

Brussels, 19 May 2026

COST 061/26

DECISION

Subject: Memorandum of Understanding for the implementation of the COST Action
“Bacteriophages for crop protection: Discovery, Exploration, Application & Society”
(Phage4Crops) CA25147

The COST Member Countries will find attached the Memorandum of Understanding for the COST Action Bacteriophages for crop protection: Discovery, Exploration, Application & Society approved by the Committee of Senior Officials at its 227th meeting held in Brussels on 19 May 2026.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA25147
BACTERIOPHAGES FOR CROP PROTECTION: DISCOVERY, EXPLORATION, APPLICATION & SOCIETY (Phage4Crops)

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to Phage4Crops action aims to explore how phage-based treatments can reduce yield losses caused by bacterial diseases, decrease pesticide dependence, and improve soil and plant health by linking researchers, regulatory experts, farmers, and industry stakeholders.. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

OVERVIEW

Summary

Sustainable management of agricultural threats, such as plant-pathogenic bacteria, is crucial for food security in the context of environmental challenges. Despite its tremendous potential, bacteriophage biocontrol is still in its infancy and many challenges – not only technical, but also at the regulatory and societal level – need to be overcome before it can be used effectively in the agri-food sector.

Inspired by the One Health concept, the Phage4Crops project proposes to build an unprecedented, multi-stakeholder network in the field of bacteriophage biocontrol in the agri-food sector. To overcome the current lack of collaboration and communication between researchers and implementors, which is wasting synergies and momentum, we will bring together previously dispersed activities, resources and manpower, including experts in the fields of bacteriophage biology, bacterial genomics, metagenomics, bioinformatics, agronomy, epidemiology, microbial ecology, plant pathology and physiology, biotechnology and social sciences.

This project is innovative and timely as it addresses fundamental questions on different pathosystems of European interest in a global context, from the discovery and exploration up to the applicability of bacteriophages as biocontrol agents. We will establish protocols to guide the selection and deployment of bacteriophage-based solutions; isolate, characterise and make accessible novel bacteriophages; educate and train next generation of experts; create bridges between researchers, society and industry to integrate bacteriophage-based biocontrol into appropriate ecological and legislative framework. The Phage4Crops action will tightly link fundamental and applied bacteriophage research, building the critical mass to drive scientific progress, thereby strengthening the European Research Area and paving the way for bacteriophage applications.

Areas of Expertise Relevant for the Action • Agriculture, Forestry, and Fisheries: Prevention and treatment of infection by pathogens (e.g. vaccination, antibiotics, fungicide) • Biological sciences: Microbiology • Biological sciences: Molecular biology and interactions • Agriculture, Forestry, and Fisheries: Agriculture related to crop production, soil biology and cultivation, applied plant biology, crop protection • Biological sciences: Virology	Keywords • Bacteriophage biocontrol • Phytopathogenic bacteria • Sustainable plant protection • Bacterial plant diseases • Agricultural innovation
--	---

Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

- 1)□establish a European network addressing the fragmented landscape of agricultural phage research by connecting experts across microbiology, bioinformatics, plant pathology, and social sciences.
- 2)□generate and disseminate integrated knowledge on phages infecting phytopathogenic bacteria through collaborative studies on plant–bacterium–phage interactions, prophage content, and bacterial defence systems
- 3)□develop shared resources, including a European phage repository and an open-access database linking bacterial hosts, phage genomes, and phenotypic data, to facilitate comparative studies and rational cocktail design

- 4) □ validate phage efficacy in controlled and field conditions, producing standardised application protocols to guide deployment under different environmental contexts
- 5) □ encourage teaching and training for future research on phages of phytopathogenic bacteria and to promote the use of phages by proactively informing regulatory authorities, farmers, and industry, providing evidence-based recommendations for safe and effective phage use as sustainable alternatives to harmful agrochemicals

Capacity Building

- 1) □ provide continued education of European investigators and build bridges between research teams and companies in different countries through annual conferences, fostering innovation and cross-sector collaboration
- 2) □ coordinate target-oriented training of European young researchers and innovators (YRIs) through dedicated workshops and training schools
- 3) □ propagate inter-laboratory exchange of personnel, enabling direct skill transfer and standardisation of experimental workflows across partner institutions
- 4) □ lower entrance hurdles for young scientists and newcomers in the field by collecting, drafting, and making open-access guidelines for experimental approaches
- 5) □ foster contacts with key stakeholders (e.g., farmers organisations, extension services, the European Food Safety Authority, committees of the European Parliament, national regulatory authorities) to translate research findings into policy and practice

TECHNICAL ANNEX

1. EXCELLENCE IN S&T AND NETWORKING

A. Main challenge

Sustainable management of agricultural pests and diseases is crucial for food security in the face of accelerating environmental challenges. Inspired by the One Health approach ^[1] and aligned with the *United Nations Sustainable Development Goals* (<https://sdgs.un.org/goals>), the PHAGE4CROPS COST Action proposes to build a multidisciplinary network to establish and demonstrate a reliable scientific basis for the use of bacteriophages (hereafter phages), the viruses of bacteria, as biocontrol agents of bacterial plant diseases. Phages, as part of the natural microbiota, are promising alternatives to antibiotics in the medical sector, which faces the emergence of antibiotic-resistant bacterial infections. In the medical field, over 200 patients in therapeutic dead-ends have been treated compassionately with phages across twelve countries (notably Belgium) in the past decade ^[2], and large-scale clinical trials are expected soon in Europe. The European Commission recently demonstrated its commitment by funding three international phage therapy trials under the HORIZON programme (expected 2026). Applications of phages in the food industry and the veterinary field are also exploding in order to replace antibiotics. In the veterinary sector, phage-based feed additives have recently been authorised at the European level. For example, *Proteon Pharmaceuticals SA* received EU approval in July 2025 for a phage preparation targeting *Salmonella enterica* in poultry ^[3]. In agriculture, commercial phage-based products such as *Erwiphage* (Hungary), used against fire blight in apple and pear orchards (*Erwinia amylovora*), have already shown promising results ^[4]. Comparable phage preparations are also marketed in the food industry, e.g., the USDA FDA-approved *PhageGuard L* against *Listeria monocytogenes*, illustrating the rapid diversification of phage applications ^[5].

Phage biocontrol in crops is still emerging, with limited studies on phage-bacterium interactions in agricultural systems. To design effective and durable treatments, it's crucial to expand phage collections, improve genetic characterisation of both phages and pathogens, and study bacterial defence systems, which remain poorly understood in plant pathogens. Deeper insight into phage-bacterium coevolution will enable the development of tailored, resistance-resilient phage therapies ^[6]. Beyond fundamental research, PHAGE4CROPS aims to demonstrate how phage biocontrol can translate into tangible benefits for European agriculture. The COST Action will explore how phage-based treatments can reduce yield losses caused by bacterial diseases, decrease pesticide dependence, and improve soil and plant health. By linking researchers, regulatory experts, farmers, and industry stakeholders, the network will also contribute to harmonising European regulatory frameworks and ensuring that phage products can reach the market safely and efficiently.

The European research landscape on phages in the agricultural context currently suffers from uncoordinated, isolated and parallel efforts from discovery to application of phages. Unfortunately, many initiatives are restricted to the national or regional level, which is not adapted to the widespread, EU- or even world-wide appearance of the phytopathogens. Studies are also impaired by lack of knowledge about initiatives in other countries and the lack of a phage repository for comparative studies and the rational design of phage cocktails.

Finally, the Action acknowledges and will collaboratively address ethical and societal questions, including biosafety, intellectual property, and public perception, to ensure responsible and socially accepted adoption of phage-based solutions ^[7,8,9]. It is therefore of uttermost importance to link fundamental and applied research tightly, to build the critical mass to drive scientific progress, thereby strengthening the European Research Area, and to pave the way for assessing phage applications at the regulatory and societal level.

B. Objectives

There are two broad, interlinked groups of objectives relating to research coordination and capacity building, which we will discuss in detail below.

