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SCIENTIFIC OPINION

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Safety and efficacy of a feed additive consisting of narasin (Monteban® G100) for chickens for fattening (Elanco GmbH)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of the coccidiostat narasin (Monteban® G100) for chickens for fattening. In a previous opinion, uncertainties remained on the identification and characterisation of the non-genetically modified production strain of the active substance narasin. The Panel could not conclude either on the safety of Monteban® G100 for chickens for fattening or on the efficacy of the additive at the minimum applied concentration. The FEEDAP Panel excluded risks for environment but the risk for sediment compartment could not be assessed. The applicant provided supplementary information to cover the data gaps and substituted the narasin production strain from *Streptomyces* spp. NRRL 8092 to *Streptomyces* spp. NRRL B-67771. The information submitted to taxonomically identify the production strain did not allow to assign it to any described microbial species. Based on the information provided, the Panel concluded that the use of Monteban® G100 did not raise safety concerns as regards the production strain for the target animal, consumer, user and environment. The Panel concluded that 70 mg narasin/kg complete feed was safe for chickens for fattening with a margin of safety of 1.4; narasin from Monteban® G100 was unlikely to increase shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*. Narasin, when used in chickens for fattening at 70 mg/kg feed, was not expected to pose a risk to the aquatic compartment and to sediment, while a risk for the terrestrial compartment could not be excluded. No risk for groundwater was expected, nor for secondary poisoning via the terrestrial food chain, but the risk of secondary poisoning via the aquatic food chain could not be excluded. The Panel concluded that 60 mg narasin/kg feed was efficacious in controlling coccidiosis in chickens for fattening.

KEYWORDS

chickens for fattening, coccidiostats, efficacy, Monteban® G 100, narasin, safety

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1 | INTRODUCTION

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

Regulation (EC) No 1831/2003 establishes rules governing the Community authorisation of additives for animal nutrition and, in particular, Article 9 defines the terms of the authorisation by the Commission. The applicant, Elanco GmbH,[1] is seeking a Community authorisation of Monteban® G100 containing granular narasin, equivalent to 100 g narasin activity/kg as a feed additive to be used as a coccidiostat for chickens for fattening (Table 1).

TABLE 1 Description of the substance.

Category of additive	Coccidiostat and histomonostats
Functional group of additive	Coccidiostat and histomonostats
Description	Monteban® G100 containing granular narasin, equivalent to 100 g narasin activity
Target animal category	Chickens for fattening
Applicant	Elanco GmbH
Type of request	New opinion

On 3 October 2018, the Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety Authority ("Authority"), in its opinion on the safety and efficacy of the product, could not conclude on the safety of Monteban® G100 containing granular narasin, equivalent to 100 g narasin activity due to insufficient data on the safety and efficacy. After discussion with the Member States on the Standing Committee, it was suggested to check for the possibility to demonstrate safety and efficacy.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been received on 05 June 2020 and were already transmitted to the EFSA by the applicant.

In view of the above, the Commission asks the Authority to deliver a new opinion on Monteban® G100 containing granular narasin, equivalent to 100 g narasin activity/kg as a feed additive for chickens for fattening based on the additional data submitted by the applicant.

1.2 | Additional information

EFSA issued an opinion on the safety and efficacy of this product for chickens for fattening (EFSA FEEDAP Panel, 2018a).

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of additional information[2] to a previous application of the same product.[3] The dossier was received on 29/5/2020 and the general information and supporting documentation are available on Open.EFSA at https://open.efsa.europa.eu/questions/EFSA-Q-2020-00557.

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

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of narasin (Monteban® G100) is in line with the principles laid down in Regulation (EC) No 429/2008[4] and the relevant guidance documents: Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b), Guidance on the characterisation of microorganisms used as feed

[1]Elanco GmbH, Heinz-Lohmann-Str. 4, 27,472 Cuxhaven – Germany.

[2]FEED dossier reference: FAD-2020-0042.

[3]FEED dossier reference: FAD-2013-0041.

[4]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.

additives or as production organisms (EFSA FEEDAP Panel, 2018c) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

3 | ASSESSMENT

Monteban® G100, containing granular narasin, is a feed additive intended to be used in the prevention of coccidiosis in chickens for fattening at a concentration of 60–70 mg narasin/kg complete feed.

