Mandate for an EFSA scientific opinion as regards specific **maximum levels of cross-contamination for 24 antimicrobial** active substances in non-target feed

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION:

Combatting antimicrobial resistance (AMR) is a priority in the European Union (EU). Several measures have already been put in place to limit its development. In 2006, the EU banned the use of antibiotics as feed additives for growth promotion. The provisions established in the new Medicated Feed Regulation[1] are further concrete actions to deal with the issue.

The cross-contamination of non-target feed (*feed, whether medicated or not, which is not intended to contain a specific active substance*) with antimicrobials has been identified as one of the core issues addressed in this context.

Cross-contamination may occur during manufacture, processing, storage or transport of feed where the same production and processing equipment, including for mobile mixing, storage facilities or means of transport are used for feed with different components. For the purposes of the Medicated Feed Regulation, the concept of cross-contamination is used specifically to designate the transfer of traces of an active substance contained in a medicated feed to a non-target feed. Contamination of non-target feed with active substances contained in medicated feed should be avoided or kept as low as possible.

The respective Article 7 on cross-contamination stipulates in paragraph 3:

The Commission shall, by 28 January 2023, adopt delegated acts in accordance with Article 20 in order to supplement this Regulation by establishing, as regards the antimicrobial active substances listed in Annex II, specific maximum levels of cross-contamination for active substances in non-target feed and methods of analysis for active substances in feed. Regarding maximum levels of cross-contamination, those delegated acts shall be based on a scientific risk assessment carried out by EFSA.

Moreover, recital 17 of that Regulation highlights the *protection of animal health, human health and the environment* and suggests *EFSA to do the risk assessment in cooperation with the European Medicines Agency (EMA).*

Finally, Article 107 of the new Regulation on veterinary medicinal products[2] stipulates in its paragraph 2: *Antimicrobial medicinal products shall not be used in animals for the purpose of promoting growth nor to increase yield.*

The development of AMR and the resulting impact on human health, animal health and the environment represents an important consequence of low-level concentration of antimicrobials in feed. Only very limited data are available on the chain between a low concentration of an antimicrobial in feed, the development of resistance in microbial agents relevant for human and animal health (zoonotic bacteria, commensals, animal pathogens) and the possible transfer of resistance determinants and/or resistant agents to humans. Therefore, it would be appropriate to investigate the effect of the exposure to the antimicrobials at low concentrations via feed on the microbiota of animals, and in particular the selection for resistance in microbial agents relevant for human and animal

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1 Regulation (EU) 2019/4 of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC (OJ L4, 7.1.2019, p. 1)

2 Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L4, 7.1.2019, p. 43)

health. Subject to availability of supporting scientific evidence, the impact of the low-level presence in feed on the environment should be considered, too.

Further, in order to avoid any misuse of the antimicrobials, use levels of the antimicrobials for promoting growth or increasing yield should, where applicable, be identified and assessed.

With respect to the scope of the non-target feed to be addressed it has to be noted that medicated feed for food-producing animals and medicated pet food are produced and distributed in separate way. Moreover, the antimicrobials at stake are not authorised for incorporation into medicated pet food. Therefore, the scope of this assessment should be focused on the low-level concentration of the antimicrobials in feed for food-producing animals.

The European Commission will mandate the European Union Reference Laboratory (EURL) for Feed Additives (Commission Directorate General JRC, Geel) to recommend methods of analysis for the antimicrobials in feed. For this task, some data might be relevant which is to be compiled for the assessment of the cross-contamination levels. Therefore, an exchange of information between the EURL, EFSA and EMA, including national authorisation authorities, would be useful.

In order to protect animal health, human health and the environment, maximum levels of cross-contamination for active substances in non-target feed should be established, based on a scientific risk assessment performed by the European Food Safety Authority (EFSA) and in cooperation with EMA. The maximum levels should be compared with the use levels of the antimicrobials for promoting growth or increasing yield, where applicable, to determine a final appropriate level.

TERMS OF REFERENCE AS PROVIDED TO EFSA:

The European Commission requests the EFSA to assess the impact of the presence of low-level concentration in feed of the antimicrobial active substances listed in the Annex on animal health, human health and, where possible, on the environment.

In particular, EFSA, in close collaboration with EMA, is asked, by 30 September 2021:

1. To assess the specific concentrations of antimicrobials resulting from cross-contamination in non-target feed for food-producing animals, below which there would not be an effect on the emergence of and/or selection for resistance in microbial agents relevant for human and animal health, i.e. the endpoint for this assessment should be the excretion of resistant bacteria from the animals. However, the assessment should also consider the impact on the environment of the low-level concentrations in feed, where possible.

2. To assess which levels of the antimicrobials have a growth promotion/increase yield effect**.**

Annex: List of antimicrobial active substances to be assessed

Active substance
1. Amoxicillin
2. Amprolium
3. Apramycin
4. Chlortetracycline
5. Colistin
6. Doxycycline
7. Florfenicol
8. Flumequine
9. Lincomycin
10. Neomycin
11. Spectinomycin
12. Sulfonamides
13. Tetracycline
14. Oxytetracycline
15. Oxolinix Acid
16. Paromomycin
17. Penicillin V
18. Tiamulin
19. Tiamfenicol
20. Tilmicosin
21. Trimethoprim
22. Tylosin
23. Valnemulin
24. Tylvalosin