B.1. Research coordination objectives

The project's general aims with respect to research coordination are:

- 1) **establish a European network** addressing the fragmented landscape of agricultural phage research by connecting experts across microbiology, bioinformatics, plant pathology, and social sciences;

- 2) **generate and disseminate integrated knowledge** on phages infecting phytopathogenic bacteria through collaborative studies on plant–bacterium–phage interactions, prophage content, and bacterial defence systems;
- 3) **develop shared resources**, including a **European phage repository** and an open-access database linking bacterial hosts, phage genomes, and phenotypic data, to facilitate comparative studies and rational cocktail design;
- 4) **validate phage efficacy in controlled and field conditions**, producing standardised **application protocols** to guide deployment under different environmental contexts; and
- 5) **encourage teaching and training** for future research on phages of phytopathogenic bacteria and to promote the use of phages by proactively **informing regulatory authorities, farmers, and industry**, providing evidence-based recommendations for safe and effective phage use as sustainable alternatives to harmful agrochemicals.

This project will generate new and integrated knowledge on phages of phytopathogenic bacteria. The approaches include studying plant-bacteria-phage interactions, characterizing bacterial defences and prophages in genomes, and developing an educational curriculum on phage discovery and characterisation. It will also explore front science strategies based on modelling of phage control of plant diseases and metagenomic analysis of phage diversity and prevalence in the agricultural landscape. The COST Action takes a multidisciplinary approach that will explore evolutionary, ecological and molecular interactions and will translate them into practical and sustainable biocontrol solutions.

To ensure feasibility and measurable impact, **key deliverables** will include:

- ≥200 novel phages isolated across Europe (≥100 of them genetically characterised), with metadata curated in a public database,
- at least **three cross-country validation trials in agricultural relevant settings** (*i.e.*, greenhouse or field assays) assessing phage biocontrol efficacy, coordinated via the Action but financed outside COST (*e.g.*, *E. amylovora*, *Pseudomonas syringae*, *Ralstonia solanacearum*),
- **best-practice guidelines** for phage formulation, application, and regulatory compliance, and
- a **stakeholder engagement report** summarising farmer feedback and regulatory perspectives.

To expand the network of proposers, relevant partners will be identified at the beginning of the project through systematic surveys. The national agronomic and phage societies will be approached to create a database of target bacteria of priority importance for European agriculture and the available studies on them. In order to reach a broad consensus, interested partners will be asked to answer a questionnaire on which bacterial models they work, which resources they have, which gaps they identify that prevent them from breakthrough discoveries or product development. Additionally, the *European and Mediterranean Plant Protection Organization* (EPPO) recommends that several of these pathogens be regulated as quarantine pests, as they are either absent or not widely distributed in the EPPO region^[10]. These pathogens are therefore particularly relevant to the EU and will receive special attention in the proposed COST Action.

Based on the results of the stakeholder survey, scientific and economic criteria^[11], and EPPO recommendations, this Action will focus on several bacterial phytopathogens (at least four) that are highly likely to respond well to phage biocontrol. Among them are the causative agents of severe bacterial diseases on economically important crops such as cucurbit plants (*Acidovorax citrulli*), horseradish, grape vines, rhubarb, stone fruits, nut trees and sugar beet (*Agrobacterium tumefaciens*), bell pepper and tomato (*Clavibacter michiganensis*), bean, soybean, red beet, onion bulb rot and tulip (pathovars of *Curtobacterium flaccumfaciens*), fruit trees including apple and pear (*E. amylovora*), carrots, potato and tomato (Soft rot *Pectobacteriaceae*), cabbage and melon (*Pantoea* spp.), prunus trees like apricot, cherry and plum, tomato, bacterial blight of common bean and melon (*P. syringae*), potato and tomato (members of the *R. solanacearum* species complex), cabbage, carrot, lettuce, bell pepper, tomato, strawberry, hazelnut and walnut (*Xanthomonas* spp.) and olive, grapevine and a range of perennial hosts (*Xylella fastidiosa*).

B.2. Capacity-building objectives

At the start of the COST Action, we will promote the project and use interactive online tools with interested partners to identify their resource needs (website, databases and bioinformatics tools) and knowledge gaps in their own expertise (specific skills, technologies). Building on this overview, we will plan **workshops and training schools** and offer internship opportunities among the PHAGE4CROPS partners, supported by the COST networking instrument of **short-term scientific missions** (STSM). Specifically, we wish to organise training schools and workshops, where we will address various aspects in the field of phage research, such as (i) “*Hunt for Phages*” (*i.e.*, phage isolation from field samples), (ii)

phage genome analysis, preferentially of own samples, (iii) phage host range analysis methods, and (iv) phage applications.

Many researchers of the PHAGE4CROPS consortium teach at Bachelor's, Master's and/or PhD level, so we can ensure the **dissemination of knowledge** generated in this COST Action to students. Phages, which were at the dawn of molecular genetics (Luria–Delbrück and Hershey–Chase experiments ^[12,13], Nobel Prize in 1969), still serve as a guide for the development of innovative teaching modules. In this context, we will align our initiative with the *Marie Skłodowska-Curie Actions* (MSCA). If the agenda allows, we will establish a consortium of interested partners from the academic and non-academic sectors to build a doctoral network to train highly skilled doctoral candidates, stimulate their creativity, enhance their innovation capacities and boost their employability in the long-term. This initiative will make use of the profoundly cross-cutting nature of phage studies, linking bacteria-phage interactions within the environment, genetics, bioinformatics, applications and legislation. The doctoral network is thus meeting the increasing demand from students for new content and methods that can also promote their autonomy, motivation and group cohesion.

Specifically, our COST Action will:

- 1) provide continued education of European investigators and build bridges between research teams and companies in different countries through **annual conferences**, fostering innovation and cross-sector collaboration;
- 2) coordinate target-oriented **training** of European young researchers and innovators (YRIs) through dedicated **workshops** and **training schools**, involving **60 trainees**, which will introduce the concepts of phage biocontrol, methods and tools, along with hands-on training to foster familiarity with these techniques,
- 3) inter-laboratory exchange of personnel through at least **40 STSM grants**, enabling direct skill transfer and standardisation of experimental workflows across partner institutions;
- 4) lower entrance hurdles for young scientists and newcomers in the field by collecting, drafting, and making **open-access guidelines** for experimental approaches, thus avoiding time-consuming, erroneous investments; and
- 5) foster contacts with key **stakeholders** (e.g., farmers organisations, extension services, the *European Food Safety Authority*, committees of the *European Parliament*, national regulatory authorities) to translate research findings into policy and practice, through visits and invitations to the COST Action events.

Collectively, the capacity building modules will secure the continuity, visibility, and resilience of the COST Action network while providing tangible, measurable outputs:

- ≥200 trained young researchers across Europe,
- ≥10 collaborative research outputs (joint publications incl. YRIs, shared datasets), and
- ≥100 stakeholders actively engaged through surveys, consultation, workshops, and dissemination events.

C. State-of-the-art

Pathogenic bacteria are an increasing threat to human, animal and plant health, posing serious risks to food security. Phages are emerging as promising biocontrol agents ^[14]. Large community-driven efforts are devoted to accelerating phage treatments of human bacterial infections because of the emerging threat of multidrug resistant bacteria. Clinical trials and compassionate, last-option use of phage therapy treatments are currently being tested in several European countries and around the world against diseases caused by multidrug-resistant bacteria ^[15,16,17]. Although the regulatory framework for phage use in food safety remains under development, the *European Court of Justice* has issued a court order in 2019 that allows food companies to use phages to eliminate *Listeria* in ready-to-eat food. Since then, phage cocktails have been marketed against various food-borne pathogens in food products and surfaces.

Phages may also represent a source of innovation for agriculture, offering an environmentally safe alternative to chemical pesticides. Current management of bacterial plant diseases often relies on compounds such as copper, which present ecological risks and declining efficacy. By contrast, phages are specific, self-replicating, and biodegradable, making them ideal tools for integrated pest management and sustainable agriculture. Although studies are in progress on several pathogens, research on phage in agriculture is heavily underdeveloped in comparison to the medical field (Table 1). Therefore, the COST Action seeks to achieve a deep understanding of phages for some of the most important bacterial plant pathogens in order to develop phages as biocontrol agents, thus improving the management of crop diseases.

Table 1. Status of phage research and applications, depending on the context.

