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Safety and efficacy of IMP (disodium 5′-inosinate) produced by fermentation with *Corynebacterium stationis* KCCM 80161 for all animal species

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Abstract

Following a request from the European Commission, the Panel on Additives and Products or substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of disodium 5′-inosinate (IMP) produced by fermentation using *Corynebacterium stationis* KCCM 80161 when used as a sensory additive (flavouring compound) in feed and water for drinking for all animal species. The production strain is not genetically modified. Viable cells of the production strain were not detected in the final additive. The additive does not give rise to any safety concern regarding the production strain. IMP produced using *C. stationis* KCCM 80161 is considered safe for the target species, for the consumer and for the environment. IMP produced using *C. stationis* KCCM 80161 is considered not toxic by inhalation, not irritant to skin or eyes and not a dermal sensitiser. The FEEDAP Panel expressed reservations on the use of the additive in water for drinking due to concerns on its impact on the hygienic conditions of the water. The Panel concluded that the additive is efficacious to contribute to the flavour of feed.

Keywords: Sensory, flavouring compounds, disodium 5′-inosinate, IMP, safety, efficacy

Requestor: European Commission

Question number: EFSA-Q-2019-00040

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7.

The European Commission received a request CJ Europe GmbH[2] for authorisation of the product disodium 5′-inosinate (IMP), when used as a feed additive for all animal species (category: sensory additives; functional group: flavouring compounds).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive). The particulars and documents in support of the application were considered valid by EFSA as of 1 March 2019.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product disodium 5′-inosinate (IMP), when used under the proposed conditions of use (see Section 3.1.5).

1.2. Additional information

The product under assessment is based on the disodium salt inosine 5′-monophosphate (also called disodium 5′-inosinate; disodium inosinate; IMP) produced by fermentation using a non-genetically modified strain of *Corynebacterium stationis* (KCCM 80161). It is not authorised as a feed additive in the European Union.

EFSA has issued an opinion on the safety and efficacy of disodium 5′-ribonucleotides, disodium 5′-guanylate, disodium 5′-inosinate for all animal species (EFSA FEEDAP Panel, 2014). Disodium 5′-inosinate produced by RNA hydrolysis is currently authorised as a sensory additive for use in all animal species in accordance with Regulation (EU) 2018/238.[3]

Disodium inosinate has been evaluated by the Scientific Committee for Food (SCF; European Commission, 1991) and by the Joint WHO/FAO Expert Committee on Food (JECFA; WHO, 1974, 1993) and is currently authorised as a food additive (E 631) ('additives other than colours and sweeteners', 'group I-with a maximum of 500 mg/kg', 'other additives that may be regulated combined').[4]

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[5] in support of the authorisation request for the use of IMP (disodium 5′-inosinate) produced by *C. stationis* KCCM 80161 as a feed additive.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the IMP (disodium 5′-inosinate) in animal feed. The Executive Summary of the EURL report can be found in Annex A.[6]

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] CJ Europe GmbH, Ober der Roeth 4, 65824 Schwalbach am Taunus, Germany.
[3] Commission Implementing Regulation (EU) 2018/238 of 15 February 2018 concerning the authorisation of disodium 5′-ribonucleotides, disodium 5′-guanylate and disodium 5′-inosinate as feed additives for all animal species. OJ L 53, 23.02.2018, p.1.
[4] Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives Text with EEA relevance OJ L 295, 12.11.2011, p. 1.
[5] FEED dossier reference: FAD-2018-0094.
[6] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/finrep-fad2018-0094-imp.pdf

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of IMP (disodium 5′-inosinate) produced by *C. stationis* KCCM 80161 is in line with the principles laid down in Regulation (EC) No 429/2008[7] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEEDAP Panel, 2017a), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

3. Assessment

This opinion assesses the safety and efficacy of IMP (disodium 5′-inosinate; IMP) produced by fermentation using *C. stationis* KCCM 80161 as a sensory additive (functional group: flavouring compounds) in feed and water for drinking for all animal species.

