RP1052 Assessment of the application for L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with Corynebacterium glutamicum KCCM 80216 or KCTC 12307BP as a feed additive for all animal species

Maes o ddiddordeb ymchwil: Research projects
Statws y prosiect: Wedi'i gwblhau
Cod prosiect: RP 1052
Awduron: Risk Assessment Unit Science, Evidence and Research Division, FSA
Cynhaliwyd gan: Risk Assessment Team Science Division, FSS
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1.Executive summary

The Food Standards Agency (FSA) and Food Standards Scotland (FSS) have undertaken a safety assessment of application RP 1052 for the use of L-lysine monohydrochloride (? 99% (footnote 1)) and concentrated liquid L-lysine (base) (? 50%1) produced by fermentation with *Corynebacterium glutamicum* KCCM 80216 or KCTC 12307BP as a feed additive for all animal species, from Daesang Europe B. V. Van Heuven Goedhartlaan 935, 1181 LD Amstelveen, Netherlands (category: nutritional additives; functional group: amino acids, their salts and analogues).

A feed additive application has been received by Great Britain (GB) where EFSA, prior to the end of the transition period, evaluated an application for the product. FSA/FSS have reviewed the EFSA opinions (EFSA Journal 2020;18(12):6334, EFSA Journal 2020;18(12):6333) and confirm that they are adequate and relevant for GB risk analysis and used this to form the basis of the GB opinion.

The FSA/FSS risk assessors concluded that the EFSA opinions are adequate and relevant for GB risk analysis and therefore, the use of the L-lysine additive, as described in this application, is safe and is not liable to have an adverse effect on the target species, worker safety, environmental safety and human health at the intended concentrations of use.

There are no specific conditions or restrictions in relation to handling, labelling, post-market monitoring requirements and use of this additive as described in this application. Maximum Residue Limits (MRLs) are not required for this additive.

2.Background and purpose of review

EFSA Journal 2020; 18(2):6334,

EFSA Journal 2020; 18(2):6333,

Question number: EFSA-Q-2020-00134 , EFSA-Q-2020-00326

In accordance with Retained EU Regulation 1831/2003 on feed additives, the application RP 1052 for the use of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with *Corynebacterium glutamicum* KCCM 80216 or KCTC 12307BP as a feed additive for all animal species from Daesang Europe B. V. has been submitted for authorisation in GB.

Whilst it was a Member State of the EU, the UK accepted the assessments of EFSA in respect of authorisations for regulated food and feed products. Since the end of the transition period, FSA/FSS has adopted equivalent technical guidance and quality assurance processes to be able to undertake GB safety assessments for regulated product applications.

Where EFSA, prior to the end of the transition period, evaluated an application for the product for which an application is now made to GB, FSA/FSS has decided to make use of the EFSA risk assessment, where this is appropriate, in forming its opinion. Therefore, FSA/FSS safety assessors have reviewed the EFSA opinions (footnote 2), (footnote 3) for the application below in the context of intended GB use and have concluded that the intended uses are safe.

In reviewing the EFSA risk assessment opinion the reviewers have verified that the standard approach as outlined in the relevant guidance (footnote 4) has been followed and the arguments made are consistent with the data summarised in the opinion. Consideration has been given to the processes undertaken to ensure the opinions are robust and whether there are any aspects that would require further review such as specific issues for the countries of the GB. The result of the assessment is that the EFSA scientific opinions are adequate also for GB risk analysis.

3.Details of the EFSA assessment

3.1 Methodology applied in the EFSA opinions

EFSA FEEDAP guidance: Guidance on the assessment of the safety of feed additives for the environment **(2019)**, Guidance on the assessment of the safety of feed additives for the target species **(2017a)**, Guidance on the identity, characterisation and conditions of use of feed additives **(2017b)**, Guidance on the assessment of the safety of feed additives for the consumer **(2017c)**, Guidance on the characterisation of microorganisms used as feed additives or as production organisms **(2018a)**, Guidance on the assessment of the efficacy of feed additives **(2018b)**, Guidance on studies concerning the safety of use of the additive for users/workers **(2012)** and principles in Regulation (EC) No 429/2008 (not explicitly stated whether applicable SC guidance applied).

3.2 Source/organism

The additive contains L-lysine produced by fermentation with *Corynebacterium glutamicum* (KCCM 80216 or KCTC 12307BP). The application is for the additive as two forms, a solid as L-lysine monohydrochloride and a concentrated liquid (base).

The production strain of the L-lysine is from the species *C. glutamicum* which is designated as eligible for the Qualified Presumption of Safety (QPS) assessment approach.

The production strain was sequenced using a whole genome approach and evaluated for susceptibility to antibiotics. From this it was concluded that the strain is resistant to Streptomycin.

3.3 Genetic modification step

The assessment of the genetic modification of the production strain was performed. There are no safety concerns noted relating to the inserted genes and the production strain does not contain acquired (by modification) additional antimicrobial resistance genes.

3.4 Specification

Information provided on the identity, composition and specifications of the production species does not raise safety concerns (the published EFSA opinions are redacted whilst confidentiality claims are determined.)

Physiochemical properties, homogeneity data and stability data (as shelf life of the products) were presented for both solid and liquid additive forms. Both forms are highly purified. Stability data for the additive within an exemplar feed ration and a feed pre-mix were provided from one study only for the solid L-Lysine- monohydrochloride form.