Medicine	Agriculture
On-going clinical assays	Very few field assays
Extensive phage collections	Few phages isolated
Molecular details on phages available	Molecular details of phages poorly characterised
Multiple evolutionary studies	Insufficient evolutionary studies
Profound knowledge on phage communities in humans	Knowledge gap on phage communities in plants

Phage applications in agriculture can target several stages of the production chain: (i) Seed and nursery treatments, preventing early-stage bacterial infections, (ii) soil and rhizosphere applications, reducing soil-borne pathogen loads and promoting beneficial microbiota, (iii) foliar sprays and drip irrigation, widely tested in greenhouse and field trials, (iv) injection or vascular delivery systems, applied in high-value perennial crops such as olive or citrus trees infected by *X. fastidiosa*. To enhance stability and field persistence, encapsulation strategies (e.g., alginate beads, chitosan nanoparticles, liposomes, and biodegradable polymers) are being developed to protect phages from UV light, desiccation, and temperature stress, while enabling controlled release. Combining such technological advances with ecological modelling will improve phage performance under diverse climatic conditions. Phages may complement other agroecological practices and unchain the potential use of microbiota in plant diseases. However, a deeper fundamental and applied knowledge on phages in the agricultural context is key to advance their development as biocontrol agents in agriculture, enhancing food security. This is especially true in Europe, where efforts in phage research are mainly devoted to human, industrial or pure molecular biology contexts. The COST Action will close this gap by bringing together phage and bacteria experts working in fundamental research and/or agricultural applications, along with farmers and regulatory stakeholders.

Notably, phages have already been proven useful in greenhouse and field trials against some major plant pathogens, including *E. amylovora*, *Pectobacterium* spp., *R. solanacearum*, and *Xanthomonas* spp. [18,19,20,21] More and more companies invest into this sector. *APS Biocontrol Ltd.* (UK), *De Ceuster Meststoffen NV* (Belgium), *Enviroinvest Zrt.* (Hungary), *OmniLytics Inc.* (USA) and *Phagelux Inc.* (China) have commercialised - or are in the process of obtaining authorisation for commercialisation - of the first phage preparations against plant pathogens. Although there is clearly great potential for the use of phages as biocontrol agents in crop production, only a limited number of phages have been commercialised in the agri-food sector, particularly in Europe, not only for technical but also for legal reasons [22].

Despite tremendous interest in phage applications in agriculture, the EU's research and development (R&D) landscape is fragmented and in need of better coordination. The proposed project will promote the emerging research community that is working on phages in the agricultural sector. The proposers are not aware of any comparable initiative that links fundamental and applied research so closely at the European level. The COST Action will thus enable the creation of an unprecedented, innovative, multidisciplinary network with critical mass in the field of phage biocontrol in the agri-food sector.

D. Rationale for choosing networking to address the main challenge

The awakening interest in phages in EU agriculture is reflected in several previous or ongoing projects that involve phages in different ways, i.e., H2020 "VIROPLANT: Virome NGS analysis of pests and pathogens for plant protection" (2018-2021), H2020 "PhageFire: An effective and environmentally friendly solution to control fire blight disease caused by *E. amylovora* in pome fruit crops" (2020-2024), COST Action CA16107 "EuroXanth: Integrating science on *Xanthomonadaceae* for integrated plant disease management in Europe" (2017-2021), and HORIZON EUROPE "BeXyl: Beyond *Xylella*" (2022-2026). The current proposal aims to include experienced members of these projects as well as new members interested in phages development and application.

In the last years, researchers have taken the initiative to create dedicated national networks to promote research on phages in Europe and beyond, such as the *Belgian Society for Viruses of Microbes*, the *Belgian Phage Valley*, the *Réseau Bactériophage France*, the priority program SPP2330 and the DZIF *TransPhage-Net* in Germany, the Spanish *FAGOMA thematic network*, *phageSuisse*, *Phage-UK*, *PHAGE Canada*, the *Africa Phage Forum* and the non-profit organisation *Phages for Global Health*. The COST Action will create and strengthen links between the various national initiatives and stimulate the creation of new organisations or societies.

In the private sector, of the approximately twenty companies around the world which have invested in the field phage biocontrol in agriculture, only few are European (e.g., *Bactolytix/Greenphage*, *Bioline AgroSciences Ltd.*, *Enviroinvest Zrt.*, *APS Biocontrol Ltd.*, *De Ceuster Meststoffen NV*). Our goal is to

build a network of research and application and create synergies that will endure over time and lead to sustainable and efficient applications of phages. Importantly, experts in agriculture and legal aspects will influence and enrich the consortium. Our project will also inform all relevant stakeholders about this initiative and how to get connected, and this networking initiative will facilitate the exchange of biological samples and trained personnel among the partner countries.

The proposed COST Action will promote the emerging research community of phages in the agricultural sector. The proposers are not aware of any comparable initiative on such a large geographical scale that combines fundamental and applied research so closely within a multidisciplinary framework. The COST Action will initially evaluate at least four important groups of phytopathogenic bacteria based on surveys and scientific/economic criteria^[11]. These bacterial pathogens cause significant losses to important crops in Europe (cf. Section 1B) and/or pose a threat to crops in countries where some of the diseases are not currently present. This project will produce useful protocols guiding the isolation, genomic characterisation, choice and use of candidate phages against emergent plant bacterial pathogens in Europe and how to match applications with a suitable ecological and evolutionary framework.

The COST Action is thus a pivotal, transversal and federative initiative for the development of agricultural phage biocontrol in Europe. It will also complement and strengthen alternative efforts on the development of biocontrol strategies, such as those involving microorganisms, macro-organisms, or natural substances^[23]. In this context, links exist to several previously established COST Actions, *i.e.*, CA21134 “Towards zero Pesticide AGRiculture: European Network for sustainability” (T0P-AGRI-Network) (2022-2026), CA22158 “Exploiting Plant-Microbiomes Networks and Synthetic Communities to improve Crops Fitness (MiCropBiomes)” (2023-2027) and CA22142 “Beneficial root-associated microorganisms for sustainable agriculture (ROOT-BENEFIT)” (2023-2027), although none of them explicitly mentions “phages” in their memorandum of understanding. Our COST Action will capitalise on the outcomes of these related initiatives to create synergies and prepare new European collaborative proposals within the forthcoming HORIZON programmes, including FARM2FORK and BIODIV.

Building on these various, partially overlapping initiatives and consortia, the COST Action will have an integrating and synergistic effect by creating a multidisciplinary phage biocontrol consortium working with agricultural pests that includes experts (*i.e.*, agronomists, bacteriologists, virologists, theoretical researchers and social scientists) who are not yet connected, thus pushing forward biocontrol organisms – from discovery and understanding to application – into a new dimension.

E. Critical mass of the network

PHAGE4CROPS brings together partners with the ensemble of competences and experience needed to achieve the objectives of the project. Our consortium covers the following disciplines: Agriculture; Agronomy; Biochemistry; Bioinformatics; Biotechnology; Ecology; Microbiology; Molecular Biology; Social Sciences; Structural Biology; Taxonomy; Virology. Specifically, we have profound insight and competences in Phage biology; Bacterial genomics; Microbial ecology; Plant pathology and physiology; Phage-bacteria coevolution; Biocontrol; Epidemiological modelling; Metagenomics; Educational competence; Sociological studies.

The initial network of 87 proposers includes 55 laboratories from 25 COST countries, among them 16 Inclusiveness Target Countries (ITC) (64%). 45 proposers are women and 42 are men, thus representing a balanced gender ratio. 31 proposers are YRIs (f40 years old) (36%). 43 partners are lecturers or professors at universities, thus ensuring a strong link to teaching and training of the next generation of YRIs. Several of our academic partners already collaborate with the private sector, including both large companies as well as small and medium-sized enterprises (SMEs), or have created their own spin-offs.

In addition to partners from COST countries, partners from near neighbour countries (NNC) or international partner countries (IPCs) in Africa, Asia, Oceania, North America and South America are also involved, making this action a truly international endeavour that extends far beyond Europe. These international partners include leading experts in phage research, plant pathogens, epidemiology, taxonomy, theoretical biology, bacterial and phage genomics. They will benefit from the project's multidisciplinary approach and contribute their own expertise. Thanks to numerous personal contacts and links to national initiatives in the field of phage research and biological pest biocontrol, the initial network of proposers is expected to grow rapidly.