3.1. Characterisation

3.1.1. Characterisation of the production organism

According to the applicant, IMP is produced by a [redacted] strain of *Corynebacterium ammoniagenes* which is deposited at the Korean Culture Centre of Microorganisms (KCCM) with the accession number KCCM 80161.[8] The data provided to support the taxonomic identification of the production strain allocated the strain to the species *C. stationis*. The taxonomic identification of the production strain was done [redacted][9,10]

The production strain was obtained from *C. stationis* ATCC 6872 [redacted][11]

The production strain was tested [redacted] in the Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018a).[12] [redacted] by FEEDAP (EFSA FEEDAP Panel, 2018a). [redacted]

The WGS of the production strain was interrogated for the presence of antimicrobial resistance (AMR) genes [redacted]

[7] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.
[8] Technical dossier/Section II/ Annex/Confidential Annex/Annex_CONFID_II_2_01.
[9] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190814/03_IMP, Annex_SIN_CONFID_01 and Annex_SIN_CONFID_02.
[10] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190604/03_SIN_CJ_IMP.
[11] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190604/Annex_CONFID_SIN_01.
[12] Technical dossier/Supplementary information February 2020/Annex/Conf_Annex_SIN_01_CJ_IMP.
[13] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190814/03_IMP.

The WGS of the production strain was also interrogated for the presence of toxin and virulence factor genes [redacted]

3.1.2. Manufacturing process

IMP is produced by fermentation with *C. stationis* KCCM 80161.[15] [redacted]

[16]

3.1.3. Characterisation of the additive

Disodium 5′-inosinate (International Union of Pure and Applied Chemistry (IUPAC) name: disodium [(2*R*,3*S*,4*R*,5*R*)-3,4-dihydroxy-5-(6-oxo-3H-purin-9-yl)oxolan-2-yl]methyl phosphate (synonyms inosin-5′-monophosphatedisodium; sodium5-inosinate; inosine5′-monophosphatedisodium), a compound identified with the Chemical Abstracts Service (CAS) No 4691-65-0 and the European Inventory of Existing Commercial chemical Substances (EINECS) No 225-146-4 is the active substance of the additive and has a molecular weight of 527.12 g/mol (392.17 g/mol, anhydrous). The molecular formula is $C_{10}H_{11}N_4Na_2O_8P{\cdot}7.5H_2O$ and the molecular structure is given in Figure 1.

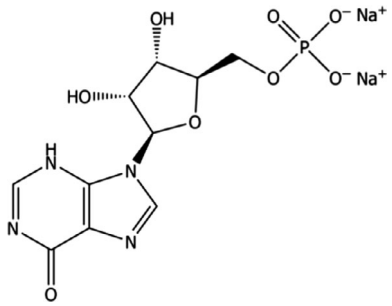

Figure 1: Molecular structure of IMP

The additive contains by specification ≥ 97% IMP (on a 'dry matter basis') and ≤ 28.5% water.[17] The analysis of five batches showed an average value of IMP 99.4% on 'dry matter basis' (range 98.6–99.9%) with an average water content of 25.7% (range 25.1–26.2%).[18]

In another analytical report,[19] the applicant analysed five additional batches for IMP (average 98.9% (range 98.7–99.0%) on dry matter basis); water (26.1%); nitrogen containing components (ammonium, nitrates, nitrites and betaine, not detected); free amino acids (not detected); nucleoside, nucleotide and base (inosine 0.01% in two batches and adenosine monophosphate (AMP) 0.04% (0.03–0.05%) 'as is' basis); organic acids (formic, acetic, citric, malic, succinic, lactic, not detected) and other elements (sodium 8.7% (8.7–8.8%) 'as is' basis, potassium 0.12% (0.10–0.14%) 'as is' basis, phosphate 0.02% (0.01–0.03%) 'as is' basis, magnesium, calcium, fluoride, bromide, chloride, sulfate, not detected). IMP produced by fermentation with *C. stationis* KCCM 80161 is a product with less than 1% unidentified material on dry matter basis.

