Quality by Design-Driven Process Characterization of Bacteriophage Production to Combat Antimicrobial-Resistant *P. aeruginosa*

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Antimicrobial resistance (AMR) is recognized by the World Health Organization (WHO) as the fifth most critical global public health threat. The rapid spread of drug-resistant pathogens threatens our ability to treat even common bacterial infections with existing antibiotics. New treatments for bacterial infections are urgently needed. One possibility is the use of 'lytic' bacteriophages, or phages for short, which are viruses that very specifically infect and kill bacteria.

This lecture will highlight the importance of integrating Quality by Design principles into the development of phage manufacturing processes.

Quality by Design (QbD) is essential for ensuring the consistency, safety, and efficacy of bacteriophage-based therapies, particularly as these treatments gain increasing interest as alternatives to antibiotics. Applying QbD during the development of phage manufacturing processes allows for a systematic understanding of critical factors influencing phage amplification, purification, and stability. By identifying and controlling critical quality attributes (CQAs) and process parameters early on, QbD minimizes batch-to-batch variability, enhances scalability, and ensures regulatory compliance. Integrating QbD principles into development studies is crucial to accelerate the path to clinical and commercial application.

More precisely, the production process for *Pseudomonas aeruginosa* phages developed at the CHUV (University Hospital Lausanne) by Dr. Grégory Resch is used as a case study. *P. aeruginosa* is a gram-negative bacterium, which under certain conditions can be pathogenic.

The *P. aeruginosa* phage production process is being assessed and characterized using a Quality by Design (QbD) approach in a well-controlled bioreactor environment to enable process optimization and redesign. A Failure Modes and Effects Analysis (FMEA) risk assessment was conducted to evaluate the criticality of process parameters, material attributes, and in-process testing involved in phage production and purification. This assessment, aligned with QbD principles recommended by the International Council on Harmonisation (ICH), provides a foundation for further characterization and optimization of the *P. aeruginosa* phage manufacturing process.

The QbD approach and the ongoing process characterization studies will be presented.

Project partners:

- Laboratory of Bacteriophages and Phage Therapy, Center for Research and Innovation in Pharmaceutical Clinical Sciences (CRISP), Lausanne University Hospital (CHUV), Dr. Grégory Resch
- Cell Production Center (CPC) Service of Pharmacy, Lausanne University Hospital (CHUV), Dr. Jean-François Brunet
- HES-SO Valais, Prof. Wolfram Brück