As outlined in Sections 2B and 3B, specific measures will be taken to identify underrepresented stakeholders and encourage their engagement in our project. The Stakeholder Coordinator will play a key role in this process. Our consortium already includes eleven partners from the private sector, around half of which are SMEs. Additionally, we will specifically approach partners from the European seed

sector such as those active in research, breeding, production and marketing of seeds of agricultural, horticultural and ornamental plant species to connect with our initiative. We will also learn from legislative efforts and procedures in related sectors, such as phage therapy in aquaculture and livestock, as well as from the legislation of other plant protection products.

2. IMPACT

A. Impact related to objectives

Bacterial infections cause major crop losses, yet effective prophylaxis or curative solutions remain unauthorized. Phages offer a safe, environmentally sound alternative due to their host-specificity and self-limiting biology when the host is absent.

The COST Action seeks to advance the field of phages as biocontrol tools by providing the scientific basis that will allow the development of commercial applications for agriculture. Our multidisciplinary COST Action will contribute with: phage collections, expert-annotated phage genomic data, understanding of phage-bacteria interactions, and biocontrol tests. Along the way, we will produce protocols, field survey analyses, bioinformatic pipelines and public databases. This basic and advanced knowledge will be useful not only for public research and academic teaching programs, but also for agriculture institutions, companies and farmers associations. Our results will provide objective arguments to advertise and advocate the use of phages in agricultural applications and they may drive changes in the current legislation. Only through a joint effort can we accelerate research and application of phages in the agricultural sector in Europe. In this sense, the COST Action will have a ground-breaking role for plant-associated phage research and in shortening the delays of application of phage biocontrol measures in agriculture.

Based on a stakeholder-wide consensus and considering the importance of dissemination of quarantine pests listed above (cf. Section 1B), specific activities of our COST Action (*i.e.*, training schools) will focus on four groups of important bacterial phytopathogens (cf. Section 3B). However, other activities, such as conferences and workshops, will also consider other pathogens (cf. Section 1B). Thus, this initiative will have a broader impact as our results, methods and approaches can easily be transferred to such other pathogens.

The heavy metal copper is the most widely used phytosanitary product, causing ecotoxicological problems and driving resistance ^[24]. Phages, given their high specificity, could reverse this pattern. Successful results with phage biocontrol will exemplify the potential of this approach to reduce the use of chemicals against other phytopathogens as well. Our approach is original and can put Europe at the forefront of phage research by producing unique and significant results for agriculture in Europe.

Based on the two interlinked objectives established for the PHAGE4CROPS COST Action (cf. Section 1B), **results of general scientific interest generated by the project** include:

- 1) As part of the COST Action, new phages will be isolated and characterised in **training schools**, which represents a “quantum leap” at European level. Indeed, phage genomes are being added to the databases at breath-taking rate, but by far most of these phages infect medically relevant bacteria, and there is a quantitative drop in plant-associated phages. Compiling phage data in agricultural-dedicated databases and providing access to phages via an international repository will accelerate the field of phage research and application.
- 2) Compared to marine aquatic environments and mammals, there are only very few studies on phages in the agricultural environment. The analysis of phage-bacteria interactions (host range, receptors, metagenomic) data will expand our perspectives on plant disease, microbial communities and host-pathogen evolution. Our project will stimulate a **complementary mix of bioinformatic and laboratory approaches**. Their combination will shed light on the importance of phages in the ecology and evolution of phytopathogens. The prophage content in genomes of bacterial phytopathogens, CRISPR-Cas and many other defence mechanisms against phages will be analysed using *in silico* tools.
- 3) We seek to establish **guidelines** for the rational choice of phage biocontrol candidates and cocktails, formulations and application protocols. Molecular, *in silico* and evolutionary criteria will be determined, consolidating methodological approaches. Thus, our initiative will open the door to incorporate phages in **integrated pest management** strategies against bacterial plant diseases.
- 4) We will organise at **least four different workshops** to exchange expertise between partners and train students and YRIs. This ambitious plan of sharing knowledge, following a rigorous Data Management Plan, and the training schools on “phage discovery” related to plant-pathogenic bacteria will ensure the continuity and scientific quality in this field in the future.

- 5) Our work will have a stimulating and triggering effect for potential **stakeholders** that have interest in phage biocontrol and that have the capacity to develop and distribute commercial products, including scale-up and bioprocessing of phages, optimisation of formulation and ecotoxicology assessment. Interested players will be in close relationship with the COST Action. Future funding opportunities will be considered as part of the exploitation plan for the project.

Besides these results, the network of researchers and stakeholders developed thanks to the PHAGE4CROPS COST Action will allow:

- training of more than 200 YRIs across Europe ($\geq 50\%$ from ITC) and beyond its borders (IPC),
- isolation and characterisation of at least 200 phages infecting phytopathogenic bacteria,
- whole genome sequencing and genome annotation of more than 100 phages,
- establishing a European repository of phages infecting phytopathogenic bacteria,
- at least 100 stakeholders actively engaged through surveys, workshops, and dissemination events,
- collaborative research outputs (≥ 10), such as joint publications, shared datasets, protocols and outreach material.

B. Involvement of stakeholders

A detailed roadmap for engaging key stakeholders (e.g., smallholder farmers, policymakers, companies, non-European collaborators) at different stages of the project, along with metrics to evaluate their involvement, will be developed within the first six months of the action. To strengthen stakeholder trust and ensure sustained involvement, we plan to appoint a Stakeholder Coordinator to the Action9s Core Group (cf. Section 3A).

A few European companies have invested in the development of phage biocontrol agents, most of them SMEs (cf. Section 1D). Using the network's competence and insight, we will search for additional activities in the private sector, including companies of the European seed sector, and discuss with them the possibility of including phages in their product development. Fortunately, some companies have already expressed their interest in collaborating with us as part of a COST Action and a few of them have even indicated their willingness to nominate colleagues for the Management Committee.

We will identify national activities in the field of phage research and phage biocontrol in Europe (cf. Section 1D), and invite them to participate in the COST Action. To improve engagement with various stakeholders, we will establish national clusters and contact points. In this way, the COST Action will have a federative effect at European level and bring together colleagues who do not know each other, even though they are working on very similar projects. We will evaluate opportunities to organise national meetings back-to-back with the annual COST Action conferences.

Not only will we advocate the COST Action at national level in the participating countries through microbiological, virological and phytopathological societies, but will also promote the Action at the international level via the *International Society for Viruses of Microorganisms* and its biannual *Viruses of Microbes* conferences. Achieving this goal will involve the use of invitations to these conferences and the COST networking tool of Dissemination Conference grants.

We will approach European authorities and organisations in plant protection and food safety, namely the *European and Mediterranean Plant Protection Organisation* (EPPO) and the *European Food Safety Authority* (EFSA), and ask them to get connected to the COST Action. Moreover, we will compile the various national authorities and ask them to join our COST Action.

We will also engage with policymakers and use the COST Association's connections to the European Parliament and its committees to meet the most suitable dialogue partners and discuss with them the development and implementation of phage biocontrol in the agri-food sector in the European Union.

The application of novel biological factors and the release of microorganisms into the environment are sensitive to public opinion and a valid concern. We will therefore inform the general public and describe our activities in a way that leads to a positive and inclusive public perception (cf. Section 2C).

C. Communication, dissemination and valorisation

C.1. Knowledge creation, transfer of knowledge and career development

Thanks to the establishment of a pan-European consortium of experts and the efficient use of COST networking tools, the COST Action will provide new insights into phage biology and may lead to new biocontrol applications using well-characterised phages in optimised formulations. Notably, this Action will facilitate exchange between academia and private partners in the agri-food sector, and thus support technological development. Generated knowledge will be published under open-access and will be promoted on the PHAGE4CROPS website and using social media and newsletters. A website-hosted

online blog and press releases will be used to announce breakthrough discoveries and other important achievements. This way, decision-makers will be informed and guided in implementing effective biocontrol strategies.

Annual conferences will gather members of the COST Action, where R&D and societal aspects of phage biocontrol will be discussed. Workshops (in-person, online or hybrid) will be used to address specific aspects of the project, as exemplified in Section 3. The PHAGE4CROPS website will introduce the consortium, present our objectives and achievements, inform about COST networking tools and corresponding calls (STSM, ITC conference grants), announce and summarise PHAGE4CROPS events (*i.e.*, annual conferences, WG meetings and workshops), and provide links to PHAGE4CROPS-supported publications and relevant websites.