Three batches of the additive were analysed for other chemical impurities. Heavy metals (lead, cadmium and mercury) and arsenic were below the limits of detection (LODs).[20] Aflatoxins (B1, B2,

[14] Technical dossier/Supplementary information February 2020/03_SIN_CJ_IMP.
[15] Technical dossier/Section II/Annex/Confidential Annex/Annex_CONFID_II_3_01.
[16] Technical dossier/Section II/ Annex/Confidential Annex/Annex_CONFID_II_3_27.
[17] Technical dossier/Section II/Annex/Annex_ II_1_01.
[18] Technical dossier/Section II/Annex/Annex II_1_02.
[19] Technical dossier/Section II/Annex/Annex_II_1_03. Clarification received by email on 3 April 2020: LODs were 0.01 mg/kg for nitrogen containing components and inorganic anions and cations; 0.5 mg/kg for free amino acids; 1 mg/kg for nucleoside, nucleotide and base and orgaic acids.
[20] Technical dossier/Section II/Annex/Annex II_1_04. LOD (in μg/kg) were 1 for arsenic, lead and cadmium, 5 for mercury.

G1, G2), ochratoxin A, zearalenone, deoxynivalenol, fumonisins B1 and B2 were below the corresponding LODs.[21] In the same batches, nitrofurans (furazolidone, furaltadone, nitrofurazone and nitrofurantoin) and nitrofuran metabolites (amino oxazolidinone, amino morpholino oxazolidinone, semi carbazide, amino hydantoin) were below the corresponding LODs.[22] A multiresidue pesticide analysis showed that none of the 358 pesticides analysed was detected in the three batches.[23]

In another analytical report[24] the applicant analysed three additional batches of the product for chemical and microbiological contamination: heavy metals (lead, cadmium and mercury), arsenic and chromium,[25] aflatoxins (B1, B2,G1, G2), ochratoxin A, deoxynivalenol and zearalenone[26] were below their corresponding limits of quantification (LOQs). Dioxins (polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/F)), dioxin-like polychlorinated biphenyls (DL-PCBs) and non-DL-PCBs were analysed. The following values were reported for dioxins: 0.07 ng WHO-PCDD/F-TEQ/kg; for the sum of dioxins and DL-PCBs: 0.14 ng WHO-PCDD/F-DL-PCB-TEQ/kg; and non-DL-PCBs: 0.6 μg/kg. *Salmonella* spp. was absent in 25 g, yeasts < 100 CFU/g, moulds ≤ 100 CFU/g, Enterobacteriaceae < 10 CFU/g and *Escherichia coli* < 10 CFU/g.

Three batches of the product were tested in triplicate for the presence of viable cells of the production strain [redacted]

To exclude the presence of DNA from the production strain in the final product, three batches were analysed in triplicate by PCR.[12] [redacted]

The additive is a white crystalline powder of colourless/white crystals with a solubility in water of 3.6 g/L and a bulk density between 500 and 800 kg/m^3 (average in five batches analysed: 580 kg/m^3).[28] The dusting potential of the additive measured in three batches following the Stauber–Heubach method gave results ranging from 6.4 to 6.7 g/m^3.[29] The particle size distribution was measured by sieving method, particles below 105 and 44 μm diameter were 45 and 17% (w/w), respectively.[30]

3.1.4. Stability

The shelf-life of the additive was determined by monitoring three batches stored at 25°C, 60% relative humidity (RH) for a period of 36 months, when stored in bags corresponding to the commercial packaging.[31] No losses were observed up to 36 months.

The stability of IMP (three batches) in a vitamin and mineral premixture for chickens for fattening (without choline chloride) was studied when added at 5% and stored at 25°C, 60% RH for 6 months (in closed bags). No losses were observed in the content of IMP in the premixture up to 6 months.[32]

The stability of IMP (three batches) was evaluated when added at 0.4% to a mash[33] and pelleted[34] feed for chickens for fattening (without choline chloride) after storage at 25°C, 60% RH for 3 months (in closed bags). Pelleting temperature was 72°C. In the mash feed, no losses of the active substance were observed in two batches while one batch showed a loss of 7.7% after 3 months. No losses were observed in the content of IMP in pelleted feed up to 3 months.

