route for addressing challenges regarding efficacy, combined with considerate regulatory frameworks⁴⁷.

Nonetheless, to ensure sustainable, long-term efficacy epidemiological monitoring of target bacterial species is necessary. This enables monitoring evolving patterns of resistance, as well as identifying problematic bacterial species. As noted by several of the contributors to this report, the necessary infrastructure to report and track the emergence of bacterial disease in the AgriFood sector does not exist in many African countries. As a result, phage products could theoretically be implemented for certain applications, but ensuring their sustained efficacy would be challenging.

Stability

There are several factors which can affect phage activity in different environments. These include pH, moisture levels, presence of organic matter, temperature, and UV⁴⁸. A number of these factors either individually or in combination can cause phage inactivation. When considering the stability of a phage product, each stage of the supply and transport chain should be considered. For example, a product may need to withstand higher pH levels in the environment to have its desired effect, but it would be practical to ensure that it also remains stable at ambient room temperature to accommodate for any limitations in the provision of cold chain.

Administration of phage products

Within the AgriFood sector, many phage products will be used by farmers and primary producers. As such, it is important to consider their perspective when designing a novel product. A key aspect to consider is the route of administration. Innovation in antimicrobial treatments should not increase the complexity of current processes. For example, if a primary producer in aquaculture has an existing vaccine schedule for their fish it would be optimal for them to incorporate a phage-based prophylactic or therapeutic with the vaccine, so they only need to treat the fish once. This ensures the process of disease management remains straightforward while also limiting how often the fish are handled and helping to maintain their welfare. In addition, information about dosing and frequency of treatment should be made readily available and easy to understand. Making this information accessible to the end user helps to minimise misuse and encourage stewardship practices regarding the use of antimicrobials. Cost must be considered relative to other technologies. Since the commercialisation of phage products is in its infancy this is hard to refer to in terms of the actual cost of future products, but price point will be key to ensuring adoption.

Systematic barriers

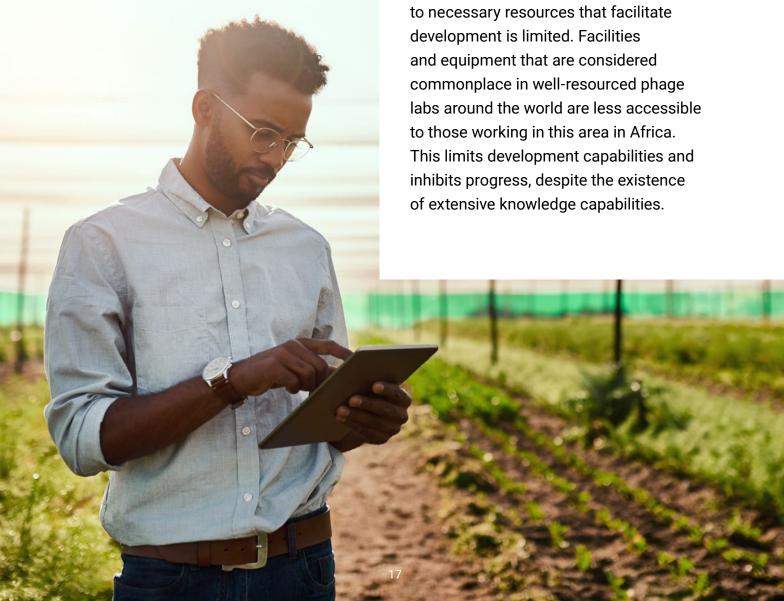
While addressing technical barriers is key to successfully developing efficacious phage products, it is also important to consider the systematic challenges that exist and need to be addressed to ensure preparedness for novel, innovative technologies. The systematic barriers described here were highlighted by experts in Africa working in the development and implementation of phage-based products.

Regulatory readiness

It was highlighted by experts from several countries that regulatory frameworks for phage-based products do not yet exist. Without clarity on the classification of phage products, it is challenging for developers to progress. In addition, the perception of regulatory ambiguity regarding phage products disincentivises investment in their development.

Capacity for development

Scarce funding means that access to necessary resources that facilitate development is limited. Facilities and equipment that are considered commonplace in well-resourced phage to those working in this area in Africa. This limits development capabilities and inhibits progress, despite the existence of extensive knowledge capabilities.