The COST Action will open opportunities to establish networks of academic training/supervision through the organisation of scientific/training activities (*e.g.*, specialised training schools, workshops, MSCA Doctoral School). We will pay great attention to gender and regional balance and to the involvement of YRIs and actively encourage and support them to take on leadership roles within the project.

YRIs will specifically benefit from these opportunities, which are intended to help them in their career development. This COST Action will also promote the scientific community and YRIs training by providing mobility grants (STSM). National and international funding opportunities will be sought and YRIs will be supported in applying for R&D grants. Thus, the COST Action will produce a new generation of professionals who will bring phages to a marketable level of sustainable biocontrol beyond the duration of the COST Action.

C.2. Plan for dissemination and exploitation and dialogue with the general public and policy

To increase international visibility, we will create a website with the goals of the COST Action and how to participate in this bottom-up initiative. The network of proposers will announce the COST Action and its website to their peers, using mailing lists, social media and national societies. In preparing the website, we will launch a competition to design a logo for the COST Action. This way, we will early on create a stimulating and inspiring atmosphere within the network. We will also prepare a flyer and a poster that introduce the COST Action along with its objectives, tasks and Working Groups (WGs). This information will be shared at national gatherings and meetings. In addition, we will make use of the COST networking tool of Dissemination Grants, thus further promoting the COST Action using the prepared poster and flyers.

The annual conferences will not only be an event where scientific results will be discussed among COST Action's participants, as we will also extend invitations to other stakeholders, such as EFSA, EPPO, farmers organisations, national plant protection services and regulatory bodies. Social media (*e.g.*, LinkedIn) will be used to advertise and increase the impact of the meetings.

The promotion of novel biological factors and the release of microorganisms or the use of molecular tools (*e.g.*, genetic engineering) in the environment are sensitive to public opinion and a valid concern. It is therefore extremely important to describe our innovations and present them to the general public in an easily understandable but accurate language. In the COST Action, we aim to describe the environmental benefits of phages and foster the design of inclusive and sustainable research and innovation with a positive and embracing public perception. To reach the general public, we will use popular communication media such as cartoons and comics.

We also want to engage with policymakers and use the COST Association's connections to the European Commission to meet the most suitable dialogue partners and discuss with them the development and implementation of phage biocontrol in the agri-food sector in the European Union.

3. IMPLEMENTATION

A. Action Structure

The Management Committee (MC) is the main decision-making authority of the project. It consists of one or two representatives from each participating COST country. The MC will meet in person once per budget period. These yearly MC meetings will ensure that activities will be organised according to the defined objectives of the four WGs and the capacity-building objectives, as defined in Section 1B. These meetings will also serve to report on and plan activities in line with the budget.

The COST Action will be coordinated by the Chair and Vice-Chair, managed by the grant holder institute and supported by the COST Science and Administrative Officers. The Chair and Vice-Chair will lead a **Steering Committee**, a.k.a. **Core Group**, consisting of the WG Leaders and Vice-Leaders, a Science Communication Coordinator, a Grant Awarding Coordinator and a Stakeholder Coordinator. This group

will be responsible for directing the scientific, organisational and financial management. The **Core Group** will comprise representatives from a variety of scientific disciplines, as well as stakeholders from universities, research organisations, and companies. The group will be representative in terms of geographic coverage, gender balance, and career stage. The Core Group will hold quarterly online meetings to review the COST Action's achievements, adjusting the scientific strategy and expenses as necessary. The meetings will also evaluate project progress and ensure that contingency plans are developed promptly if required. The Core Group will write yearly reports to update the MC on project progress and issues, and to encourage effective feedback. This will also facilitate the transfer of information to WG4 regarding available training, teaching and outreach knowledge.

The **WG Leaders and Vice-Leaders** will coordinate WG activities and ensure collaboration between partners within and between groups. Specifically, they will organise online meetings, training school and workshops as part of their work plans. They will also follow their own outreach agenda, which includes preparing guidelines, pipelines, protocols, databases and publication manuscripts (see below). Seven major goals will be addressed by four complementary and interconnected WGs (see Figure 1):

- 1) establish an R&D network on phage research in the agri-food sector in Europe and train YRIs in the field of phage biology and application (WG1-WG4);
- 2) discover and characterise new phages and to promote the establishment of at least one international repository for phages with relevance to agriculture (WG1);
- 3) assess phage-related traits in bacterial genomes allowing to develop predictive tools and get fundamental evolutionary insights in phytopathogens (WG1, WG2);
- 4) develop databases on metagenomic, host range and molecular phage-bacteria interactions in agricultural environments (WG2, WG3);
- 5) determine the effects of phages on bacteria at the molecular level to identify efficient phage candidates for long-term biocontrol strategies (WG2, WG3);
- 6) provide guidelines on the use of phages and phage cocktails, on formulations and on application protocols (WG3); and
- 7) deliver knowledge on the feasibility and acceptance of biocontrol strategies based on the use of phages against phytopathogenic bacteria (WG3, WG4).

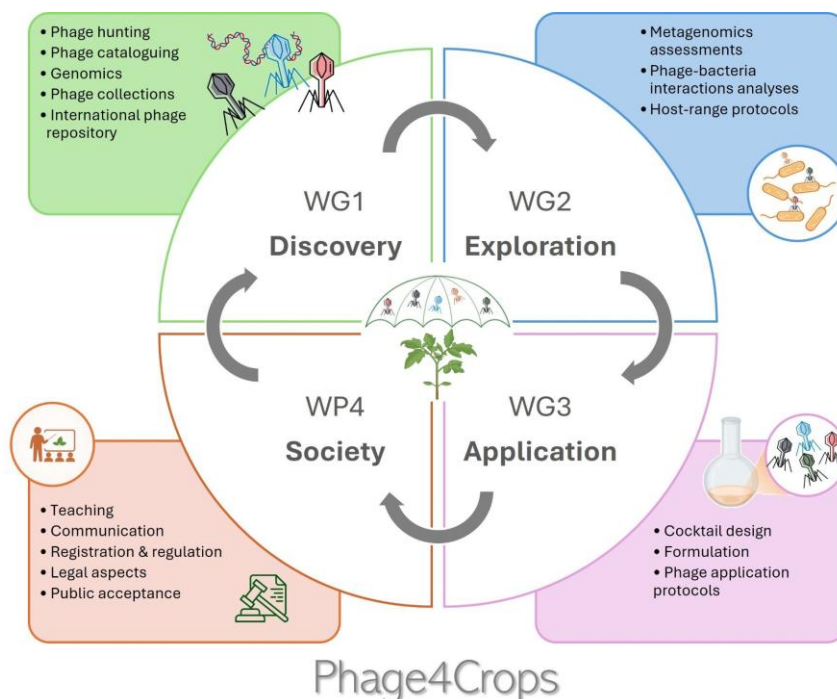


Figure 1. Illustration of the PHAGE4CROPS COST Action. *Discovery* is the basis for *Exploration*. Both *Discovery* and *Exploration* will guide *Application*. *Application* and *Society* will influence each other strongly. Both *Discovery* and *Exploration* will inform *Society*. *Society* will also shape *Discovery* and *Exploration*.

Over the four years, annual conferences open to all stakeholders and respecting career stage, gender and geographical balance will be organised to favour scientific exchange, preferentially back-to-back with other relevant events (e.g., conferences of other COST Actions or conferences of national societies)

(cf. Section 1D). Co-organisation with high-impact conferences (e.g., *Viruses of Microbes*, *International Congress of Plant Pathology*, *International Conference on Plant Pathogenic Bacteria & Biocontrol*) will be considered. Such joint events will provide each participant with an in-depth insight into the methodology and results of the other partners, across different scientific disciplines and pathosystems. They will also help to create an open-minded and trusting atmosphere, supported by social activities at our face-to-face events.

In preparing the proposal, we performed a risk analysis and developed a contingency plan. This plan will be reassessed by the MC at the project kick-off meeting, where potential risks will be re-evaluated and categorised according to probability and severity. The risk mitigation plan will also be revised. To date, we have identified two high-impact risks with a moderate probability and high severity. One of these is the low involvement of key stakeholders. To mitigate this risk, we will appoint a Stakeholder Coordinator to join the Core Group. Based on the **Science Communication Plan**, which will be drafted in the first six months of the Action by the Science Communication Coordinator in collaboration with WG4, the Stakeholder Coordinator will define strategies to approach, inform and motivate stakeholders to participate in the COST Action. This activity will include identifying national contact points, as well as approaching national phage networks, farmers' organisations, and societies. Another possible risk is data loss. Therefore, the Core Group will implement a **Data Management Plan** within the first six months of the Action to ensure the integrity and security of the data throughout the duration of the Action and beyond.