[21] Technical dossier/Section II/Annex/Annex II_1_04. LOD (in μg/kg) was 0.1 for aflatoxins (B1, B2, G1, G2) and ochratoxin A; 1.5 for zearalenone; 0.5 for deoxynivalenol and 5 for fumonisin B1 and B2.
[22] Technical dossier/Section II/Annex/Annex II_1_04. LOD (in μg/kg) was 0.09–0.15 for nitrofurans and 0.11–0.16 for nitrofuran metabolites.
[23] Technical dossier/Section II/Annex/Annex II_1_05. LOD (in μg/kg) was 0.5-8 depending on the pesticide considered.
[24] Technical dossier/Supplementary information February 2020/Annex/Annex_SIN_01_CJ_IMP.
[25] Technical dossier/Supplementary information February 2020/Annex/Annex_SIN_01_CJ_IMP. LOQ (in mg/kg) were 0.015 for lead, 0.01 for cadmium and mercury, 0.04 for arsenic and 0.2 for chromium.
[26] Technical dossier/Supplementary information February 2020/Annex/Annex_SIN_01_CJ_IMP. LOD (in μg/kg) were 0.2 for aflatoxins (B1, B2, G1, G2), 0.5 for ochratoxin A, 50 for deoxynvalenol and 10 for zearalenone.
[27] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190814/Annex_SIN_CONFID_03.
[28] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190604/Annex_SIN_02.
[29] Technical dossier/Section II/Annex/Annex_II_1_07.
[30] Technical dossier/Section II/Annex/Annex_II_1_06.
[31] Technical dossier/Section II/Annex/Annex_II_4_01.
[32] Technical dossier/Section II/Annex/Annex_II_4_04.
[33] Technical dossier/Section II/Annex/Annex_II_4_02.
[34] Technical dossier/Section II/Annex/Annex_II_4_03.

Analytical data on the stability in water of three batches of IMP have been provided. A total of 1.0 g of IMP was suspended in 1 L of drinking water at 30°C and stored at 25°C or 40°C. The content of IMP was measured in 10 subsamples after 0, 3, 6, 24 and 48 h. No losses were observed in IMP content after 48 h at 25 or 40°C.

3.1.5. Conditions of use

IMP is intended to be used in feedingstuffs/complementary feedingstuffs or water for drinking in all animal species as a flavouring compound. The applicant proposes a maximum use level of 50 mg IMP/kg feed. For its use in water, the applicant recommends 25 mg/L water for drinking for rabbits, poultry species and pigs. For the rest of the species, the applicant recommends that the use in water should not exceed the daily amount that would be consumed via feed.[35]

3.2. Safety

Safety concerns from the additive may derive either from the active substance or from the residues of the fermentation process/production strain remaining in the final product. The product under assessment is highly purified (less than 1% unidentified material is present in the additive). The production strain *C. stationis* KCCM 80161 was not genetically modified and was shown not to carry acquired antimicrobial resistance genes. Based on the WGS data provided, the production strain is not expected to produce any toxic compound during fermentation. In addition, no viable cells of the production strain were detected in the final product. It can be concluded that no safety concerns for target animals, consumers and the environment would arise from the use of *C. stationis* KCCM 80161 as the production strain.

IMP is widely distributed in all tissues of animals and plants. Its role in purine metabolism, as well as its breakdown to uric acid and to allantoin (in mammals except for primates), is well known. The recommended levels of use of IMP in feed would be in the range of the total nucleotides levels that may be present in feedstuffs like soybean meal and fish meal, which contain 38 and 75 mg of total nucleotides/kg, respectively (Mateo and Stein, 2004). Therefore, no concerns for the target animals would arise for the supplementation of the diets with IMP at 50 mg/kg feed. The applicant established conditions of use in water that would mirror the intakes resulting from the supplementation in feed; however, the FEEDAP Panel has reservations on the use of the additive via water due to hygienic reasons (EFSA FEEDAP Panel, 2010).