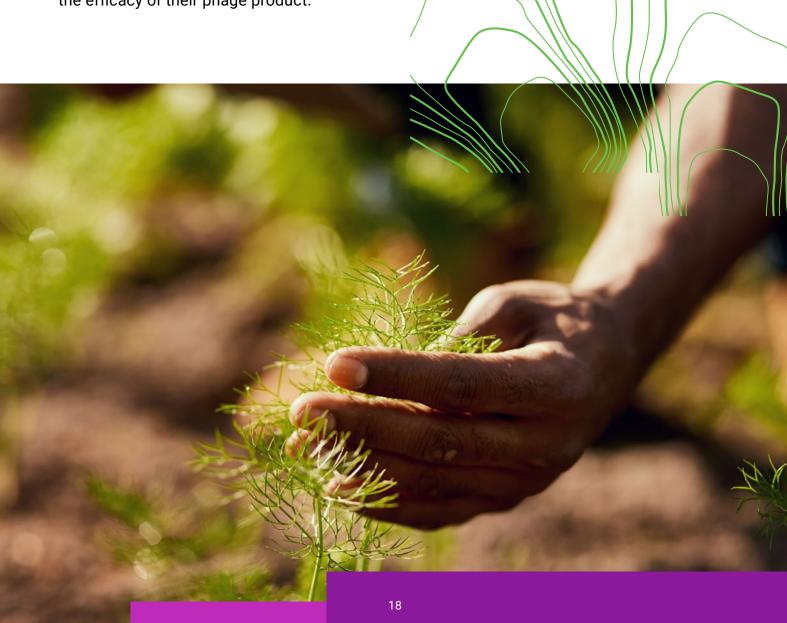


Limited epidemiological information

Knowledge of key bacterial pathogens and prevalence antibiotic resistance is key when developing sustainable infection control practices to address AMR. The dataset to inform this knowledge does not exist in many African countries. Outbreaks caused by bacterial pathogens are seldom monitored or reported. As previously described, having this information is key to ensuring the longevity of efficacy of a phage product. With this aspect of infrastructure lacking, it is challenging for developers to ensure they are targeting the appropriate strains of bacterial pathogens and ensure the efficacy of their phage product.

End-user acceptance

Crucial to the success of phage-based products in Africa is engagement with the different communities of end-users. Currently, there is limited understanding of AMR as an issue and phages as a solution. Ensuring that these communities are prepared for the emergence of innovative antimicrobial approaches within their sector is fundamental to ensuring the necessary impact the use of alternative antimicrobial approaches could have on addressing AMR.





AMR is a global challenge. Collaboration is crucial to finding and implementing novel approaches and solutions to support health and food security.

Through this work multiple areas in which collaboration and knowledge sharing would support in the development of PBTs have been identified. These areas focused around: capacity building, networking, and sharing of best practice. There is a history of international collaborations in this area, including projects supported by UKRI. There is an opportunity to build on these international collaborations and utilise the activities of global networks, such as the Innovate UK Phage Innovation Network and Phages for Global Health, as well as existing relationships between organisations to further the development of PBTs and their implementation in African countries.

Building the capacity of phage researchers and institutions is required to help minimise the impact of AMR within Africa, especially as this is a region which is expected to be disproportionately affected. Utilising the existing and growing networks of researchers globally to connect scientists and entrepreneurs is key to ensuring that connections are made between current and future experts. This could include sharing of ideas through collaborative R&D projects between UK and African organisations to develop phage-based solutions across two geographies and ensuring that there are routes for researchers globally to access equipment, for example sequencing or imaging tools. There are also opportunities for transfer of existing solutions between geographies and proven in the UK, to trial or test these in African environments. Similar opportunities for use and implementation of PBTs exist globally and challenges and interests are shared too, therefore collaboration should be encouraged regardless of geographic location.

19

Case studies

Using bacteriophages to reduce Salmonella infection in chicken-processing facilities in South Africa

Project partners: The Centre for Food Safety, Stellenbosch University, South Africa; Micreos, Switzerland

Challenge

Non-typhoidal Salmonella is estimated to cause 93 billion cases of gastroenteritis infection, and approximately 155,000⁴⁹ fatalities globally each year⁵⁰. The emergence of multi-drug resistant Salmonella is an increasing public health concern. Infection in humans is often caused by consumption of uncooked meat or meat products⁵¹. Salmonella is naturally present in the gut microbiome of chickens and can be transferred into the food supply chain when carriers are slaughtered and processed. Managing and reducing the contamination of food products intended for human consumption is critical within the poultry processing industry to reduce the incidence of foodborne Salmonella. Current methods to reduce the presence of Salmonella in processing include the use of chemicals, such as chlorine. Chlorine-resistance by salmonella bacteria is being observed, further driving the need for alternative processing approaches such as PBTs.

Research findings

During a four-week trial in a poultry-processing plant in South Africa, four million carcasses were sprayed with the commercially available bacteriophage product PhageGuard S (PGS), produced by Micreos⁵². The aim of this was to determine its impact on the presence of Salmonella within this supply chain. PGS is a water-based phage solution which contains Salmonella specific bacteriophages. It is approved for commercial use by both the FDA and USDA as a food processing aid. The trial found that use of PGS, combined with chlorine wash, on fresh meat pre-grinding or pre-packaging reduced the presence of Salmonella significantly. A spray system was designed to ensure that phages were not damaged during application, that coverage was sufficient, and that it could be delivered within the normal processing line.