Deliverables: MC meeting minutes; Yearly Core Group reports; Open access citable proceedings of the Annual Conferences; Risk contingency plan; Science Communication Plan; Data Management Plan; Calendar: Annual MC Meetings and Conferences; Trimestrial online meetings of the Core Group.

B. Work plan (tasks, activities and timeframe)

WG1. DISCOVERY: From the field to the lab: Identifying the diversity of phages of plant-pathogenic bacteria in agricultural environments

Task 1.1. Cataloguing the pan-European landscape of phage research in the agricultural context

Objective: Identifying national projects and institutional collections of phages in the agricultural context.

By contacting EU-wide and national phage networks and associations (cf. Section 1D), this COST Action will sum up the current status quo of the general EU phage landscape in the agricultural context to identify putative cooperation partners, phage sources and other relevant plant-pathogenic bacteria, beside the four primary bacterial groups targeted by the project. A questionnaire will be compiled to query information on individual institutes, research groups or companies, their expertise and scientific interests, available bioresources and identified research gaps. A comprehensive overview of identified national phage projects and thus linked institutional collections will be used to **create a database** to reflect this information and make it publicly accessible (e.g., on the PHAGE4CROPS website). Data on the available phages will be deposited in that phage-dedicated database, including metadata and links to genome sequence information, alongside with information on model phytopathogenic strains used to study phage-bacterium interactions. In parallel, if cooperation partners agree, available corresponding bioresources will be deposited in European public microorganisms' collections to create an **international repository for phages** with agricultural importance to facilitate the transfer of phages between the PHAGE4CROPS network and safeguard the phages isolated thanks to this initiative (e.g., from the training schools, see task 1.2).

Deliverables: **One** questionnaire to assess the status quo of phage biocontrol initiatives in the EU and partner countries. **One** map and **one** database of laboratories, institutions, companies and biological resources (i.e., phages and bacterial hosts) with relevance to phage biocontrol. Establishment of **one** publicly accessible phage collection for research purposes.

Task 1.2. Hunting for phages specific to phytopathogenic bacteria

Objective: Expanding phage collections infecting phytopathogenic bacteria by sampling and characterizing phages from agricultural environments.

Phage collections targeting plant pathogens need to be increased substantially at the European level. For the four groups of pathogens on which this project focuses, only a few phages are available and stored in institutional collections. Therefore, an unprecedented collective effort involving **two "Hunt for Phages" training schools** will be organised to isolate and characterise new phages in various European agricultural regions. The proposers' experience and knowledge from the literature confirm the presence of phages of bacterial phytopathogens in the rhizosphere and phyllosphere, irrigation water, soil, compost accumulations or in general wastewater. Depending on the ecology of each plant

pathogen, the most appropriate sampling strategy will be proposed to the trainees. The aim of these training schools is to **introduce and teach phage isolation and propagation**, as well as phage biology, and the associated methods and protocols for studying them. The expected outcome of them is to isolate ≥ 200 new phages, thereby largely increasing the number of available phages. The phages isolated during the training schools will be deposited in the phage repository created in Task 1.1. To this end, guidelines on how to preserve and deposit the phages will be developed.

Deliverables: Two “Hunt for Phages” training schools, each with 16 trainees and their respective syllabus describing laboratory methods and protocols. **2 x 100 new phages** (100 per training school). **One** step-by-step protocol for phage preservation and submission to the phage repository.

Task 1.3. Genomics of phages infecting phytopathogenic bacteria

Objective: Improving our understanding and prediction of genes encoded in phage genomes

With the increased interest in phage research and accessibility to modern sequencing technologies (Illumina, Nanopore), there is also an increased need for proper **phage genome assembly and annotation** guidelines. To meet this need, two workshops on “Phage genome analysis and annotation” will be organised to provide an overview of the process of phage genome assembly and annotation, from raw reads to genome submission. A bioinformatics pipeline will be developed for this, and phage genomes identified in the database created in Task 1.1 will be initially used for this purpose. Trainees will be also encouraged to bring their own datasets for analysis. In parallel, genome sequencing of 100 phages isolated during the “Hunt for Phages” training schools will be performed by cooperation partners and by leveraging institutional, national and/or international funding. This approach will allow us to infer phylogenetic relationships between the newly isolated phages and their genomic features, taxonomy, replication strategies and evolution. This strategy will allow us to share fully annotated phage genomes, as well as writing a paper describing the phages isolated and sequenced during this COST Action.

Deliverables: One phage collection database, integrating phage’s genomic information, will be available to the MC of the COST Action. **Two** workshops on “Phage genome analysis and annotation”. **100** new annotated phage genome sequences. **One** paper describing phages isolated in training schools (Task 1.2.) fully sequenced and annotated.

WG2. EXPLORATION: Determining phage prevalence and host range in agricultural environments to identify efficient phage candidates for sustainable biocontrol

Task 2.1 Insights from metagenomics

Objective: Obtaining insight into the biogeography and ecological role of phages of phytopathogenic bacteria in the agricultural context and their contribution to plant disease dynamics.

Explore the diversity, distribution, and dynamics of **phage communities** in the agricultural landscape by analysing datasets from high-throughput sequencing and linking it to different environmental and agroecological parameters, noticeably climate variables, disease incidence, agricultural practices, plant varieties and water and soil data. Compared to other virus domains ^[25], plant-associated phage communities have been poorly explored and their data is not integrated into any database. We will therefore build an open-access database dedicated to phage metagenomic data of agricultural relevance, gathering both published and at least five ongoing projects, as a crucial and early effort to coordinate and optimise data sharing. Recently developed metagenomic analysis tools and pipelines will be compiled and shared, e.g., on GitHub, to promote reproducibility and interoperability among research teams. In the long term, these resources will underpin the rational design of biocontrol strategies by identifying phage–pathogen associations across diverse agroecosystems.

Deliverables: One metagenomics phage **open-access** database of agricultural relevance. **One** validated bioinformatic pipeline and protocol for microbiota-derived metagenomic analyses in agriculture, shared on GitHub. **One report and webinars** summarising current trends and knowledge gaps in agricultural viromics.

Task 2.2. Phage-host interaction

Objective: Improving our understanding and prediction of the host range and specificity of phages infecting phytopathogenic bacteria.

Phages are known to be, in general, species- or even subspecies-specific, which is an advantage for a safe and sustainable biocontrol agent. Leveraging several projects, we will analyse current available data on the host range of phages of phytopathogenic bacteria. We will compile and share the **host range** data of 100 phages on a panel of bacteria representing the genetic diversity of the host species and more distantly related bacteria, using quantitative approaches. This work will rely on phages that are already available or will be sampled in Task 1.2., which will be tested on well-characterised bacteria

from European strain collections (BCCM-LMG, CIRM-CFBP, NCPPB). Metadata on bacteria will be included, such as genomic information, available mutants, transposon mutant libraries, phage receptors, etc. We thus propose to test genomics-informed panels of bacteria for host range studies. All in all, this will contribute to a better characterisation of phage collections and their diversity (Task 1.1). All data and protocols will be openly shared to foster reproducibility and facilitate cross-laboratory comparison, thereby contributing to a unified framework for evaluating phage efficacy and biosafety.

Deliverables: **One** set of guidelines and standardised protocols for analysing the host range testing of phages, including information on panels of strains and the type strains of each bacterial species. **One** training school with 16 trainees on host range laboratory methods and analysis. **One** meta-analysis manuscript on host range patterns and molecular determinants of susceptibility among phytopathogenic bacteria, with the aim of identifying efficient phages for biological control.

Task 2.3. Mechanisms of bacterial resistance to phages

Objective: Assessing phage-related traits and resistance mechanisms in plant bacterial genomes to develop predictive tools for phage–bacterium coevolution.