The FEEDAP Panel adopted its first opinion on the re-evaluation of this additive in 2018 (EFSA FEEDAP Panel, 2018a). In this opinion, the Panel concluded that the use of Monteban® G100 in chickens for fattening at the maximum concentration proposed, and without applying a withdrawal period, is safe for the consumer. A maximum residue limit (MRL) of 50 µg narasin/kg for all wet tissues ensure consumer safety. The Panel also concluded that Monteban® G100 is irritant to the eyes but not to the skin and is a skin sensitiser. Inhalation exposure would pose a risk to persons handling the additive. Moreover, narasin, when used as a feed additive for chickens for fattening at 70 mg/kg feed, was not expected to pose a risk to the environment and did not have a bioaccumulation potential. In this opinion, the risk for sediment compartment could not be assessed due to lack of data. The Panel was not in the position to unequivocally identify the production strain NRRL 8092 as *Streptomyces aureofaciens* and could not conclude on the absence of genetic determinants for antimicrobial resistance (AMR) in the strain of *Streptomyces* spp. under assessment. Based on the available tolerance studies, the safety of Monteban® G100 for chickens for fattening could not be established and no conclusion on the efficacy of the additive could be drawn at the minimum applied concentration of 60 mg narasin/kg complete feed for chickens for fattening.

In the current opinion, the FEEDAP Panel assessed the information submitted by the applicant to address the above-mentioned data-gaps.

3.1 | Characterisation

3.1.1 | Characterisation of the production microorganism

In its previous opinion of 2018, the FEEDAP Panel noted that uncertainties remained on the identification and characterisation of the production strain, including the presence of AMR genes. Moreover, no analytical data were provided on the presence of viable cells/spores of the production strain and on the presence of DNA of the production strain in the final additive. For the current assessment, the applicant submitted data to address the above-mentioned gaps.

In the former application, the applicant reported that narasin was produced by fermentation with a *Streptomyces aureofaciens* (synonym of *Kitasatospora aureofaciens*) strain deposited in the Agricultural Service Culture Collection (USA) under the deposition number NRRL 8092 (EFSA FEEDAP Panel, 2018a). Based on the newly submitted information, the current production process foresees the use of a new strain, deposited in the Agriculture Research Culture Collection (NRRL) with the accession number NRRL B-67771, [redacted].[5]

[redacted] The data suggest that the production strain NRRL B-67771 does not belong to *K. aureofaciens* but may belong to a new species of the *Streptomyces* genus [redacted].[6]

The production strain was tested according to the Clinical and Laboratory Standards Institute (CLSI) against the nine antibiotics recommended for '*Corynebacterium* and other Gram-positive' in the Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018c).[5] [redacted] Therefore, the strain is considered to be susceptible to all relevant antibiotics.

The WGS data of the production strain *Streptomyces* spp. NRRL B-67771 were interrogated for the presence of antimicrobial resistance (AMR) genes against [redacted]. No genes of concern were identified.

The WGS data of the production strain *Streptomyces* spp. NRRL B-67771 were interrogated for the presence of genes coding for toxins or virulence factors [redacted] no genes of concern were identified.

[5]Technical dossier/Annex II_11.0_Conf Tech Report on Charact of production strain.pdf.

[6]Technical dossier/Annex II.2_00_Conf Add info Charac strain.pdf.

[7]Technical dossier/Monteban_Elanco_Suppl_Data_4_Conf.pdf.

Regarding antimicrobial activity, the product was considered to be free of antimicrobial activity other than narasin, based on a study previously assessed (EFSA FEEDAP Panel, 2018a).

New data have been submitted to exclude the presence of viable cells in the additive. [redacted] No colonies were detected in the batches tested.[8]

The FEEDAP Panel notes that the toxicological profile of the active substance and the antimicrobial activity of the feed additive were evaluated in studies made with [redacted] NRRL 8092 [redacted] To establish the equivalence from a toxicological viewpoint, [redacted] the FEEDAP Panel considers the toxicological and antimicrobial studies made with narasin produced from [redacted] NRRL 8092 an adequate surrogate for the feed additive produced with the strain under assessment (NRRL B-67771).