Further work

Future work aims to troubleshoot the process of applying phages in this way and identify areas for improvement. In addition, engagement with government and regulators will be necessary to clarify regulatory classification of phage products used in this context and facilitate scale-up of use.

Development of bacteriophage cocktails as disease biocontrol agents for improved aquaculture productivity, food and nutrition safety in Ghana and Uganda

Project partners: CSIR-Food Research Institute, Ghana; CSIR-Water Research Institute, Ghana; Department of Fisheries and Aquatic Science, University of Cape Coast, Ghana; Noguchi Memorial Institute for Medical Research, Ghana; Department of Electron Microscopy and Histopathology, University of Ghana, Ghana; Department of Infection, Immunity and Inflammation, University of Leicester, UK

Challenge

Bacterial pathogens are of significant economic importance to the farming of tilapia in Ghana and Uganda. In Ghana fish mortality can be as high as 75-85% after stocking with fingerlings, and problems due to fish disease are the largest single cause of economic losses in aquaculture (Sudheesh et al., 2012).

Ongoing research

Led by the CSIR Food Research Institute, the SafeFish project⁵³ has identified species of *Aeromonas, Yersinia, Serratia*, and *Streptococcus* as relevant bacterial pathogens in fish in Uganda and Ghana. They aim to establish local banks of phages and formulate and evaluate phage-based products for aquaculture. Raising awareness to ensure future buy-in for biocontrol agents is a crucial part of the project, as well as capacity building for the research and development of phage technologies in East and West Africa.

Further work

Covid-19 lockdowns have impacted project progress; however, work is ongoing and collaborators are identifying production practices that influence the occurrence of fish spoilage; establishing the effectiveness of different phage combinations; and optimising formulation of phage cocktail products for use on fish farms. The beneficial impact of phage therapies in aquaculture globally are clear, with extensive work on the application of phages in this sector being carried out in the UK, Norway, Denmark, and Chile.



Application of Xanthomonas phages to control banana Xanthomonas wilt in Uganda

Project lead: Kyambogo University, Uganda



Banana *Xanthomonas* Wilt (BXW) threatens banana production and food security in Uganda¹⁶. Banana is a staple food crop which provides up to 25% of daily caloric intake. Conventional agricultural management practices, including the use of copper-based pesticides and antibiotics, are ineffective at controlling the disease but also contribute to antimicrobial resistance and pose an environmental hazard.

Ongoing research

With the aim of assessing the application of phages as a biocontrol agent to prevent BXW, the research team at Kyambogo University are working to isolate phages targeting Xanthomonas campestris pv. musacearum. Phages have been successfully isolated from diseased banana

plants and soil and are currently being studied for their antibacterial properties⁵⁴.

Further work

Globally, two Xanthomonas phage products manufactured by AgriPhage⁵⁵ have been shown to successfully control pathogens that cause tomato and pepper spot disease and citrus canker disease. The ongoing work at Kyambogo University will utilise the phages that have been identified in the development of a cocktail effective at controlling BXW and carry out field trials to test the efficacy of this cocktail. Future activity will look to establish scalable production processes for the cocktail and commercialise this product.

Development of a phage product to control Campylobacter contamination in poultry in Kenya⁵⁶

Project partners: University of Nottingham, UK; Makerere University, Uganda; Sokoine University of Agriculture, Tanzania; Kampala International University, Uganda

Challenge

Campylobacteriosis infection is a significant global health concern and is considered to be the most common type of gastroenteritis in humans worldwide with more than 95 million cases of foodborne illness attributable to Campylobacter infection^{57,58}. In Africa specifically, a recent analysis indicated that Nigeria had the highest overall prevalence of Campylobacter in humans of all ages and Kenya reported the highest prevalence in children under the age of five⁵⁹. The same study reported a high incidence of resistance to antibiotics frequently used to treat campylobacteriosis and an increase in the number of resistant Campylobacter strains. Considering the escalating rates of antibiotic resistance in Campylobacter, there is a critical need for sustainable alternative antimicrobial approaches to managing contamination of food products and preventing infection in humans.

Research findings

Through this project the research team have determined that phages could be added to the drinking water for chickens to prevent the introduction of *Campylobacter* into the food supply chain. Extended storage

stability is particularly crucial for disseminating products to developing nations, where access to refrigeration facilities necessary for biologicals in liquid form may not always be feasible. Through this work, the research team have effectively generated phage products targeting *Campylobacter* with a prolonged shelf life by using spray-drying and lyophilisation technologies.

