IABS meeting

"Avoiding antimicrobial resistance: Veterinary use of phages for prevention, therapy and control of bacterial infections"

Conclusions & Recommendations

The workshop focused on the implemention of phage therapy in veterinary medicine and consequently the potential of phages to reduce the use of antibiotics. Presentations were given on the successful application of phages to control infectious pressure by pathogenic bacteria in aquaculture environments, control of *Campylobacter* in the poultry rearing environment and in-feed use to reduce zoonotic pathogen contamination along the poultry and pork food chains. On the therapeutic use of phages, studies in dogs and in ruminants were presented.

Invited oral and poster presentations illustrated the current breadth of the phage research field. Panel discussions focused on the provisions for manufacture, and the potential for licensing of phage-based products via medicinal and non-medicinal legislation.

Conclusions

There is a high level of scientific interest globally for the veterinary use of phages in prevention, therapy and control of bacterial infections, with the aim of reducing the use of antibiotics and fighting against multidrug-resistant bacteria.

Phages are required to follow different regulatory pathways to market depending on national legislation and the way in which they are presented and used, including marketing as: veterinary medicinal products (VMP), feed additives, biocides, or conditioning agents for use on foodstuffs of animal origin. Even when used to treat bacterial infections in animals, national legislative frameworks are not harmonized at the moment, directing phage-based products through options ranging from magistral preparations, through borderline products, to fully authorised novel therapy veterinary medicinal products. Each of these pathways differs in terms of requirements and in how, or if, changes in active pharmaceutical ingredients can be accommodated within an existing approval procedure. Therefore, differences in approach and requirements can cause a wide range of economic cost-benefit analysis outcomes depending on the chosen or prescribed route to market.

It was debated whether all therapeutic use of phages in individual, named animals or, if the legislation allows, in small groups of animals could and should be considered as magistral preparations prescribed by a veterinarian, like the current situation in human clinical medicine.

However, different economic drivers between human and veterinary medicine allow for high fees to be charged in human clinical situations, meaning that the costs for human products are substantialy higher compared to veterinary products and therefore presenting an uneven economic field.

For all fields of use (targeted decontaminants, feed additives, prophylaxis, therapy) the regulatory situation is currently not conducive to developing phage products and in many cases is actually blocking developmental progress. In particular, the classification of phages as novel therapies under recently revised EU legislation (thereby requiring central licensing by the EMA) acts as a disincentive to the development of phage products as fully authorised VMPs.

Recommendations

New measures to encourage access to market of phage products should be considered in an overall strategy to reduce the use of antibiotics. The current high political profile of AMR calls for directing resources toward control and prevention approaches that use phages as part of global and national AMR control strategies, not exclusively as an option for medicinal therapy.

The introduction of flexibility is required for manufacturing of phage-based VMPs, following a risk based approach and focussing in particular on the quality of the final product, including effective record systems to assure consistent quality of production.

The provisions for the quality of manufacture (GMP), the requirements on quality, safety and efficacy of the final product, as well as the regulatory pathways for approval/ licensing, need thorough re-evaluation and adaptation to the biology of phages, their narrow host specificity and the relatively small return on investment expected for the great majority of veterinary phage products. This is needed in order to unleash the potential of this technology within the veterinary domain.

Specific guidance is needed for this type of biological product in view of the urgent need to develop VMPs that have the potential to reduce or replace the use of conventional antibiotics. Such guidance would include the development of mechanisms for alleviating the risk of phage resistance, that is adapted for the different fields of use. Adaptation should take into account all aspects of veterinary medicine from mass treatment of production animals in different farming environments, to individual treatment of companion animals more related to human therapy. Where appropriate, it should include systems to monitor phage use and to conduct surveillance to detect emerging phage-resistance, in a similar way to systems for monitoring use and resistance have been set up for conventional antibiotics.

Follow up publication:

The current regulatory situation and the challenges will be described in a publication in the TOPRA journal 'Regulatory Rapporteur' by David Mackay as first author.

A detailed meeting report will be published in Biologicals, the IABS Journal, by Céline Antoine volunteering as first author and rapporteurs as co-authors, Etienne Thiry being the last and corresponding author.