Regarding the safety for consumers, IMP is metabolised and excreted efficiently by the target animals. It is not expected that the composition of tissues and products of animal origin will be affected by the use of IMP as a feed additive. The FEEDAP Panel also notes that the same substance is authorised as an additive in food at levels up to 500 mg/kg.

IMP is naturally present in tissues of animals and plants. The use of IMP as a feed additive at the levels proposed is not expected to increase its concentration in the environment and therefore, it is of no safety concern for the environment.

Overall, the FEEDAP Panel concludes that IMP produced by *C. stationis* KCCM 80161 is safe under the proposed conditions of use for the target species, for the consumer and for the environment. However, the Panel has reservations on the use of the additive in water for drinking of the target animals due to concerns on its impact on the hygienic conditions of the water.

3.2.1. Safety for user

3.2.1.1. Effects on the respiratory system

The dusting potential of the additive measured in three batches following the Stauber–Heubach method was up to 6.7 g/m^3.[29] The additive contains particles of < 100 and < 50 μm diameter. The users can be exposed by inhalation.

A valid acute inhalation test in laboratory animals, performed according to the Organisation for Economic Co-operation and Development (OECD) guideline 403, showed an LC_{50} greater than 5.23 mg/L in male and female rats.[36,37]

[35] Calculated values would equate (in mg/day) to 100 for veal calf, 454 for cattle for fattening, 1,136 for dairy cow, 68 for sheep/goat, 454 for horses, 14.2 for dog and 3.4 for cats.
[36] Technical dossier/Section III/Annex/Annex_III_3_03.
[37] Technical dossier/Supplementary information August 2019/CJE_SIN_IMP_FAD-2018-0094_190604/Annex/Annex_ SIN_03.

3.2.1.2. Effects on skin and eyes

The skin irritation potential of the additive was tested in a study[38] performed according to OECD guideline 439. The results of the study indicate that the additive should not be considered as a skin irritant.

The eye irritation potential of the additive was tested in a valid study performed according to OECD guideline 437. The results of the study indicate that the additive should not be considered as an eye irritant.[39]

In a valid dermal sensitisation study following OECD guideline 429 (local lymph-node assay) and Method B42 skin sensitisation (local lymph node assay) of Commission Regulation (EC) No 440/2008, the additive did not show any skin sensitisation potential.[40]

3.2.1.3. Conclusions on safety for the user

IMP produced by *C. stationis* KCCM 80161 is considered not toxic by inhalation, not irritant to skin or eyes and not a dermal sensitiser.

3.3. Efficacy

IMP is mentioned in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2010), by the Flavour and Extract Manufactures Association (FEMA) as a flavour enhancer, i.e. a substance with no specific taste on its own but which has an ability to enhance existing flavours. Furthermore, IMP is authorised under Commission Regulation (EU) No 1129/2011 on food additives.

The Panel considers that the effect of IMP to increase the taste of food is well documented and therefore no further demonstration of efficacy when used in feed or water for drinking is necessary.

4. Conclusions

The additive is produced by a non-genetically modified strain of *C. stationis,* KCCM 80161, and no viable cells of the production strain were detected in the final additive. The additive does not give rise to any safety concern regarding the production strain.

IMP produced by *C. stationis* KCCM 80161 is considered to be safe for the target species, for the consumer, users and for the environment. However, the use of the additive in water for drinking raises concerns for the target species due to its likely impact on the hygienic conditions of the water.

The FEEDAP Panel concludes that the additive is efficacious to contribute to the flavour of feed and water for drinking.