Further work

Insights gained from this work support the cost-effective preparation of other phage formulations and biologics intended for global transportation. Community engagement with farmers during this project indicated that there is a clear inclination towards a powdered formulation that can be administered to poultry orally, either mixed in water or food. These key messages should be the focal point of further engagement activities with government stakeholders.

Applying phages to reduce post-harvest loss by controlling potato soft rot in Kenya

Project lead: Technical University of Kenya, Kenya

Challenge

Potatoes are the third most important food crop, after wheat and rice^{60,61,62} with global production reaching 376 million tonnes in 2021³⁰. Pectobacterium carotovorum causes tuber soft rot in stored farm produce. affecting many economically important vegetables including potatoes and causing significant crop loss (Onkendi and Moleleki, 2014; Muturi et al., 2018). Infection can occur during cultivation, harvesting, handling, transportation of farm produce, or during storage. Globally, current disease control approaches involve the sorting of tubers, ensuring sanitary procedures during processing, the use of potato varieties resistant to P. carotovorum, and crop rotation. Antibiotics and copper-based pesticides have been applied to inhibit P. carotovorum but with the emergence of antibiotic-resistant bacteria there is need for alternative disease management strategies.

Ongoing research

Phages effective against Kenyan isolated *P. carotovorum bacterium* have been isolated and characterised in China. Laboratory experiments demonstrated that these were effective at preventing infection of potato tubers⁶³.



Options to control soft rot disease in contaminated tubers could involve spraying phages onto potatoes after harvest or before storage. Trials in Russia indicated that use of phages in potato storage warehouses via the humidity maintenance systems could result in a decrease in the growth of phytopathogenic bacteria on tubers, with no soft rot symptoms being observed during the study⁶⁴. Research into the application methods of phages against soft rot suggests static application methods, such as sprinkling or spraying treatment with suspensions of phages, rather than washing, may be most effective⁶⁵. Alternatively, potato seeds could be inoculated with phages before planting to protect the seed tubers from infection. The development and testing of commercial products applying this research must be carefully designed to align to the storage and processing methods of farmers and producers. This is to both ensure their efficacy and secure adoption.

References

- 1 Antimicrobial Resistance Collaborators (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, Lancet, 399: 629–55 https://thelancet.com/action/ showPdf?pii=S0140-6736%2821%2902724-0
- 2 United Nations Environment Programme, Geneva (2023) Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance https://www.unep. org/resources/superbugs/environmental-actio n?gclid=CjwKCAjw7oeqBhBwEiwALyHLM1VFS Gu_qlTrUXY6x0zrKoPz0E2947dsnzfAXONgP5oN meGHtAjfVhoCmUAQAvD_BwE
- 3 https://www.woah.org/en/what-we-do/globalinitiatives/one-health/
- 4 World Organisation for Animal Health, Accessed 19 Dec 2023 https://www.woah.org/en/what-wedo/global-initiatives/one-health/
- 5 Phages against Pathogenic Bacterial Biofilms and Biofilm-Based Infections: A Review (2022) Siyu Liu, Hongyun Lu, Shengliang Zhang, Ying Shi and Qihe Chen, Pharmaceutics, 14(2):427 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8875263/#:~:text=As%20 natural%20enemies%20of%20bacteria%2C%20 phages%20can%20eradicate%20biofilms%20 through,infections%20of%20the%20host%20 bacteria
- 6 Chang Cheng, Yu Xinbo, Guo Wennan, Guo Chaoyi, Guo Xiaokui, Li Qingtian, Zhu Yongzhang, (2022) Bacteriophage-Mediated Control of Biofilm: A Promising New Dawn for the Future, Frontiers in Microbiology, 13 https://www.frontiersin.org/ articles/10.3389/fmicb.2022.825828
- 7 Joshua M. Borin, Sarit Avrani, Jeffrey E. Barrick, Katherine L. Petrie and Justin R. Meyer (2021) Coevolutionary phage training leads to greater bacterial suppression and delays the evolution of phage resistance, PNAS, 118 (23) https://www.pnas.org/doi/10.1073/pnas.2104592118#:~:text=A%20major%20barrier%20to%20successful,to%20evolve%20to%20counter%20resistance.
- 8 Elina Laanto, Kati Mäkelä, Ville Hoikkala, Janne J. Ravantti and Lotta-Riina Sundberg, (2020) Adapting a Phage to Combat Phage Resistance Antibiotics (Basel), 9(6): 291, doi: 10.3390/ antibiotics9060291 https://www.ncbi.nlm.nih. gov/pmc/articles/PMC7345892/