3.1.2 | Characterisation of the additive

Monteban® G100 is specified to contain 95.0–107.5 g narasin activity/kg.[9] Narasin is produced by fermentation and not isolated/purified after the fermentation process. It is included in Monteban® G100 as 'narasin granulated' which contains 13% narasin activity, 28% mycelial solids, 6% dipotassium hydrogen phosphate and 53% montmorillonite clay. The final additive is produced by mixing 'narasin granulated' with 10–25 g mineral oil, 10–20 g vermiculite (expanded vermiculite magnesium-aluminosilicate mineral)[10] per kg additive with rice hulls (up to 100%).

The additive was characterised in the previous opinion of the FEEDAP Panel (EFSA FEEDAP Panel, 2018a). The applicant submitted additional information to assess the presence of small/nano particles described below.

3.1.3 | Physical properties of the additive

The applicant submitted particle size analysis data using scanning electron microscopy (SEM) method.[11] The product consists of different components and the applied methodology does not allow to differentiate the particles of each components. A descriptive SEM analysis was presented without complementary size estimation or measurement. Constituent particles were not measurable due to presence of agglomerates. These shortcomings identified in the submitted data performed with the additive Monteban® G100 did not allow the FEEDAP Panel to conclude on the absence of (a fraction of) small particles including nanoparticles in the additive. In absence of adequate data on the decision criteria for particle size, the FEEDAP Panel considered the following elements: (i) Pure narasin is very slightly soluble in water[12] (102 mg/L); the octanol/water partition coefficient (log K_{OW}) varies from 4.8 to 5.0 depending on the pH (EFSA FEEDAP Panel, 2018a); (ii) The test items used in the ADME, residue and toxicological studies, including tolerance studies, were representative of the active substance (EFSA FEEDAP Panel, 2018a). The results from these studies are in general sufficient to cover nanoscale considerations since the administration mimics the actual use in animals (also in terms of the studied doses).

Considering the above and in line with the appraisal route described in Section 4 of the Guidance on technical requirements (EFSA Scientific Committee, 2021), the Panel concludes that the safety of narasin from Monteban® G100 can be adequately covered by the conventional risk assessment and any risks from particles that are potentially in the small particle/nano range have already been covered by the existing data.

3.1.4 | Conditions of use

Monteban® G100 is intended to be used in the prevention of coccidiosis in chickens for fattening at a concentration of 60–70 mg narasin/kg complete feed.

[8]Technical dossier/Annex II_11.1_Conf Adamson, 2019.

[9]The concentration of narasin is expressed as narasin activity which includes the relative biopotency of the different narasin variants (EFSA FEEDAP Panel, 2018a, 2018b, 2018c).

[10]The FEEDAP Panel notes that vermiculite is not authorised anymore as a feed additive (withdrawn by: Commission Implementing Regulation (EU) 2023/1173 of 15 June 2023, OJ L 155, 16.6.2023, p. 28–32) and is neither an authorised feed material.

[11]Technical dossier/Supplementary information 2023/Annex II.1_13 and II.1_14.

[12]The value is below the threshold set in Section 2.3.1 of the Guidance on technical requirements (EFSA Scientific Committee, 2021).

3.2 | Safety

3.2.1 | Safety of the production strain

The active substance narasin is produced by a non-genetically modified strain of *Streptomyces* spp. (NRRL B-67771). The data submitted to taxonomically identify the strain do not allow to assign NRRL B-67771 to any described microbial species. The production strain *Streptomyces* spp. NRRL B-67771 was shown to be free of AMR genes and genes encoding for toxins or virulence factors. No viable cells of the production organism were detected in the active substance, representative of the final additive. Therefore, it can be concluded that the use of Monteban® G100 does not raise safety concerns as regards the production strain for the target animals, consumer, user and environment.

Based on the WGS analysis, the FEEDAP Panel considers the toxicological and antimicrobial studies made with narasin produced from NRRL 8092 an adequate surrogate for the strain under assessment (NRRL B-67771).