5. Documentation as provided to EFSA/Chronology

Date	Event
21/12/2018	Dossier received by EFSA. IMP (disodium 5′-inosinate) produced by fermentation with *Corynebacterium ammoniagenes* KCCM 80161 for all animal species. Submitted by CJ Europe GmbH.
18/01/2019	Reception mandate from the European Commission
01/03/2019	Application validated by EFSA – Start of the scientific assessment
29/03/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation, target species safety, user safety*
01/06/2019	Comments received from Member States
21/06/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: methods of analysis*
23/09/2019	Reception of supplementary information from the applicant – Scientific assessment re-started
24/09/2019	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
27/11/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation*

[38] Technical dossier/Section III/Annex/Annex_III_3_05.
[39] Technical dossier/Section III/Annex/Annex_III_3_04.
[40] Technical dossier/Section III/Annex/Annex_III_3_06.

Date	Event
12/02/2020	Reception of supplementary information from the applicant – Scientific assessment re-started
07/05/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

Burdock GA, 2010. Fenaroli's handbook of flavor ingredients. 6th Edition. CRC press, Taylor & Francis Group. Boca Raton, FL, 143 pp.

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances Used in Animal Feed), 2010. Scientific Opinion on the use of feed additives authorised/applied for use in feed when supplied via water. EFSA Journal 2010;8(12):1956, 9 pp. https://doi.org/10.2903/j.efsa.2010.1956

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Abbreviations

AMP	adenosine monophosphate
AMR	antimicrobial resistance
CAS	Chemical Abstracts Service
CFU	colony forming unit
DL-PCB	dioxin-like polychlorinated biphenyl
EINECS	European Inventory of Existing Commercial chemical Substances
EURL	European Union Reference Laboratory
FAO	Food and Agriculture Organization of the United Nations
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
FEMA	Flavour and Extract Manufactures Association
HPLC-UV	high-performance liquid chromatography coupled to UV detection
IMP	disodium inosinate
IUPAC	International Union of Pure and Applied Chemistry
JECFA	Joint WHO/FAO Expert Committee on Food
KCCM	Korean Culture Centre of Microorganisms
LC_{50}	lethal concentration, medium
LOD	limit of detection
LOQ	limit of quantification
OECD	Organisation for Economic Co-operation and Development
PCDD/F	polychlorinated dibenzo-*p*-dioxins and dibenzofurans
RH	relative humidity
SCF	Scientific Committee for Food
WGS	whole genome sequence
WHO	World Health Organization

Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Disodium 5′-inosinate (IMP) produced by fermentation with *Corynebacterium ammoniagenes*[41] KCCM80161

In the current application authorisation is sought under Article 4(1) for *disodium 5′-inosinate (IMP)* produced by fermentation with *Corynebacterium ammoniagenes* KCCM80161 under the category/ functional group 2(b) 'Sensory additives' / 'flavouring compounds' according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of the *feed additive* for all animal species and categories.

The *feed additive* consists of a minimum of 97% of *disodium 5′-inosinate (IMP)* as an active substance, which is produced by fermentation with a strain of *Corynebacterium ammoniagenes KCCM80161*.

The *feed additive* is intended to be used directly into *feedingstuffs* or through *premixtures* and in *water* for drinking with proposed maximum levels of 25 mg *IMP/kg feedingstuffs*.

For the identification of *IMP* in the *feed additive*, the Applicant proposed the internationally recognised FAO JECFA monograph "disodium 5′-inosinate", which is comprised of various fit-for-purpose tests that are based on measuring solubility, absorbance signals in spectrophotometric measurements, presence of sodium, ribose and organic phosphate.

The EURL recommends for official control the above mentioned tests of the FAO JECFA monograph for the identification of *IMP* in the *feed additive*.

For the determination of *IMP* in raw materials, *flavouring premixtures* and *water* the Applicant submitted the method based on high performance liquid chromatography coupled to UV detection (HPLC-UV).

Based on the available performance characteristics, the EURL recommends the HPLC-UV method submitted by the Applicant for the determination of *disodium 5′-inosinate (IMP)* in the *feed additive*, *flavouring premixtures* and *water*.

As no protocol of the method or experimental data were provided by the Applicant for the determination of IMP in *feedingstuffs*, the EURL could not evaluate nor recommend the method for official control to determine IMP in *feedingstuffs*.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.

[41] During the assessment the strain was identified as *Corynebacterium stationis*.