A huge gap exists in the knowledge of **bacterial defence systems** mechanisms and **prophage** content in phytopathogenic bacteria compared to human-related ones. We propose to fill this gap by joining efforts in analysing and sharing data of a set of 100 high-quality genomes representing the genetic diversity of major phytopathogenic species. A bioinformatic pipeline will be developed, made available on GitHub, and applied to systematically detect: (i) phage-resistance systems (e.g., CRISPR–Cas, BREX, DISARM, restriction–modification) and (ii) prophage content and diversity, as indicators of past phage–bacterium interactions and potential immunity barriers. Our strategy will be to share genomes and pipelines, as well as writing papers on the novel results, and including a review or meta-analysis paper summarising trends and implications for biocontrol.

Deliverables: **One** bioinformatic pipeline to analyse genomes of plant-associated bacteria, shared on GitHub. **One** bioinformatic online training workshop. **One** manuscript on phage-related genomic traits in bacteria of agricultural relevance.

WG3. APPLICATION: From the lab back to the field: Phages as biocontrol agents for sustainable plant disease management

Task 3.1. Cocktail design

Objective: Establishing guidelines for designing cocktails of synergistic phages that prevent or overcome bacterial resistance and ensure broad-spectrum efficacy.

The host range of phages is usually narrow, and the targeted phytopathogenic bacteria can become resistant or tolerant against the applied phages. One solution is to form phage cocktails to broaden the host range of the bacteriophage-based product and/or to bypass bacterial phage defence systems. Several factors are critical when forming a phage cocktail. As well as the host spectra, the receptor specificity of the phages must be considered. Phage cocktails can overcome this limitation by combining complementary phages with different receptor specificities and infection strategies. This task will evaluate criteria for **phage compatibility**, **receptor diversity**, and **synergistic interactions**, enabling the rational design of cocktails with durable activity. Antagonistic or neutral effects among phages will also be documented to optimise formulations.

Deliverables: Guidelines for or rational phage cocktail design for integrated pest management. **One** review **article** summarising current strategies and bottlenecks in phage cocktail development. **One** training school with 12 trainees on phage cocktail design and formulation (cf. Task 3.2).

Task 3.2. Formulations

Objective: To develop and share best practices for phage formulations that enhance stability, persistence, and efficacy under agricultural relevant conditions.

The application of phages faces different challenges in the field, such as UV radiation, desiccation, temperature extremes, and pH fluctuations all of which can drastically reduce phage viability. To address this, WG3 will compile and test formulation strategies that protect phages and improve delivery. Both dry formulations (powders, granules, seed coatings) and liquid formulations (suspensions, emulsions) will be considered. Protective strategies include:

- Co-application with non-pathogenic host bacteria, e.g., *Pantoea agglomerans* to maintain *E. amylovora* phage populations.
- Addition of UV protectants, such as skim milk or natural polymers.
- Encapsulation technologies, including chitosan–alginate–Ca, starch, cellulose, or sporopollenin exine capsules, to achieve timed release and environmental protection.

- Adjuvants such as alginate to prevent wash-off and increase adhesion on plant surfaces.

The task will culminate in the definition of standardised formulation protocols optimised for stability and efficiency across major crop systems.

Deliverables: **One** set of guidelines for phage formulation and stabilisation in agricultural applications. **One** training school with 12 trainees on phage cocktail design and formulation (cf. Task 3.1). **One** review article on advances in formulation strategies for phage-based biocontrol.

Task 3.3. Application protocols

Objective: Evaluating data on the application of phage-based biopesticides, including the timing of the applications, dosage, and integration with existing agricultural practices.

The application's aims could be prophylactic or curative. This is determined by the nature of the pathogenic bacteria (epiphytic or endophytic), the anatomy of the plants (e.g., hydathodes can provide natural openings enhancing the infiltration and translocation of phages), and the possible timing of the application. Timing is crucial as infective phages are present in the field only for a limited time and must coincide with bacterial infection windows.

Application protocols involve the treatment of the seeds and seedlings prior to transplantation, treatment of plants and fields prior to or when the targeted bacterium is present, as well as post-harvest treatments. Methods (including meteorological-based and direct detection of the phytopathogens) helping in the proper timing of the application can boost the efficacy of disease management. Not only the timing but also the correct dosage can contribute to the positive outcome of the treatments.

To ensure the practical viability of the developed protocols, three pilot field trials will be coordinated in collaboration with partner institutions and local stakeholders. Each trial will target a different pathosystem and climatic region (e.g., temperate, Mediterranean, continental) to capture environmental variability. The trials will: evaluate phage cocktail performance under real agricultural conditions, test formulations optimised in Task 3.2 for persistence and efficacy, quantify disease incidence reduction, yield impact, and economic feasibility, collect stakeholder feedback (farmers, cooperatives, agricultural advisors) to inform adoption barriers and user perceptions. Results will serve as **proof-of-concept** for large-scale applications and will feed into EU and national biocontrol guidelines.

Deliverables: **One** set of general guidelines for phage applications, either prophylactic or curative. At least **three coordinated pilot field trials**, each focusing on a distinct crop–pathogen system, with open-access reports and standardised data collection templates. **One** stakeholder conference/workshop with farmers and agricultural advisors. **One** review article summarising lessons learned from field trials and implementation pathways.

WG4. SOCIETY: Outreach - Education, communication, stakeholder engagement, public acceptance and legal perspective

Objectives: Communication, advertising and public relations for the COST Action

Task 4.1. Teaching and communication activities

Our expertise in phage research will have a direct impact on academic education, as almost half of the network's partners are heavily involved in teaching (cf. Section 1E). Our common goal is to disseminate profound knowledge about phages that infect plant pathogens in our respective academic programs and to be a resource for interested colleagues from other universities. The COST Action will communicate using web-based solutions, through Gold Open Access publications and at meetings with both the public and professionals, e.g., agricultural cooperatives and phytosanitary services, chambers of agriculture and agricultural associations. We will create a monthly "Phage Club" where members of the consortium, interested parties and invited speakers will discuss various aspects of their work, covering scientific, legal and societal topics, similar to the *ASPB Plantae* webinars, the webinar series of the *American Phytopathological Society* and the *BeXyl Xylella* seminars.

A dedicated website and a blog will be available at month 4 and will disseminate material, such as posters and publications, and provide relevant news and information. Regular newsletters and yearly press releases will inform the various stakeholders about the network, its goals, achievements and opinions. The COST Action will be publicised to the research community, the agricultural industry and the general public via social media presence (e.g., Bluesky, LinkedIn) and press releases. Our goal is to have 250 newsletter subscribers after one year and 500 subscribers by the end of the Action. "Popular Science" material on the use of phages in biocontrol in agriculture will be produced, such as podcast contributions (inspired by the *Plantopia* podcast), virtual farm tours showcasing phage applications and visual material (e.g., short videos, photo exhibitions or comics).

Deliverables: Innovative and research-oriented academic programs on phages. **One** website, **one** blog, at least **24** newsletters and regular social media activity. **One** poster, **one** flyer and **yearly** press releases describing the aims and achievements of the COST Action. “Popular Science” materials, such as **one** photo collection, **one** comic on phages and their use in biocontrol for the general public, and **regular** podcast contributions and/or webinars (10 per year).

Task 4.2. Registration, regulation and legal aspects

The legal context of the application of phages in agriculture is mostly limited to their consideration as biocide biocontrol agents or “processing aids” [26]. The latter excludes the need for labelling or toxicity testing and has been adopted by commercial phage preparations in Europe. The *Agriphage*® products are EPA (*Environmental Protection Agency*) authorised biopesticides in the USA, already registered for 20 years, that treat and control pathogens on several crop plants. At the EU level, an authorisation for phage products as an actual plant protection product (under COMMISSION REGULATION (EU) 2022/1438 of 31 August 2022 amending Annex II to Regulation (EC) No 1107/2009) is pending for potato soft rot control (by the UK-based company *APS Biocontrol*) and for fire blight in apple and pear (by the Belgian company *DCM*). Another fire blight product against *E. amylovora* infections, *Erwiphage*, received an emergency authorisation in Hungary for several years as crop protection product, but is not generally authorised at the EU level.

In this task, we propose an action plan and a workshop to compare how regulation is managed and evolves in the EU. Literature and websites will be analysed to understand and anticipate the data generation required for the authorisation forms. We will communicate with companies, national bodies, EFSA and the legal services in the participating countries. Measures are being taken to transfer knowledge, such as identifying suitable partners involved in the production and marketing of phage products, and contact is being made with politicians in the committees of the European Parliament. These activities will provide guidance on the legislation of phages as a “plant protection product”.

