Assessment : Assessment of the application for L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with *Corynebacterium glutamicum* KCCM 80183 as a feed additive for all animal species, from CJ Europe GmbH

Reference Number RP 1199

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29th August 2023

Contents

1.Executive summary

The FSA/FSS have undertaken an assessment of application RP 1199 for the use of L-lysine monohydrochloride (≥ 78%[1]) and concentrated liquid L-lysine (base) (≥ 50%[1]) produced by fermentation with *Corynebacterium glutamicum* KCCM 80183 as a feed additive for all animal species, from CJ Europe GmbH, Unterschweinstiege 2 - 14, 60549 Frankfurt am Main, Germany (category: nutritional additives; functional group: amino acids, their salts and analogues, to satisfy the nutritional needs of the target species with this essential amino acid).

A number of feed additive applications have 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 opinion (EFSA Journal 2021;19(4):6537) and confirm that this is adequate and relevant for GB risk analysis and used this to form the basis of the GB opinion. A full risk assessment of this application was not considered necessary by FSA and FSS.

The FSA/FSS risk assessors concluded that the EFSA opinion is adequate and relevant for GB risk analysis. 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 2021; 19(4):6537

Question number: EFSA-Q-2019-00411

In accordance with Retained EU Regulation 1831/2003 on feed additives, the application RP 1199 for the use of L-lysine monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation with *Corynebacterium glutamicum* KCCM 80183 as a feed additive for all animal species from CJ Europe GmbH has been submitted for authorisation in each nation of Great Britain (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 risk assessments for regulated product applications.

However, a number of applications have been received by GB where EFSA, prior to the end of the transition period, evaluated an application for the product for which an

[1] L-Lysine was analysed by ion-exchange chromatography following the method described in AOAC official method 999.13.

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 risk assessors have reviewed the EFSA opinion[2] 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[3] 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. Therefore, a full risk assessment has not been performed by FSA/FSS.

3.Details of the EFSA assessment

Methodology applied in the EFSA opinion

EFSA FEEDAP guidance: Guidance on the assessment of the safety of feed additives for the environment (**2019a**), 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 studies concerning the safety of use of the additive for users/workers (**2012**) and principles in Regulation (EC) No 429/2008.

3.1 Source/organism

The additive contains L-lysine produced by fermentation with a genetically modified strain of *Corynebacterium glutamicum* (KCCM 80183). 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 recombinant production strain was sequenced using a whole genome approach and evaluated for susceptibility to antibiotics. From this it was concluded that the strain is not resistant to any antibiotics evaluated.

3.2 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

[2] EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2021. Scientific Opinion on the safety and efficacy of the feed additives concentrated liquid L-lysine (base) and L-lysine monohydrochloride produced by *Corynebacterium glutamicum* KCCM 80183 for all animal species (CJ Europe GmbH). EFSA Journal 2021;19(4):6537 https://doi.org/10.2903/j.efsa.2021.6537

[3] See reference list for the full set of guidance applied.

genes (detailed information in the EFSA opinion is redacted whilst confidentiality claims are determined).

3.3 Specification

Information provided on the identity, composition and specifications of the production species does not raise safety concerns (detailed information in the EFSA opinion is 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 both forms of the additive within an exemplar feed ration and a feed pre-mix were provided, but for the additive produced from a different species, *Corynebacterium glutamicum* (KCCM 10227). However, due to the similarity of the additive characteristics and production process these data, evaluated in a previous EFSA opinion (EFSA FEEDAP Panel, 2019b), are deemed to be applicable to this application.

Three batches of L-lysine (base) and 3 batches of L-lysine monohydrochloride were analysed for heavy metals (mercury, lead, cadmium and arsenic), 358 pesticides, mycotoxins (aflatoxins, ochratoxin A, zearalenone, fumonisins and deoxynivalenol) and microbiological contamination (*E.coli*, total *coliforms*, *Salmonella* spp, total viable counts, yeasts and filamentous fungi). No safety concerns were noted with results from the analyses.

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.

3.4 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.

3.5 Toxicological data

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

This application is for the use of L-lysine produced by fermentation with *Corynebacterium glutamicum* (KCCM 80183).

Acute oral toxicity studies for both L-lysine forms produced by a different production strain (*Corynebacterium glutamicum,* KCCM 10227) were undertaken but deemed not relevant as only a single dose of L-lysine was administered in both studies.

Studies relating to safety for the worker were evaluated in a previous EFSA opinion (EFSA FEEDAP Panel, 2019b), for the additive produced from a different species, *Corynebacterium glutamicum* (KCCM 10227). However, due to the similarity of the additive characteristics and production process these data are deemed to also be applicable for this application.

4. EFSA assessment and conclusions

L-Lysine produced by fermentation with *C. glutamicum* strain KCCM 80183 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 irritant and not deemed a skin sensitiser. L-lysine in both forms is considered an inhalation hazard and mild eye irritant.

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 80183).

There are no safety concerns noted relating to the inserted genes within *C. glutamicum* (KCCM 80183) and the strain does not contain acquired (by modification) additional antimicrobial resistance genes.

The use of the L-lysine additives does not raise safety concerns for the target animal provided the inclusion rates within the diet are appropriate. There are some concems noted on the addition of amino acids such as L-Lysine administered via drinking water due to hygiene implications and the risk of nutritional imbalances when also administered simultaneously in feed.

5. Caveats and uncertainties

There are no further caveats or uncertainties to highlight.

6. FSA Conclusion on reliability and applicability

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 this description is consistent with the conclusions.

6.1 Analytical Method Review

FSA/FSS accepts the EURL analytical method evaluation reports[4]. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

7. Outcome of assessment

[4] https://joint-research-centre.ec.europa.eu/system/files/2014-04/FinRep-FAD-2013-0027_L-lysine.pdf

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. A full risk assessment of this application was not considered necessary by FSA and FSS.

FSA/FSS had access to all supporting documentation that was provided to the EFSA Panel by the applicant, and subsequently used to form the EFSA opinion. FSA/FSS agree with the safety conclusions outlined in the EFSA opinions.

Following the principles outlined in the background for making use of the EFSA opinions, the FSA/FSS opinion is that the L-lysine additive in both forms, 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), 2019a. 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), 2019b. Scientific Opinion on the safety and efficacy of L-lysine

monohydrochloride and concentrated liquid L-lysine (base) produced by fermentation using *Corynebacterium glutamicum* strain KCCM 10227 for all animal species. EFSA Journal 2019;17(5):5697, 15pp. https://doi.org/10.2903/j.efsa.2019.5697

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2021. Scientific Opinion on the safety and efficacy of the feed additives concentrated liquid L-lysine (base) and L-lysine monohydrochloride produced by *Corynebacterium glutamicum* KCCM 80183 for all animal species (CJ Europe GmbH). EFSA Journal 2021;19(4):6537 https://doi.org/10.2903/j.efsa.2021.6537