- 9 Adair L. Borges (2021) How to train your bacteriophage, Proc Natl Acad Sci U S A.; 118(28), doi: 10.1073/pnas.2109434118 https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC8285965/
- 10 Helen J. Stacey, Steven De Soir and Joshua D. Jones (2022) The Safety and Efficacy of Phage Therapy: A Systematic Review of Clinical and Safety Trials, Antibiotics 11(10):1340, doi/10.1089/phage.2022.29037.inp https://www.researchgate.net/publication/364258497_The_Safety_and_Efficacy_of_Phage_Therapy_A_Systematic_Review_of_Clinical_and_Safety_Trials
- 11 https://www.phagesforglobalhealth.org/
- 12 https://apf.phage.directory/
- 13 Tobi E. Nagel, Ivy J. Mutai, Theodore Josephs and Martha R.J. Clokie (2022) A Brief History of Phage Research and Teaching in Africa, Phage, 3(4):184-193, DOI:10.1089/phage.2022.29037. inp https://www.researchgate.net/publication/366653733_A_Brief_History_of_Phage_Research_and_Teaching_in_Africa
- 14 OECD and Food and Agriculture Organization of the United Nations (2016) OECD-FAO Agricultural Outlook 2016-2025, Chapter 2. Agriculture in Sub-Saharan Africa: Prospects and challenges for the next decade https://www.oecd-ilibrary.org/sites/agr_outlook-2016-5-en/index.html?itemId=/content/component/agr_outlook-2016-5-en
- 15 Colin Buttimer, Olivia McAuliffe, R. P. Ross, Colin Hill, Jim O'Mahony, Aidan Coffey (2017) Bacteriophages and Bacterial Plant Diseases, Front. Microbiol., 7 Sec. Antimicrobials, Resistance and Chemotherapy, doi.org/10.3389/ fmicb.2017.00034 https://www.frontiersin.org/ articles/10.3389/fmicb.2017.00034/full#B144
- 16 Mansfield, J., Genin, S., Magori, S., Citovsky, V., Sriariyanum, M., Ronald, P., et al. (2012). Top 10 plant pathogenic bacteria in molecular plant pathology. Mol. Plant Pathol. 13, 614–629. doi: 10.1111/J.1364-3703.2012.00804.X. https:// pubmed.ncbi.nlm.nih.gov/22672649/
- 17 Svircev A, Roach D, Castle A. (2018) Framing the Future with Bacteriophages in Agriculture, Viruses, 10(5):218. doi: 10.3390/v10050218. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5977211/

- 18 Nakayinga, R., Makumi, A., Tumuhaise, V. et al. (2021) Xanthomonas bacteriophages: a review of their biology and biocontrol applications in agriculture. BMC Microbiol, 21, 291 https://doi.org/10.1186/s12866-021-02351-7. https://bmcmicrobiol.biomedcentral.com/articles/10.1186/s12866-021-02351-7#citeas
- 19 W K Tushemereiwe, O O Okaasai, J Kubiriba, C Nankinga, J Muhangi, N Odoi, F Opio. (2006) Status of Banana Bacterial Wilt in Uganda. African Crop Science, 14 (2) 73-83 https://www.researchgate.net/publication/27792000_Status_of_Banana_Bacterial_Wilt_in_Uganda
- 20 Flaherty, J.E., Somodi, G.C., Jones, J.B., Harbaugh, B.K., & Jackson, L.E. (2000). Control of Bacterial Spot on Tomato in the Greenhouse and Field with H-mutant Bacteriophages, HortScience HortSci, 35(5), 882-884 https:// doi.org/10.21273/HORTSCI.35.5.882. https:// journals.ashs.org/hortsci/view/journals/ hortsci/35/5/article-p882.xml?tab_body=pdf
- 21 Jillian M. Lang, David H. Gent, and Howard F. Schwartz (2007) Management of Xanthomonas Leaf Blight of Onion with Bacteriophages and a Plant Activator, Plant Disease, 91:7, 871-878. https://apsjournals.apsnet.org/doi/epdf/10.1094/PDIS-91-7-0871
- 22 B. Balogh, J. B. Jones, M. T. Momol, S. M. Olson, A. Obradovic, P. King, and L. E. Jackson (2003) Improved Efficacy of Newly Formulated Bacteriophages for Management of Bacterial Spot on Tomato, Plant Disease 87:8, 949-954. https://apsjournals.apsnet.org/doi/epdf/10.1094/PDIS.2003.87.8.949
- 23 FAO (2022) The State of World Fisheries and Aquaculture 2022. Towards Blue Transformation. https://doi.org/10.4060/cc0461en https://www.fao.org/3/cc0461en/online/sofia/2022/keymessages.html
- 24 Babatunde Adeleke, Deborah Robertson-Andersson, Gan Moodley & Simon Taylor (2021) Aquaculture in Africa: A Comparative Review of Egypt, Nigeria, and Uganda Vis-À-Vis South Africa, Reviews in Fisheries Science & Aquaculture, 29:2, 167-197, DOI: 10.1080/23308249.2020.1795615. https://www. tandfonline.com/doi/full/10.1080/23308249.202 0.1795615
- 25 Irshath AA, Rajan AP, Vimal S, Prabhakaran VS, Ganesan R. (2023) Bacterial Pathogenesis in Various Fish Diseases: Recent Advances and Specific Challenges in Vaccine Development. Vaccines, 11(2):470 doi: 10.3390/vaccines11020470. PMID: 36851346; PMCID: PMC9968037. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9968037/