3.2.2 | Safety for the target species

In its former opinion on the re-evaluation of Monteban® G100 (EFSA FEEDAP Panel, 2018a), the FEEDAP Panel could not conclude on the safety of the highest proposed dietary concentration of narasin (70 mg/kg) for chickens for fattening and also derive a margin of safety, as none of the studies submitted showed full compliance with the requirements of Regulation (EC) No 429/2008. The applicant provided a new tolerance study in chickens for fattening.[13] In addition, three new studies were provided to demonstrate the effect of narasin supplementation in chickens for fattening on the shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*.[14]

Tolerance study

A total of 800 one-day-old male Ross 308 chickens were randomly allocated to four treatment groups which were fed diets unsupplemented or supplemented with Monteban® G100 to provide narasin at 70 mg/kg (1× maximum use level), 105 mg/kg (1.5×) and 140 mg/kg (2×) complete feed, respectively, for 35 days. The analysed levels of narasin corresponded to 1.4× and 1.8× of the maximum use level, respectively (Table 2). The study followed a randomised complete block design with eight blocks distributed among four rooms (i.e. two blocks per room). Blocks consisted of four pens with each treatment group represented by one pen. Group size was 200 birds per treatment (8 replicates with 25 birds each).

The birds received two basal diets, starter (1–14 days) and grower (15–35 days), which were mainly composed of wheat, soybean meal, soybean oil, and were supplemented with methionine, lysine and threonine. The starter diet (crumbs) and the pelleted grower diet contained 23.6% and 20.4% crude protein (CP) by analysis, respectively (metabolisable energy was calculated as 11.9 and 12.4 MJ/kg, respectively).

Bird health, mortality (including culling) and litter conditions were recorded daily. Birds were weighed by pen on Days 1, 14 and 35. Feed remaining in each pen was weighed and recorded on Days 14 and 35. Other zootechnical parameters (weight gain and average daily gain, feed intake and feed to gain ratio) were calculated. On Days 35, 36 and 37 blood samples were collected from a total of 5 preselected birds per pen and haematology[15] and routine clinical biochemistry[16] were assessed. The same birds were killed, necropsied, and organ and tissue samples collected[17] and weighed.[18] Since no treatment specific macroscopic alterations were seen in these organs, histopathological examinations were not performed.

Statistical evaluation was based on a generalised linear mixed model using the pen as the experimental unit, the treatment as the fixed effect, and the following random effects: room, block and the 'treatment group × room' interaction. Narasin treated groups were compared to the control treatment by linear contrasts through a Dunnett test when the statistical analysis indicated a significant overall treatment effect. All tests were two-sided and conducted at 5% significance level.

The main results are summarised in Table 2. Overall mortality was low (2.5% on average) and without differences between the groups.

Final body weight and average daily weight gain of chickens receiving Monteban® G100 at the maximum use level was significantly higher in comparison to the control. In contrast, birds receiving the additive at 2× had a significantly reduced final body weight and average daily gain in comparison to the control. No effects were seen in feed intake or feed to gain ratio.

[13]Technical dossier/Annex III_1_01.

[14]Technical dossier/Annexes 32, 33, 34.

[15]Red blood cells, haemoglobin, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, thrombocytes, white blood cells, heterophils, eosinophils, basophils, monocytes, lymphocytes and fibrinogen.

[16]Aspartate aminotransferase, alanine aminotransferase, amylase, creatine kinase, alkaline phosphatase, total protein, albumin, globulins, uric acid, cholesterol, glucose, phosphate, magnesium, calcium, total bilirubin, sodium, potassium chloride.

[17]Tissues observed and collected during necropsy: lung, liver, kidneys, heart, spleen, pancreas, adrenal gland, thymus, thyroid gland, testes, proventriculus, duodenum, je.junum, ileum, colon, caecum, cloaca (including Bursa of Fabricius), skeletal muscle (left M. quadriceps femoris).

[18]The following samples were weighed: liver, heart, and both kidneys.

TABLE 2 Effect of narasin on the performance and serum biochemistry parameters in chickens for fattening (35 days).

