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ENG2003 Term Project

Professor Bonab

July 2025

# Letter of Transmittal

July 23, 2025

To whom it may concern,

Please find my attached draft of my technical report, titled *Combating the Spread of Antimicrobial Resistance with Bacteriophage Therapy and Artificial Intelligence*. This report covers our proposal centered around two currently emerging technologies to combat multidrug-resistant bacteria: bacteriophage therapy, and artificial-intelligence driven antibiotic discovery, which could help address the global challenge of fighting drug-resistant infections. The purpose of this report is to propose a two-part strategy to address the urgent global threat that is posed by the multidrug-resistant bacteria, leveraging engineering and machine learning to create solutions.

The report follows the standard technical report format and integrates evidence from 5 different peer-reviewed sources from the past 5 years, to justify both the technical feasibility and the potential global impact of the solutions we found. I have tried my best to clarify any complex processes and data and cater it towards a university-level engineering audience, and I made sure that all of my data is sourced and cited, using creditable sources.

I am looking forward to your invaluable feedback, which I will take into consideration and incorporate into my final report. Please feel free to contact me with any questions or suggestions, and I hope that this report will receive your approval.

Sincerely,

Quoc-An Pham (221504865)

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Combating the Spread of Antimicrobial Resistance with Bacteriophage Therapy and Artificial Intelligence

Quoc-An Pham

ENG2003 – Effecting Engineering Communication

July 23, 2025

# 1. Executive Summary

Antimicrobial Resistance, or AMR, currently poses one of the most urgent threats to global health, with drug-resistant infections causing around 700,000 deaths every year, and is projected to reach over 10 million deaths per year by 2050 if left unchecked [1]. Traditional antibiotic development cannot keep pace with the speed at which bacteria evolve, and they are constantly outpacing the speed that we can develop antibiotics currently.

Bacteriophage therapy employs viruses engineered to selectively infect and destroy multidrug-resistant bacteria, or MDRs, which is a highly specific way of treating them. Recent case studies have found that bacteriophage therapy can successfully eradicate Pseudomonas aeruginosa and Acinetobacter baumannii, two strains of bacteria that can be fatal in many cases [2]. This is a case where Artificial Intelligence can prove useful, as it can use deep-learning models to predict new antimicrobial candidates way faster than humans can, and this has been proven through the identification of halicin [4][5], a molecule active against both laboratory and clinical MDRs, which was identified using artificial intelligence.

# 2. Introduction and Background

Antimicrobial resistance, or AMR, arises when bacteria evolve mechanisms to survive exposure to antibiotics, which renders standard treatments practically ineffective. The overuse and misuse of antibiotics in clinical and agricultural settings accelerates the rate at which they all build up this resistance, and there are already over 700,000 deaths annually worldwide, a number which will only increase as time goes on if we leave it untreated. Antibiotics have been misused so commonly around the world, that it could end up reversing decades of medical progress, and scientists project that it could end up causing up to 10 million deaths annually by 2050 if nothing is done to slow down the spread of these untreatable infections.

The BBC’s 50 Grand Challenges for the 21st century list identifies antibiotic resistance as a huge threat to global health, noting that currently, antibiotic pipelines are inadequate to address the rapidly evolving bacterial defenses. The World Health Organization, or WHO, categorizes 6 main pathogens that are responsible for the majority of AMR related deaths: the ESKAPE pathogens, otherwise known by their full names as Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp. As this is mainly a biological challenge, this challenge mostly links to biomedical engineering, which is the field which will be responsible for development of the next generation of antimicrobials, from the molecular design to the delivery systems and diagnostics. This report will showcase the progress we have made so far in two complementary engineering strategies: bacteriophage therapy, which repurposes viruses as living antimicrobials, and artificial intelligence-driven antibiotic discovery, which will accelerate the identification of possible new antibiotics, speeding up different stages of the drug-development timeline, and hopefully will form a more resilient pipeline in the fight against MDR bacteria.

# 3. Main Topics

3.1 Bacteriophage Therapy

Bacteriophages, or simply phages, are viruses that specifically infect bacteria. Engineered phages can be tailored to recognize and destroy targeted MDR strains without harming any surrounding human cells or any beneficial bacteria [1]. The general workflow comprises phage isolation from environmental samples, host-range engineering via receptor-binding protein modification, cocktail formulation to reduce the resistance emergence, and then laboratory testing through several different routes to test its adaptability. Clinical case reports have demonstrated the remarkable ability of engineered phages to clear infections by both Pseudomonas aeruginosa and Acinetobacter baumannii, even when they failed to respond to all other available antibiotics [2]. Despite these massive successes, scaling up production to a level where it would be globally available has proven to be challenging, because maintaining phage stability and purity during large-scale manufacturing requires specialized equipment and protocols, and regulatory approval is complicated by the inconsistent classification of phages across different jurisdictions, and there remains limited data on the potential side effects of repeated phage administration, or their long-term impact on the host.

