Assessment : Assessment of the application for disodium 5'-guanylate produced by *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067 as a feed additive for all animal species, from CJ Europe GmbH

Reference Number RP 1200

Risk Assessment Unit
Science, Evidence and Research Division, FSA

Risk Assessment Team
Science Division, FSS

29th August 2023

Contents

1.Executive summary

The FSA/FSS have undertaken an assessment of application RP 1200 for the use of disodium 5'-guanylate (≥ 97%, on a dry matter basis[1])) produced by fermentation with *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067 as a feed additive for all animal species, from CJ Europe GmbH, Unterschweinstiege 2 - 14, 60549 Frankfurt am Main, Germany (category: sensory, functional group: flavouring compounds, to enhance the flavouring of feed).

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(6):6619) 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. and therefore, the use of the disodium 5'-guanylate 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(6):6619

Question number: EFSA-Q-2020-00267

In accordance with Retained EU Regulation 1831/2003 on feed additives, the application RP 1200 for the use of disodium 5'-guanylate produced by fermentation with *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067 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] Disodium 5'-guanylate was measured by high-performance liquid chromatography coupled with UV detection.

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 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 (**2018**),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 disodium 5'-guanylate (disodium-GMP) produced from 5'-guanylic acid (guanosine monophosphate, GMP) by fermentation with two non-genetically modified strains of *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067. The application is for the additive as disodium 5'-guanylate in its hydrated form. Disodium 5'-guanylate is a sodium salt that is the disodium salt of GMP.

The *C. stationis* KCCM 10530 production strain of disodium 5'-guanylate has been characterised using a whole genome approach and evaluated for susceptibility to antibiotics and production of toxic compounds with no concerns (detailed information in the EFSA opinion is redacted whilst confidentiality claims are determined).

[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 a feed additive consisting of disodium 5'-guanylate produced with *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067 for all animal species (CJ Europe GmbH). EFSA Journal 2021;19(6):6619, 15 pp. https://doi.org/10.2903/j.efsa.2021.6619

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

The *E.coli* K12 KFCC 11067 strain is a derivative of *E.coli* K12 which is well characterised in the literature (Gorbach, 1978), with its genome fully sequenced. No safety concerns are expected with the use of this production organism.

Additionally, viable strains of the production organisms were not detected in the final additive product.

3.2 Genetic modification step

Not applicable for this application. The production organisms are not genetically modified.

3.3 Specification

Information provided on the identity, composition and specifications of the production species does not raise safety concerns (the details on the characterisation of the production strains and information on the manufacturing process in the EFSA opinion is redacted whilst confidentiality claims are determined.)

Physiochemical properties and stability data (as shelf life of the products) were presented for the additive, which is highly purified. No data were provided to evaluate the additive's distribution (i.e. homogeneity) in feed. Stability data for the additive within three batches of final product, batches of exemplar feed rations (three batches for mash and three for pelleted forms) and three batches of feed pre-mix were provided. No losses were recorded over 36, 3 or 6 months for the stability studies for the additive product (as is), in feed ration or in feed pre-mix respectively.

Three batches of the additive were analysed for heavy metals (mercury, lead, cadmium and arsenic), dioxins, dioxin-like polychlorinated biphenyls (PCBs) and non-dioxin like PCBs, mycotoxins (aflatoxins, ochratoxin A, zearalenone and deoxynivalenol), bacterial endotoxin activity and microbiological contamination (*E.coli*, total *Enterobacteriaceae, Salmonella* spp, yeasts and moulds). No safety concerns were noted with results from the analyses.

This application included the request for use within all species with a maximum inclusion rate of 50 mg/kg of complete feed and/or water. However, when used in water the proposed concentration for poultry, porcine species and rabbits should be at least two times lower. Overall, if used in both feed and water simultaneously, the inclusion rates should not exceed the concentration that would result from intake with the inclusion in feed at 50 mg/kg.

3.4 Exposure assessment

Not required as GMP is a natural component of tissues of all plants and animals, is metabolised and excreted efficiently by the target species, and it is not expected that the composition of tissues and other products of animal origin will be affected by the use of disodium-GMP as a feed additive under the proposed conditions of use.

3.5 Toxicological data

This application is for the use of disodium 5'-guanylate produced by fermentation with *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067.

Disodium 5'-guanylate is currently authorised as a food additive (E 627) with a maximum use of 500 mg/kg and has been evaluated by the Scientific Committee for

Food (European Commission, 1991) and by the Joint WHO/FAO Expert Committee on Food (WHO, 1993).

The additive has particles of inhalable, and respirable sizes and therefore the worker may be exposed through inhalation. An acute inhalation toxicity test was performed in rats under GLP and following OECD TG 403. The inhalation lethal concentration LC_{50} was estimated to be > 4.28 mg/L air, therefore the additive was not given a classification for inhalation toxicity.

The skin irritancy potential of the additive was tested in a GLP study performed according to OECD TG 439. The additive was concluded to be non-irritant to skin. A skin sensitisation test was undertaken in a GLP study performed according to OECD TG 429 which found the additive to not be a skin sensitiser.

The potential eye irritancy of the additive was tested in a GLP study performed according to OECD TG 437. The results showed the additive to not be an eye irritant.

4. EFSA assessment and conclusions

The additive production strains are not genetically modified, show no acquired resistance to antimicrobials and are well characterised. No safety concerns are expected with the use of either strain and additionally there were no viable production strain cells detected in the final product.

Disodium 5'-guanylate produced by fermentation with *Corynebacterium stationis* KCCM 10530 and *Escherichia coli* K-12 KFCC 11067 raises no concerns for the consumer of the products obtained from animals fed the additive. It is also noted that the same chemical is authorised as an additive in food at concentrations up to 500 mg/kg.

Regarding safety for the worker, the additive is not a skin or eye irritant, not deemed a skin sensitiser or toxic by inhalation. The bacterial endotoxin activity (analysed in three batches) was below the limit of detection of 0.5 EU/g. When comparing the calculated potential inhalation exposure of endotoxins per day of 0.86 EU (using the limit of detection of the endotoxin analytical method) against the provisional inhaled endotoxin exposure limit of 900 EU, set by the UK Health and Safety Executive (HSE, 2013), there is no risk by inhalation due to endotoxins for workers.

No risks to the environment are expected since the use of disodium-GMP as a feed additive at the levels proposed is not expected to increase its concentration in the environment, and no further environmental risk assessment is required.
The use of the disodium 5'-guanylate additive does not raise safety concerns for the target animal at the proposed inclusion rate of 50 mg/kg. There are some concerns noted on the addition of the additive administered via drinking water due to hygiene implications.

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

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 disodium 5'-guanylate 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

[4] http https://joint-research-centre.ec.europa.eu/system/files/2020-10/finrep-fad-2019-0085-gmp.pdf

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Gorbach SL, 1978. Risk assessment of recombinant DNA experimentation with Escherichia coli K12. Proceedings from a workshop at Falomuth, Massachusetts. *Journal of Infectious Diseases*, 137, 613–714.

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