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Safety and efficacy of concentrated liquid L-lysine (base), L-lysine monohydrochloride and L-lysine sulphate produced using different strains of *Corynebacterium glutamicum* for all animal species based on a dossier submitted by AMAC/EEIG

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)

Abstract¹

Concentrated liquid L-lysine (base) and L-lysine HCl, produced by genetically modified (GM) strains of *Corynebacterium glutamicum*, and L-lysine sulphate (solid and liquid) produced by non-GM strains of *C. glutamicum*, were the subject of this application. The use of L-lysine HCl produced by the GM *C. glutamicum* 'A' in animal nutrition was considered a hazard due to the presence of a recombinant antibiotic resistance gene. The use in animal nutrition of concentrated liquid L-lysine (base) produced using *C. glutamicum* 'A' was considered of no concern for the target species, consumer and the environment. The FEEDAP Panel could not conclude on the safety of concentrated liquid L-lysine (base) and L-lysine HCl produced by the GM *C. glutamicum* 'B' or 'C' for the target animals, consumers and environment due to the absence of adequate data on the absence of the production strain or its recombinant DNA in the products. The identity of strain 'C' as *C. glutamicum* was also not confirmed. For L-lysine sulphate originating from non-GM strains *C. glutamicum* 'D', 'E' or 'F', the FEEDAP Panel could not conclude on the safety for the target species, the consumer and the environment due to uncertainties that these products might contain antibiotic resistance genes. In addition, the intrinsic high sulphate content in those products might have the potential to cause adverse effects in target species. The FEEDAP Panel reiterated its concerns on the safety of the administration of amino acids, including L-lysine, via water for drinking because of the risk of imbalances and for hygiene reasons. Due to the uncertainties described above, the FEEDAP Panel could not conclude on the safety for users or the environment of all products under assessment except concentrated liquid L-lysine (base) produced using *C. glutamicum* 'A'. The products under assessment would be considered efficacious sources of L-lysine for non-ruminant species. For these sources of supplemental L-lysine to be as efficacious in ruminants as in non-ruminant species, they would require protection against degradation in the rumen.

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Keywords: nutritional additive, amino acids, concentrated liquid L-lysine base, concentrated liquid L-lysine HCl, L-lysine HCl, L-lysine sulphate, safety and efficacy

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¹ This section has been amended following the confidentiality claims made by the applicant.

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Note: The full opinion will be published in accordance with Article 8(6) of Regulation (EC) No 1831/2003 once the decision on confidentiality, in line with Article 18(2) of the Regulation, will be received from the European Commission.

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Summary²

Following a request from European Commission, the Panel on Additives and Products or Substances used in Animal Feed was asked to deliver a scientific opinion on concentrated liquid L-lysine (base), L-lysine monohydrochloride (HCl) technically pure and L-lysine sulphate (solid and/or liquid) produced by fermentation by different strains of *Corynebacterium glutamicum* (hereafter referred as 'A', 'B', 'C', 'D', 'E' and 'F'), for all animal species.

L-Lysine is an essential amino acid for all animal species. L-Lysine and its salts are widely used in the feed industry to optimise the amino acid profile of diets in order to improve animal performance.

The use of the amino acid L-lysine itself in animal nutrition is considered safe for target animals, consumers, and the environment.

The use of L-lysine HCl technically pure produced using *C. glutamicum* 'A' in animal nutrition was considered a hazard for the target species, consumer, user and environment due to the presence of a recombinant antibiotic resistance gene in most batches of the product. The use of concentrated liquid L-lysine (base) produced by *C. glutamicum* 'A' in animal nutrition was considered of no concern for the target species, consumer and the environment.

The FEEDAP Panel could not conclude on the safety of the products concentrated liquid L-lysine (base) and L-lysine HCl, technically pure, produced using *C. glutamicum* 'B' (the presence of the production strain and/or its recombinant DNA could not be excluded) or 'C' (incomplete data on identification of the species, safety of the genetic modification, potential for antibiotic resistance and the presence/absence of the production strain and its recombinant DNA in the products) for the target animal species, consumer, the user and the environment.

The FEEDAP Panel could not conclude on the safety of L-lysine sulphate solid and/or liquid originating from *C. glutamicum* 'D', 'E' or 'F'. The genetic basis of resistance to at least one antibiotic used in medical and veterinary practice was not sufficiently elucidated. In addition, the intrinsic high sulphate content in the product might have the potential to cause adverse effects in target species.

Regardless of the assessment of the genetic modification, potential transmissible antibiotic resistance or absence of toxicological studies, the FEEDAP Panel had concerns on the safety of the administration of the amino acids, including L-lysine, via water for drinking because of the risk of imbalances and for hygiene reasons.

The lack of any significant dermal or eye irritant potential along with evidence for lack of respiratory toxicity and dermal sensitisation indicated that there is no significant concern regarding user safety for the L-lysine sulphate products. Concentrated liquid L-lysine (base) is considered as corrosive due to its high pH. In the absence of data, the FEEDAP Panel could not conclude on the dermal sensitisation and on the irritancy of L-lysine HCl to skin or eyes. The concerns regarding the safety of the genetic modification and potential presence of transmissible resistance to antibiotics might also have implications for the safety of the user.

Concentrated liquid L-lysine base and L-lysine HCl, technically pure produced by fermentation with strains *C. glutamicum* 'A', 'B' or 'C', and L-lysine sulphate (both solid and liquid) produced by fermentation with strains *C. glutamicum* 'D', 'E' or 'F' are regarded as efficacious sources of the essential amino acid L-lysine for non-ruminant animal species. For these sources of supplemental L-lysine to be as efficacious in ruminants as in non-ruminant species, they would require protection against degradation in the rumen.

The FEEDAP Panel made some recommendations concerning (i) the description of the additives and (ii) the importance of considering the contribution of sulphate from the additive when using L-lysine sulphate supplementation in feed.

² This section has been amended following the confidentiality claims made by the applicant.