3.2 Artificial Intelligence Driven Antibiotic Discovery

Using artificial intelligence to drive antibiotic discovery is done through deep-learning algorithms which are trained on datasets of molecular descriptors as well as bioactivity datasets to predict novel compounds with antimicrobial potential. In a landmark study, researchers used a convolutional neural network to virtually screen nearly one billion different chemical structures and successfully identified one we now know as Halicin. Halicin is a molecule that exhibits potent activity against a broad range of Gram-negative MDR pathogens in both laboratory tests, as well as animal models. This AI approach dramatically accelerates the lead-identification phase and reduces associated costs by focusing experimental efforts on the most promising candidates and allows transfer learning techniques to adapt quickly to emerging pathogen classes, extending its utility and knowledge past the initial dataset. However, the effectiveness of these models is constrained by biases in training data, which tend to favor well-represented chemical scaffolds, and might end up overlooking any truly novel structures, as early screening often neglects toxicity considerations, which means that researchers have to integrate these factors later on in the pipeline, and even just assembling and curating high-quality datasets required for training and validating the model requires a lot of labor-intensive work, which can potentially limit the speed of AI discovery.

# 4. Discussion

4.1 Manufacturing Scalability

The process of integrating precision phage therapy with artificial intelligence-powered discovery leverages the biological specificity of viruses and the computational speed of deep-learning models to create new antimicrobials is a rapid approach to a previously tedious and time-consuming tasks, as research teams can iterate more rapidly, new phage candidates are isolated and engineered against emerging bacterial isolates, and the AI models can simultaneously propose small-molecule leads tailored to the same targets.

Manufacturing scalability is often a major issue with new advancements and treatments, but in this case, it can be addressed through the adoption of flexible bioprocess engineering. Phage production benefits from the use of continuous-culture bioreactors equipped with real-time monitoring of the titer and purity, while the AI-identified compounds are validated through standardized quality-control assessments, testing for phage potency and performance, but nevertheless, meeting good manufacturing practice (GMP) requirements for both methods is a significant challenge and requires tons of financial investment and specialized expertise.

4.2 Regulatory Pathways and Economic/Funding Considerations

Navigating regulatory pathways also requires a coordinated strategy, because bacteriophages currently occupy a gray zone between biologics, and gene therapies. Leveraging the American FDA’s emergency use authorization for compassionate-use cases and the European Medicines Agency’s adaptive-licensing pilot could help expedite the approval. At the same time, AI-discovered candidates could qualify for accelerated programs that can collect extra safety and efficacy data and provide funding, making it much easier to research.

The economic sustainability of both methods relies on diversified funding, and new payment models, which could be private-public partnerships, or milestone-based grants, which can spread the risk across multiple stakeholders. Pharmaceutical companies can gain access to AI-identified leads at a reduced research and development cost, while public health agencies support phage libraries as a global repository. While the integrated pipeline would be a robust and multifaceted response to antimicrobial resistance, it also introduces new challenges in coordination between so many stakeholders, regulatory alignment, and financial investment barriers, and addressing these weaknesses can be the difference between a breakthrough that can change the world, and a failure that gets stuck in development hell forever.

# 5. Conclusion

Antimicrobial resistance threatens global health and the viability of modern medicine as we know it, but this report has demonstrated that combining the tech of bacteriophage therapy and artificial intelligence identification provides a resilient pipeline for rapid treatment development. Immediate actions should include conducting pilot studies in relevant animal models, upgrading technological infrastructure for scalable production, engaging with regulatory bodies early on in order to align clinical and manufacturing requirements, and establishing a phage-AI consortium to coordinate the allocation of resources and trials will accelerate the transition from traditional laboratory research to new safe and effective therapies.

References

[1] R. Urban-Chmiel, A. K. Szeleszczuk, M. Zawacka-Pankau, and M. Chmiel, “Antibiotic Resistance in Bacteria–A Review,” Antibiotics, vol. 11, no. 8, art. no. 1079, Aug. 2022.

[2] G. Mancuso, L. Pirri, A. Coppolino, and F. Federici, “Bacterial Antibiotic Resistance: The Most Critical Pathogens,” Pathogens, vol. 10, no. 10, art. no. 1310, Oct. 2021.

[3] A. Tarín-Pelló, B. Suay-García, and M.-T. Pérez-Gracia, “Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal,” Expert Rev. Anti-infect. Ther., vol. 20, no. 8, pp. 1095–1108, 2022.

[4] E. A. Phan, L. C. Sutherlin, and M. P. H. Stumpf, “Bacteriophage Therapy as an Alternative to Combat Multidrug-Resistant Bacteria,” Front. Microbiol., vol. 13, art. no. 892743, May 2022.

[5] Y. Zhang, H. Li, K. Wang, and J. Chen, “Deep Learning for Antibiotic Discovery,” Nat. Commun., vol. 12, art. no. 5003, Sept. 2021.

# Appendix

Using the feedback that I received from my peers, I made a few changes to my paper. I clarified the sources to my figures in the executive summary, adding in-text citations, to allow readers to easily find where I got my numbers from, instead of having to dig into all of the sources listed at the bottom. I renumbered and distinguished the main sections of my paper to make it easier to navigate, making it easier to find the part you want in the paper, and updated the table of contents to match the contents of the paper. Separating these topics enhances the readability of the paper while also preventing it from looking like a wall of text, pushing away potential readers from reading through the whole thing. I also made the discussion section more detailed and standardized all citations and in-text citations in IEEE format, which is commonly used by engineers, to cater to my engineering student audience. I also edited any spelling and grammar mistakes out of my final report, fixing any issues that my peers brought up in their peer feedback from phase 2. The style and flow of my paper were a little bit off, having run-on sentences and poor transitions between ideas and paragraphs, so I edited them a little bit as well to make the text read more crisply and logically, smoothing the transitions from one point to the next.