- 26 ACD Pharma. Custus. Accessed 19 Dec 2023 https://acdpharma.com/custusyrs-eng/
- 27 Ramos-Vivas, J.; Superio, J.; Galindo-Villegas, J.; Acosta, F. (2021) Phage Therapy as a Focused Management Strategy in Aquaculture. Int. J. Mol. Sci. 22, 10436. https://doi.org/ 10.3390/ijms221910436. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8508683/pdf/ijms-22-10436.pdf
- 28 World Bank (2017) Drug-Resistant
 Infections: A Threat to Our Economic Future,
 Washington, DC: World Bank. License:
 Creative Commons Attribution CC BY 3.0 IGO
 https://documents1.worldbank.org/curated/
 en/323311493396993758/pdf/final-report.pdf
- 29 Makumi, A.; Mhone, A.L.; Odaba, J.; Guantai, L.; Svitek, N. (2021) Phages for Africa: The Potential Benefit and Challenges of Phage Therapy for the Livestock Sector in Sub-Saharan Africa. Antibiotics, 10, 1085. https://doi.org/10.3390/ antibiotics10091085. https://www.mdpi. com/2079-6382/10/9/1085
- 30 Thanki AM, Hooton S, Whenham N, Salter MG, Bedford MR, O'Neill HVM, Clokie MRJ. (2023) A bacteriophage cocktail delivered in feed significantly reduced Salmonella colonization in challenged broiler chickens. Emerg Microbes Infect, 12(1):2217947. doi: 10.1080/22221751.2023.2217947. PMID: 37224439; PMCID: PMC10283443. https://pubmed.ncbi.nlm.nih.gov/37224439/
- 31 FAO (2011) Global food losses and food waste Extent, causes and prevention https://www.fao.org/3/i2697e/i2697e.pdf
- 32 Global Food Safety Partnership (2019)
 Food safety in Africa: Past endeavors
 and future directions. Washington, D.C.:
 World Bank. https://cgspace.cgiar.org/
 handle/10568/108321#:~:text=lt%20
 provides%20up-to-date,successful%20
 elsewhere%20but%20not%20yet
- 33 Alexander Byth Carstens, Amaru Miranda Djurhuus, Witold Kot, Lars Hestbjerg Hansen (2019) A novel six-phage cocktail reduces Pectobacterium atrosepticum soft rot infection in potato tubers under simulated storage conditions, FEMS Microbiology Letters, 366 (9) 101, https://doi.org/10.1093/femsle/fnz101
- 34 Maja A. Zaczek-Moczydłowska, Gillian K. Young, James Trudgett, Cali Plahe, Colin C. Fleming, Katrina Campbell, Richard O' Hanlon (2020) Phage cocktail containing Podoviridae and Myoviridae bacteriophages inhibits the growth of Pectobacterium spp. under in vitro and in vivo conditions, PLoS ONE 15(4): e0230842 https://doi.org/10.1371/journal.pone.0230842

