EFSA'S EXPERIENCE IN THE RISK ASSESSMENT OF BACTERIOPHAGES INTENDED TO BE USED AS FEED ADDITIVES

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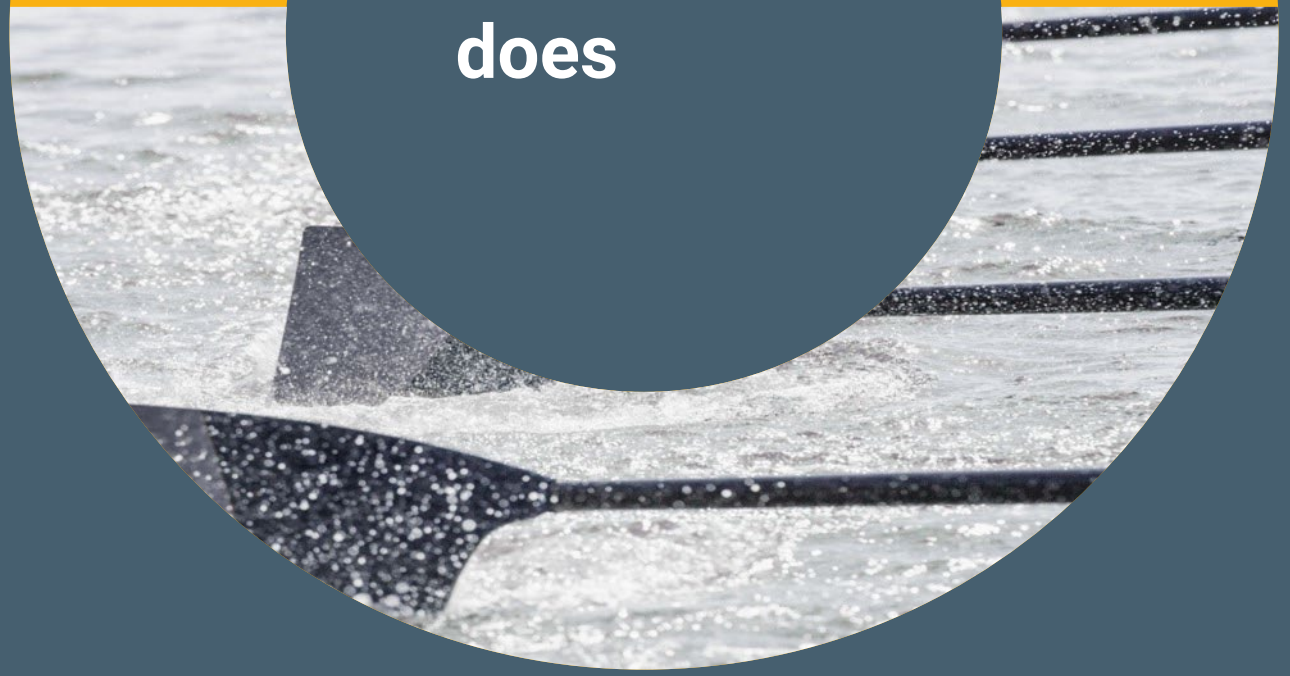
IABS meeting, 20 November 2024

EUROPEAN FOOD SAFETY AUTHORITY

What EFSA does



- Provides independent scientific advice and support for EU risk managers and policy makers on food and feed safety
- Provides independent, timely risk communication
- Promotes scientific cooperation

What EFSA does NOT do

- Develop food safety policies & legislation
- Adopt regulations, authorise marketing of new products
- Enforce food safety legislation

FEED ADDITIVES FRAMEWORK

EU Regulations

REGULATION (EC) No 1831/2003 on additives for use in animal nutrition

Commission Regulation (EC) No 429/2008 on the preparation and the presentation of applications and the assessment and the authorisation of feed additives

Other relevant legal texts (e.g. **Commission Regulation (EC) No 378/2005 on duties and tasks EURL)**

