Dr. Matthew Lamaudiere (matthew.lamaudiere1@mhra.gov.uk)

Medicines and Healthcare products Agency (MHRA)

Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 3QG, United Kingdom

Abstract: Bacteriophage, or ‘phage’ products represent a powerful strategy to combat the escalating global burden of bacterial antimicrobial resistance (AMR). The Medicines and Healthcare products Regulatory Agency is positioned to support harmonisation and innovation in the development of phage products. By working with stakeholders, we can ensure the safety, quality and efficacy of these novel products through biological standardisation and regulatory science. This includes the production of physical reference materials or ‘standards’. Primary assessments and biobanking of phage will require genomic sequencing for the purposes of taxonomic identification, and to verify a lack of deleterious genetic elements including AMR-, (endo/exo)toxin- and integrase-encoding genes. To validate and harmonise phage genome sequencing approaches we are developing a standard comprising the gDNA of 7 different phages targeting clinically relevant Enterobacteriaceae. Firstly, we consulted with industry to understand the needs of innovators and build an initial phage standard profile. Following phage cultivation and purification, gDNA was isolated, and underwent quality assessment through spectrophotometry for purity, fluorometry for yield, and capillary gel electrophoresis for integrity. We found we were able to isolate an average of 239 ng/µL of DNA from each phage with an integrity of 7.6 DNA integrity number (DIN). Lyophilisation and subsequent reconstitution and quality assessment was also conducted ahead of whole-genome sequencing for the individual and combined phage genomes. The next stages of work will comprise benchmarking and comparing the performances of different commonly used bioinformatic pipelines in the profiling and characterisation of the genomic standard.