- 35 Vikram A, Woolston J, Sulakvelidze A. (2021) Phage Biocontrol Applications in Food Production and Processing. Curr Issues Mol Biol, 40:267-302. doi: 10.21775/cimb.040.267 https://pubmed.ncbi. nlm.nih.gov/32644048/
- 36 Darshana Deka, U. S. Annapure, S. S. Shirkole, B. N. Thorat (2021) Bacteriophages: An organic approach to food decontamination https://doi.org/10.1111/jfpp.16101 https://ifst.onlinelibrary.wiley.com/doi/epdf/10.1111/jfpp.16101
- 37 Połaska M, Sokołowska B. (2019)
 Bacteriophages-a new hope or a huge
 problem in the food industry. AIMS
 Microbiol, 5(4):324-346. doi: 10.3934/
 microbiol.2019.4.324 https://www.ncbi.nlm.nih.
 gov/pmc/articles/PMC6946638/#:~:text=In%20
 biosanitization%2C%20phages%20or%20
 the,bacteria%20that%20spoil%20the%20food.
- 38 Srivastava P, Mishra CP, Nath G. (2022)
 Bacteriophages Can Make a Difference in Water
 Quality: Evidence From a Community-Based
 Study From North India. Cureus, 14(8):e27551.
 doi: 10.7759/cureus.27551 https://www.ncbi.nlm.
 nih.gov/pmc/articles/PMC9428944/
- 39 Ji, M., Liu, Z., Sun, K. et al. (2021) Bacteriophages in water pollution control: Advantages and limitations. Front. Environ. Sci. Eng, 15, 84 https://doi.org/10.1007/s11783-020-1378-y. https://link.springer.com/article/10.1007/s11783-020-1378-y
- 40 Mathieu J, Yu P, Zuo P, Da Silva MLB, Alvarez PJJ. (2019) Going Viral: Emerging Opportunities for Phage-Based Bacterial Control in Water Treatment and Reuse. Acc Chem Res, 52(4):849-857. doi: 10.1021/acs.accounts.8b00576 https:// pubmed.ncbi.nlm.nih.gov/30925037/
- 41 Braga, L.P.P., Spor, A., Kot, W. et al. (2020) Impact of phages on soil bacterial communities and nitrogen availability under different assembly scenarios. Microbiome 8, 52 https://doi.org/10.1186/s40168-020-00822-z. https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-020-00822-z#citeas

- 42 Maimaiti Z, Li Z, Xu C, Chen J, Chai W. (2023) Global trends and hotspots of phage therapy for bacterial infection: A bibliometric visualized analysis from 2001 to 2021. Front Microbiol, 13:1067803. doi: 10.3389/fmicb.2022.1067803. PMID: 36699585; PMCID: PMC9868171. https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC9868171/
- 43 Rhea Lewis, Colin Hill. (2020) Overcoming barriers to phage application in food and feed. Current Opinion in Biotechnology. 61, 38-44 https://doi.org/10.1016/j.copbio.2019.09.018. https://www.sciencedirect.com/science/article/pii/S095816691930093X
- 44 Lavilla, M.; Domingo-Calap, P.; Sevilla-Navarro, S.; Lasagabaster, A. (2023) Natural Killers: Opportunities and Challenges for the Use of Bacteriophages in Microbial Food Safety from the One Health Perspective. Foods, 12, 552 https:// doi.org/10.3390/foods12030552. https://www. mdpi.com/2304-8158/12/3/552
- 45 Fernández L, Gutiérrez D, Rodríguez A, García P. (2018) Application of Bacteriophages in the Agro-Food Sector: A Long Way Toward Approval. Front Cell Infect Microbiol, 22;8:296 doi: 10.3389/fcimb.2018.00296 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113595/
- 46 Shanshan Liu, Siew-Young Quek & Kang Huang (2023) Advanced strategies to overcome the challenges of bacteriophage-based antimicrobial treatments in food and agricultural systems, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2023.2254837. https://www.tandfonline.com/doi/epdf/10.1080/10408398.2023.2254837?needAccess=true
- 47 European Medicines Agency (2023) Guideline on quality, safety and efficacy of veterinary medicinal products specifically designed for phage therapy https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-quality-safety-and-efficacy-veterinary-medicinal-products-specifically-designed-phage-therapy_en.pdf
- 48 Shanshan Liu, Siew-Young Quek & Kang Huang (2023) Advanced strategies to overcome the challenges of bacteriophage-based antimicrobial treatments in food and agricultural systems, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2023.2254837. https://www.tandfonline.com/doi/epdf/10.1080/10408398.2023.2254837?needAccess=true
- 49 Majowicz S.E., Musto J., Scallan E., Angulo F.J., Kirk M., O'Brien S.J., Jones T.F., Fazil A., Hoekstra R.M. (2010) The global burden of nontyphoidal salmonella gastroenteritis. Clin. Infect. Dis, 50:882–889. doi: 10.1086/650733. https://academic.oup.com/cid/article/50/6/882/419872