Deliverables: **One** action plan and workshop about the EU-wide regulatory requirements of biocontrol phage products. List of key partners and meeting minutes, all published on the PHAGE4CROPS website.

Task 4.3. Society and public acceptance

A key issue besides communication is certainly the general public acceptance, but also the acceptance of stakeholders such as farmers or people working in the field of plant protection products, food safety, risk management or environmental protection. During the phage renaissance at the turn of the century, the plant sector was the first area in which phages were used for curative purposes; however, the medical sector is now much more advanced. We will therefore exchange with renowned experts in phage therapy in the medical sector to learn from their experiences, even though the specific context is quite different.

A survey will assess awareness of current measures against plant-pathogenic bacteria, perceptions of phage-based alternatives, and related ethical concerns. It will follow a two-stage process: a small-scale pilot to validate the format, followed by a broader online survey promoted through partnerships with agricultural, environmental, and consumer groups, as well as social media and email. Conducted across all participating EU countries, the survey will be complemented by an analysis of public acceptance research and stakeholder opinions in agriculture.

We are aware that such kind of outreach is usually requested in the target audience's language. Our activities will therefore be supplemented by leveraging national funding from societies and universities.

Deliverables: **One** conference/workshop with stakeholders (farmers, agricultural advisors, consumer organisations). **One** EU-wide survey on public acceptance.

C. Deliverables

The list of deliverables contains the organisation of meetings, workshops and training schools, but also guidelines, protocols, manuscripts, databases and software pipelines, as described in Section 3B and summarised in Table 2.

Table 2. List of deliverables and their timeframe (Tasks in bold; semester of delivery in brackets).

	WG1	WG2	WG3	WG4
Meetings	Annual Conferences, back-to-back with MC Meetings, and conference proceedings (2,4,6,8); Online meetings of the Core Group, and meeting minutes (each trimester) “Phage Club” webinars, coordinated by WG4 (10 per year)			

	WG1	WG2	WG3	WG4
Training Schools	1.2 “Hunt for Phages” (≥32 trained YRIs) (2x: 2,4)	2.2 Host range laboratory methods and analysis (≥16 trained YRIs) (7)	3.1/3.2 Phage cocktail design and formulation (≥12 trained YRIs) (6)	
Workshops	1.3 Phage genome analysis & annotation (2x: 3,5)	2.3 Online workshops on bacterial genome analysis (2,4)	3.3 Meet the stakeholders (7) back-to-back with WG4	4.2 Regulatory requirements of biocontrol phage products (5); 4.3 Meet the stakeholders (7) back-to-back with WG3
Guidelines/ protocols	1.2 Phage preservation in a repository (3)	2.2 Phage host range analysis (6)	3.1/3.2 Phage cocktails: design and formulation (6); 3.3 Guidelines for phage application (7)	
Manuscripts	1.2 & 1.3 Phages from the training school (4,6)	2.1 Meta-analysis on phage host ranges (7); 2.3 Phage-related traits in bacterial genomes (5)	3.1/3.2/3.3 Review on phage application in biocontrol (8)	
Others	1.1 Questionnaire on phage biocontrol initiatives in the EU (1); 1.1 Map and database of relevant EU labs (2); 1.1 European phage repository (4); 1.3 ≥200 isolated phages from training schools, ≥100 of them sequenced and annotated (5)	2.1 Database “Metagenomic data on phages in agriculture” (2); 2.1 Bioinformatic pipeline and protocols for metagenomic analyses (GitHub) (6); 2.3 Bioinformatic pipeline for genome analysis of plant-associated bacteria (GitHub) (5)	3.3 3 coordinated pilot field trials , each focusing on a distinct crop–pathogen system	4.1 Website, Blog (1); 4.1 Social media (1); 4.1 Action poster and flyer (1); 4.1 ≥24 newsletters (1-8); 4.1 Yearly press releases (2,4,6,8); 4.1 “Popular Science” material (5); 4.3 EU-wide survey on public acceptance (6)

D. Gantt chart

Progress on the tasks, as indicated in Table 3, is monitored by the Core Group, which meets online once per trimester, supplemented by one face-to-face meeting per year. These meetings also serve as a guide for technical and organisational aspects and for communication between the WGs. A mid-term report, prepared by the Core Group under the supervision of the Chair, documents progress and delays and serves as a decision-making aid for the MC for the second project phase.

Table 3. GANTT diagram (periods of high activity in dark color).

WG	Task	Semester							
		1	2	3	4	5	6	7	8
Discovery	1.1								
	1.2								
	1.3								
Exploration	2.1								
	2.2								
	2.3								
Application	3.1								
	3.2								
	3.3								
Society	4.1								
	4.2								
	4.3								

References:

- [1] Gruetzmacher et al. (2021) *Sci. Total Environ.* 764: 142919. DOI: 10.1016/j.scitotenv.2020.142919
- [2] Pirnay et al. (2024). *Nat. Microbiol.* 9: 1434-1453. DOI: 10.1038/s41564-024-01705-x
- [3] https://eur-lex.europa.eu/eli/reg_impl/2025/1390/oj/fra
- [4] Meczker et al. (2014) *FEMS Microbiol. Lett.* 350: 25-27. DOI: 10.1111/1574-6968.12319
- [5] EFSA Panel on Biological Hazards (BIOHAZ) (2016) *EFSA J.* 14: e04565. DOI: 10.2903/j.efsa.2016.4565
- [6] Subedi et al. (2025) *Nat. Microbiol.*, in press. DOI: 10.1038/s41564-025-02130-4
- [7] Korniienko et al. (2022) *Plant Protect. Sci.* 58: 81-91. DOI: 10.17221/147/2021-PPS
- [8] Lin et al. (2022) *Molecules* 27: 1857. DOI: 10.3390/molecules27061857
- [9] Halawa (2023) *J. Genet. Eng. Biotechnol.* 21: 98. DOI: 10.1186/s43141-023-00549-y
- [10] https://www.eppo.int/ACTIVITIES/quarantine_activities
- [11] Mansfield et al. (2012) *Mol. Plant Pathol.* 13: 614-629. DOI: 10.1111/j.1364-3703.2012.00804.x
- [12] Luria & Delbrück (1943) *Genetics* 28: 491-511. DOI: 10.1093/genetics/28.6.491
- [13] Hershey & Chase (1952) *J. Gen. Physiol.* 36: 39-56. DOI: 10.1085/jgp.36.1.39
- [14] Holtappels et al. (2021) *Curr. Opin. Biotechnol.* 68: 60-71. DOI: 10.1016/j.copbio.2020.08.016
- [15] Reardon (2014) *Nature* 510: 15-16. DOI: 10.1038/510015a
- [16] McCallin et al. (2019) *Viruses* 11: E343. DOI: 10.3390/v11040343
- [17] Uyttebroek et al. (2022) *Lancet Infect. Dis.* 22: e208-e220. DOI: 10.1016/S1473-3099(21)00612-5
- [18] Koskella & Taylor (2018) *Annu. Rev. Phytopathol.* 56: 361-380. DOI: 10.1146/annurevphyto-080417-045858
- [19] Stefani et al. (2021) *Microorganisms* 9: 1056. DOI: 10.3390/microorganisms9051056
- [20] Nakayinga et al. (2021) *BMC Microbiol.* 21: 291. DOI: 10.1186/s12866-021-02351-7
- [21] Farooq et al. (2022) *Viruses* 14: 171. DOI: 10.3390/v14020171
- [22] Wagemans et al. (2022) *Annu. Rev. Phytopathol.* 60: 21-42. DOI: 10.1146/annurevphyto-021621-114208
- [23] Pandit et al. (2022) *Pathogens* 11: 273. DOI: 10.3390/pathogens11020273
- [24] Wales & Davies (2015) *Antibiotics* 4: 567-604. DOI: 10.3390/antibiotics4040567

[25] Galperina et al. (2025) PLoS Comput. Biol. 21: e1012268. DOI: 10.1371/journal.pcbi.1012268

[26] Fernández et al. (2018) Front. Cell. Infect. Microbiol. 8: 296. DOI: 10.3389/fcimb.2018.00296