Guidance

Administrative guidance for the preparation of applications on additives for use in animal nutrition

Scientific guidance (sectoral and cross-cutting)

REGULATION (EC) NO 1831/2003

Feed additive: Micro-organisms or preparations, other than feed material and premixtures, which are intentionally added to feed or water in order to perform one or more of the following functions :

a) Favourably affect the characteristics of feed, animal products and the colour of ornamental fish and birds

b) Satisfy the nutritional needs of animals

c) Favourably affect the environmental consequences of animal production

d) Favourably affect animal production, performance or welfare

e) Have a coccidiostatic or histomonostatic effect

REGULATION (EC) NO 1831/2003

Feed additive vs VMP

- The feed additive **should**:
  a) Be used in **healthy animals**
  b) Be administered via **feed or water**
  c) Normally administered during the **whole life or production stage** of the animals
  d) **Fixed formulation**

EFSA OPINIONS 2021 AND 2023

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Safety and efficacy of a feed additive consisting on the bacteriophages PCM F/00069, PCM F/00070, PCM F/00071 and PCM F/00097 infecting *Salmonella* Gallinarum B/00111 (Bafasal®) for all avian species (Proteon Pharmaceuticals S.A.)

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Meta data

EFSA EXPERIENCE ON PHAGES AS FEED ADDITIVES

- First assessment ever on bacteriophages as feed additive
- No specific guidance available. Conducted according to FEEDAP guidance documents: https://www.efsa.europa.eu/en/applications/feedadditives/regulationsandguidance
- Assessment on:
  - Characterisation of the additive
  - Safety for target species, consumers, users and environment
  - Efficacy

APPLICATION

Subject

- **Product consisting of four bacteriophages infecting a strain of *S. enterica* ser. Gallinarum**
- **Zootechnical additive**

Conditions of use

- **In water and complementary feed for all poultry**

Intended effects

- **Reduction of the *Salmonella* spp. carriage in poultry**
- **Reduction of the *Salmonella* spp. load in the environment**
- **Improvement of zootechnical performance**

ASSESSMENT – ACTIVE AGENTS AND ADDITIVE

Phages → WGS and phenotypic tests

- **Taxonomic identification**
- **Type (i.e. lytic/lysogenic)**
- **Genes of concern (e.g. coding for antimicrobial resistance, toxins, virulence factors)**

Host strain → WGS and phenotypic tests

- **Taxonomic identification**
- **Antimicrobial susceptibility**
- **Genes of concern (e.g. coding for antimicrobial resistance, toxins, virulence factors)**

Additive → Experimental data

- **Purity (e.g., presence of viable cells and DNA from host strain, contaminants)**
- **Stability**

SAFETY

Safety for target species and consumer

- **Nature of the additive (i.e. phages, host strain, purity)**
- **Full toxicological package**
  - Tolerance trial with target species
  - Genotoxicity studies (in vitro mammalian cell gene mutation and three in vitro micronucleus assays)
  - Sub-chronic (90-days) oral toxicity study in rats

Safety for user

- **Eye and dermal irritation tests**
- Owing to the proteinaceous nature of the phages, the product is considered to be sensitiser

Safety for the environment

- **Based on nature and purity of the additive**

EFFICACY

Host range → *In vitro* studies

- Lytic activity against a range of strains

Zootechnical effects → *In vivo*/challenge trials

- *Salmonella* spp. counts in boot swabs and caecal content
- Zootechnical performance

LESSONS LEARNT

Characterisation of the additive

- **Characterisation of phages and their host strain**
- **Manufacturing process**
- **Characterisation/purity of final product**

Safety

- **Dependent on nature and purity of product**
- **Toxicological data**

Efficacy

- **Dependent on intended effects (i.e. specificity of lytic activity vs broad host range)**

Future/pending challenges

- **Development of resistance**
  - Post-market monitoring?

NEXT STEP

cha… … risk
assess… …ganisms
us… …ain

Public consultation 2025

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