Assessment of feed additives produced from or containing microorganisms - Tackling antimicrobial resistance risks

Rosella Brozzi (rosella.brozzi@efsa.europa.eu)

European Food Safety Authority, FEED Unit. Parma, Italy.

Regulation (EC) No 1831/2003[1] stipulates that all feed additives intended to be marketed in the European Union (EU) must be safe for the target species, the consumer of products derived from the treated animals, the user and for the environment. The European Food Safety Authority (EFSA) is the EU body in charge of conducting the risk assessment of feed additives in line with the legal requirements. This work is carried out by the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) with the support of the FEED Unit.

The FEEDAP Panel has produced a series of guidance documents intended to support applicants in the preparation of technical dossiers, and risk assessors in the evaluation of the contained data. These guidance documents are regularly updated to take advantage of the experience gained in evaluating the data and of the new findings in science and technology.

Microorganisms can be used as feed additives (e.g., probiotics, silage additives) or can be used as production strains for other additives (e.g., enzymes, amino acids, organic acids). A proper characterisation of these microorganisms is fundamental for the safety assessment. This includes, among other issues, consideration of their ability to survive antimicrobial treatments (i.e., antimicrobial resistance, AMR) and to transfer this capacity to other microorganisms. This is provision is based on the legal requirements. In fact Commission Regulation (EC) No 429/2008 prescribes that microbial feed additives should not contribute to the reservoir of antibiotic resistance genes already present in the gut microbiota of animals and the environment.

So far approximately 140 strains intended to be used as feed additives have been assessed. From these, five have been found to be resistant to one or more antibiotics (EFSA, 2010, 2011, 2012a, 2012b, 2014). However, only in two cases the genetic basis of the resistance could be identified and in only one of these, the concern related to the potential transfer of the resistance determinants to other microbes could be dismissed. Consequently, in four out of these five cases the Panel could not conclude on the safety of the strains.

The FEEDAP Panel is currently revising its guidance documents. Within this activity, a new guidance document describing the data requirements and the approach underpinning the assessment of microbial and microbial-based additives has been produced.[2] In this document, the assessment of the AMR of bacterial feed additives is based on two sets of data:

- Phenotypic testing based on determination of the minimum inhibitory concentration (MIC) for a battery of relevant antimicrobials,
- A search of the whole genome sequence for the presence of known AMR genes.

The antimicrobials are chosen to detect a wide range of antibiotic resistance determinants and to cover those relevant for use in humans and animals (i.e., critically important antimicrobials (CIAs) or highly important antimicrobials (HIAs), last revision WHO, 2016). The possibility of transfer of resistance from viable microorganisms to other microorganisms is related to the genetic basis of the resistance and is considered to be most plausible when the resistance is mediated by added/acquired genes.

---

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29–43.

[2] Draft FEEDAP Panel's guidance on the characterisation of microorganisms used as feed additives or as production organisms. Under public consultation until 15 September 2017 at http://www.efsa.europa.eu/en/consultations/call/170615

The current view of the FEEDAP Panel is:

- Bacterial strains used as feed additives or as a source of feed additives carrying acquired genes that confer resistance to relevant antimicrobial(s) are considered to represent a risk for target species and for those exposed to the additive.
- Bacterial strains used as a source of a feed additive carrying acquired AMR genes, when DNA fragments long enough to cover the corresponding complete genes are detected in the final product, the product is considered to represent a risk for target species and those exposed to the additive. However, if the absence of DNA from the production strain can be shown in the additive, this is not considered a risk.

The guidance on the characterisation of microorganisms used as feed additives or as production organisms was subject to public consultation in the period June to September 2017 and is currently under revision to take account of the comments received. It is expected to be adopted by the FEEDAP Panel and published on the EFSA website in late 2017/early 2018.

EFSA is actively involved in several other activities in the area of antimicrobial resistance. It provides independent scientific support and advice to risk managers on the risks to human and animal health related to the possible emergence, spread and transfer of antimicrobial resistance in the food chain and in animal populations, e.g., in the reduction of the need to use of antimicrobials in food-producing animals (EMA and EFSA, 2016), in the monitoring and collection of information on antimicrobial resistance in food-producing animals and food (http://www.efsa.europa.eu/en/biological-hazards-data/reports).

For further information, visit: http://www.efsa.europa.eu/en/topics/topic/antimicrobial-resistance

References:

WHO (World Health Organisation) 2016. Critically important antimicrobials for human medicine – 4th rev. WHO Press. ISBN 978 92 4 151146 9

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); 2010. Scientific Opinion on the safety and efficacy of the product Cylactin® (*Enterococcus faecium*) as a feed additive for chickens for fattening. EFSA Journal 2010; 8(7):1661. [13 pp.]. doi:10.2903/j.efsa.2010.1661

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); 2011. Scientific Opinion on the safety and efficacy of *Lactobacillus pentosus* (DSM 14025) as a silage additive for all animal species. EFSA Journal 2011;9(11):2449. [8 pp.]. doi:10.2903/j.efsa.2011.2449.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); 2012a. Scientific Opinion on the safety and efficacy of Prostora Max (*Bifidobacterium animalis*) as a feed additive for dogs. EFSA Journal 2012;10(12):2964 [14 pp.] doi:10.2903/j.efsa.2012.2964.EMA (European Medicines Agency) and EFSA (European Food Safety Authority), 2017.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); 2012b. Scientific Opinion on the safety and efficacy of Toyocerin® (*Bacillus cereus*) as a feed additive for sows, piglets, pigs for fattening, cattle for fattening, calves for rearing, chickens for fattening and rabbits for fattening. EFSA Journal 2012;10(10):2924. [34 pp.]

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2014. Scientific Opinion on the safety and efficacy of *Pediococcus pentosaceus* (NCIMB 30044) as a silage additive for all animal species. EFSA Journal 2014;12(3):3610, 12 pp.

EMA (European Medicines Agency) and EFSA (European Food Safety Authority), 2017. EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA). [EMA/CVMP/570771/2015]. EFSA Journal 2017;15(1):4666, 245 pp. doi:10.2903/j.efsa.2017.4666