- 50 Khan MAS, Rahman SR. (2022) Use of Phages to Treat Antimicrobial-Resistant Salmonella Infections in Poultry. Vet Sci., 9(8):438. doi: 10.3390/vetsci9080438 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9416511/#B8-vetsci-09-00438
- 51 Ramatla, T.; Tawana, M.; Onyiche, T.E.; Lekota, K.E.; Thekisoe, O. (2021) Prevalence of Antibiotic Resistance in Salmonella Serotypes Concurrently Isolated from the Environment, Animals, and Humans in South Africa: A Systematic Review and Meta-Analysis. Antibiotics, 10, 1435. https://doi.org/10.3390/antibiotics10121435. https://www.mdpi.com/2079-6382/10/12/1435
- 52 Phage Guard, Micreos, Phage usage in Poultry Processing https://www.fmcgis.com.au/Phage%20 usage%20in%20Poultry%20Processing.pdf
- 53 Jesca Nakavuma et al. (2019) Building capacity for phage applications in management of livestock production diseases: AU-project on tilapia disease management on aquaculture farms in Ghana and Uganda https://www.researchgate.net/publication/341089700_BUILDING_CAPACITY_FOR_PHAGE_APPLICATIONS_IN_MANAGEMENT_OF_LIVESTOCK_PRODUCTION_DISEASES_AU-PROJECT_ON_TILAPIA_DISEASE_MANAGEMENT_ON_AQUACULTURE_FARMS_IN_GHANA_AND_UGANDA
- 54 Kyambogo University (2021) Biocontrol strategies for the management of Banana Xanthomanas Wilt in Uganda: Preliminary findings https://www.youtube.com/watch?v=2vArNkaPoGI
- 55 Omnilytics, Accessed 19 Dec 2023 ttps://www.omnilytics.com/
- 56 UKRI Project Description, Development of a Bacteriophage Product to Control Campylobacter Contamination in Kenya, University of Nottingham https://gtr.ukri.org/projects?
 ref=BB%2fP02355X%2f1&pn=1&fetchSize=10
 &selectedSortableField=firstAuthorName
 &selectedSortOrder=ASC#/tabOverview
- 57 World Health Organisation, Campylobacter Fact Sheet, Accessed 19 Dec 2023 https://www.who.int/news-room/fact-sheets/detail/campylobacter
- 58 Havelaar AH, Kirk MD, Torgerson PR, Gibb HJ, Hald T, Lake RJ, et al. (2015) World Health Organization Global Estimates and Regional Comparisons of the Burden of Foodborne Disease in 2010. PLoS Med 12(12): e1001923. https://doi.org/10.1371/journal.pmed.1001923 https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001923

- 59 Gahamanyi N, Mboera LEG, Matee MI, Mutangana D, Komba EVG. (2020) Prevalence, Risk Factors, and Antimicrobial Resistance Profiles of Thermophilic Campylobacter Species in Humans and Animals in Sub-Saharan Africa: A Systematic Review. Int J Microbiol, doi: 10.1155/2020/2092478. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6983289/
- 60 Onkendi EM, Maluleke LN, Moleleki LN. (2014)
 First Report of Pectobacterium carotovorum
 subsp. brasiliense Causing Soft Rot and Blackleg
 of Potatoes in Kenya. Plant Dis, 98(5):684. doi:
 10.1094/PDIS-09-13-0988-PDN https://pubmed.
 ncbi.nlm.nih.gov/30708532/
- 61 Muturi P, Yu J, Li J, Jiang M, Maina AN, Kariuki S, Mwaura FB, Wei H. (2018) Isolation and characterization of pectolytic bacterial pathogens infecting potatoes in Nakuru County, Kenya. J Appl Microbiol., 124(6):1580-1588. doi: 10.1111/jam.13730. https://pubmed.ncbi.nlm.nih.gov/29437273/
- 62 Patil VU, Sharma NN, Chakrabarti SK. (2017) High-throughput sequencing of the potato genome. In: Chakrabarti SK, Xie C, Tiwari JK, editors. The potato genome. Berlin: Springer; 95–107. https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC6599505/#CR16
- 63 Muturi P, Yu J, Maina AN, Kariuki S, Mwaura FB, Wei H. (2019) Bacteriophages Isolated in China for the Control of Pectobacterium carotovorum Causing Potato Soft Rot in Kenya. Virol Sin., 34(3):287-294. doi: 10.1007/s12250-019-00091-7 https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC6599505/
- 64 Bugaeva, E.N.; Voronina, M.V.; Vasiliev, D.M.; Lukianova, A.A.; Landyshev, N.N.; Ignatov, A.N.; Miroshnikov, K.A. (2021) Use of a Specific Phage Cocktail for Soft Rot Control on Ware Potatoes: A Case Study. Viruses, 13, 1095. https://doi. org/10.3390/v13061095 https://www.mdpi. com/1999-4915/13/6/1095
- 65 Beňo F, Horsáková I, Kmoch M, Petrzik K, Krátká G, Ševčík R. (2022) Bacteriophages as a Strategy to Protect Potato Tubers against Dickeya dianthicola and Pectobacterium carotovorum Soft Rot. Microorganisms., 10(12):2369. doi: 10.3390/microorganisms10122369. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9785987/



iuk.ktn-uk.org/programme/agrifood-africa-connect

03333 403250 • enquiries@iuk.ktn-uk.org • @innovateuk