This application included the request for use within all species. No recommended inclusion rates were discussed in the application due to the varying concentrations that may be required due to the animal species, nutritional specification of the feed ration, environmental conditions and the current health state of the animal.

3.5 Exposure assessment

Not relevant as L-lysine is a natural component of any consumed animal products. The applicant is seeking to use L-lysine as a nutritional feed additive and the product has been assessed on this basis.

3.6 Toxicological data

L-lysine is currently authorised as a feed additive for all species as a nutritional additive, using different production species than the ones used in this application.

This application is for the use of L-lysine produced by fermentation with *Corynebacterium glutamicum* (KCCM 80216 or KCTC 12307BP).

4. EFSA assessment and conclusions

L-Lysine produced by fermentation with *C. glutamicum* strain KCCM 80216 or KCTC 12307BP raises no concerns for the consumer of the products obtained from animals fed the additive. *C. glutamicum* has QPS status.

The additive, in either form, is not a skin or eye irritant and not deemed a skin sensitiser. L-lysine monohydrochloride (the solid additive form) is not an inhalation hazard. The liquid base form was not evaluated for effects on the respiratory system.

No risks to the environment are expected and no further environmental risk assessment is required. The application does not raise safety concerns for the environment with regard to the genetic modification of the production strain *C. glutamicum* (KCCM 80216 or KCTC 12307BP).

There are no safety concerns noted relating to the inserted genes within *C. glutamicum* (KCCM 80216 or KCTC 12307BP) and the strain does not contain acquired (by modification) additional antimicrobial resistance genes.

The use of the L-lysine additive does not raise safety concerns for the target animal.

5. Caveats and uncertainties

There are no further caveats or uncertainties to highlight.

6. FSA Conclusion on reliability and applicability

FSA and FSS have access to the full dossier of information from the applicant but have used the EFSA opinion as the basis of their assessment. The FSA and FSS assessment of the EFSA opinion has confirmed the application has been assessed in line with the applicable guidance and is partially based on considerations of detailed proprietary information available to the EFSA Panel, whilst this is only briefly summarised in the EFSA opinion, this description is consistent with the conclusions.

6.1 Analytical Method Review

FSA/FSS accepts the EURL analytical method evaluation reports (footnote 5), (footnote 6). FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

7. Outcome of assessment

FSA/FSS has reviewed the EFSA opinions and consider them adequate and relevant for GB risk analysis. Therefore, the opinions were used to form the basis of the GB opinion.

FSA/FSS had access to the full dossier of information for the application supplied by the applicant but have used the EFSA opinion as the basis of their assessment. FSA/FSS agree with the safety conclusions outlined in the EFSA opinion.

The FSA/FSS opinion is that the L-lysine additive, as described in this application, is safe and is not liable to have an adverse effect on the target species, worker safety, environmental safety and human health at the intended concentrations of use.

8. References

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012. Guidance on studies concerning the safety of use of the additive for users/workers. EFSA Journal 2012;10(1):2539, 5 pp. https://doi.org/10.2903/j.efsa.2012.2539

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017a. Guidance on the assessment of the safety of feed additives for the target species. EFSA Journal 2017;15(10):5021, 19 pp. https://doi.org/10.2903/j.efsa.2017.5021

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017b. Guidance on the identity, characterisation and conditions of use of feed additives. EFSA Journal 2017;15(10):5023, 12 pp. https://doi.org/10.2903/j.efsa.2017.5023

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017c. Guidance on the assessment of the safety of feed additives for the consumer. EFSA Journal 2017;15(10):5022, 17 pp. https://doi.org/10.2903/j.efsa.2017.5022

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018a. Guidance on the characterisation of microorganisms used as feed additives or as production organisms. EFSA Journal 2018;16(3):5206, 24 pp. https://doi.org/10.2903/j.efsa.2018.5206

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018b. Guidance on the assessment of the efficacy of feed

additives. EFSA Journal 2018;16(5):5274, 25 pp. https://doi.org/10.2903/j.efsa.2018.5274

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2019. Guidance on the assessment of the safety of feed additives for the environment. EFSA Journal 2019;17(4):5648, 78 pp. https://doi.org/10.2903/j.efsa.2019.5648

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2020. Safety and efficacy of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with *Corynebacterium glutamicum* KCCM 80216 as feed additive for all animal species. EFSA Journal 2020; 18(12):6334. https://doi.org/10.2903/j.efsa.2020.6334

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2020. Safety and efficacy of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with *Corynebacterium glutamicum* KCTC 12307BP as feed additives for all animal species. EFSA Journal 2020; 18(12):6333. https://doi.org/10.2903/j.efsa.2020.6333

1. L-Lysine was analysed following the method described in section 2.2.56 (method I) of the European Pharmacopoeia 9th edition and L-Lysine monohydrochloride was calculated by stoichiometry.

2. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2020. Safety and efficacy of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with Corynebacterium glutamicum KCCM 80216 as feed additive for all animal species. EFSA Journal 2020; 18(12):6334.

   https://doi.org/10.2903/j.efsa.2020.6334

3. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2020. Safety and efficacy of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with Corynebacterium glutamicum KCTC 12307BP as feed additives for all animal species. EFSA Journal 2020; 18(12):6333.

   https://doi.org/10.2903/j.efsa.2020.6333

4. See reference list for the full set of guidance applied.

5. Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003

6. EURL evaluation report on Lysine