	Control	1×	1.5×	2×
Narasin (mg/kg complete feed)				
Intended	0	70	105	140
Analysed, starter	< LOD	61.6	93.2	119
Analysed, grower	< LOD	64.1	95.9	132
Mortality (%)	3	4	2	1
Performance parameters				
Final body weight (g)	2210	2335*	2209	2092*
Average daily gain (g/day)	62	65*	62	59*
Feed intake (g/day)	102	104	103	98
Feed to gain ratio	1.65	1.60	1.67	1.67
Serum biochemistry				
Uric acid (μmol/L)	421	415	415	462*
Amylase (U/L)	633	654	735	802*
Cholesterol (mmol/L)	3.30	3.52*	3.28	3.54*
Alkaline phosphatase (ALP) (U/L)	4851	3805	3537*	2897*

Abbreviation: LOD, limit of detection.

Note: LOD: 0.2 mg narasin/kg feed.

*Values with a superscript in the same row are significantly different ($p \leq 0.05$) from control values.

There were no statistically significant changes in the haematological parameters. Similarly, most blood biochemistry endpoints did not show significant differences. However, there were statistically significant overall treatment effects in four blood biochemistry variables: uric acid, amylase, cholesterol and alkaline phosphatase (ALP). When compared to the control group, uric acid and amylase were significantly higher in the 2× overdose group. The increases of uric acid were mild to moderate and were not associated with further renal pathological correlates. The increases in amylase, albeit minor, appeared dose related. However, the changes lack any clinical or pathological correlates. Cholesterol levels were significantly higher in the 1× and 2× groups, but not in the 1.5×, indicating a lack of a clear dose-related effect. ALP values seemed to decrease in a dose-dependent manner, differences to the control group reaching significance for the 1.5× and 2× overdose groups. The main origin of ALP is the hepatic epithelium and rapidly remodelling bone. The decreased ALP noted in the 2.0× overdose group could be due to the reduced body weight gain of this group. There were not gross pathology hepatic correlates. Owing to its dose dependency the findings in ALP should be considered with caution.

No relevant findings were found in gross pathology that could be related to the treatments.

The results of this study showed that narasin up to a 1.4× the maximum use level (analysed value 94.6 mg/kg) is tolerated by chickens for fattening, whereas the 1.8× overdose (analysed value 125.5 mg/kg) causes growth depression. Therefore, the FEEDAP Panel concludes that 70 mg narasin/kg complete feed is safe for chickens for fattening with a margin of safety of 1.4.

Microbial studies

Three studies, with similar experimental design, were provided to study the effect of narasin supplementation in chickens for fattening on the faecal shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*.[19] In each study, a total of 120 one-day-old male Ross 308 chickens were randomly allocated to three treatment groups which were fed diets supplemented with 0, 70 mg narasin/kg (1× maximum use level) and 140 mg narasin/kg (2×), respectively, for 35 days. Viable cells of the respective enteropathogen (10^5 CFU) were given by oral gavage to the animals of all groups at Day 14. The intended levels of narasin and the dose of pathogenic bacteria were analytically confirmed. Group size was 30 birds per treatment (6 replicates with 5 birds each).

Cloacal swabs were collected from each animal at Day 12 to confirm the counts of enteropathogens presenting pre-challenge, and again on Days 15, 19, 26 and 35 to evaluate faecal shedding. Enteropathogens counts were performed on appropriate selective media. The narasin supplementation did not affect the counts of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni* in the excreta samples at any time.

The FEEDAP Panel concludes that the use of narasin as a feed additive in chickens for fattening is unlikely to increase shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*.

[19]Technical dossier/Annexes 32, 33, 34.

Conclusions on safety for the target species

Based on the results of the new tolerance study in chickens for fattening, the FEEDAP Panel concludes that Monteban® G100 at the maximum use level of 70 mg narasin/kg complete feed is safe for chickens for fattening with a margin of safety of 1.4.

Based on recent shedding studies, the FEEDAP Panel concludes that the use of narasin as a feed additive in chickens for fattening is unlikely to increase shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*.

3.2.3 | Safety for the consumer

In its previous opinions (EFSA Panel, 2004; EFSA FEEDAP Panel, 2018a), the FEEDAP Panel assessed a series of toxicological studies (in vitro and in vivo genotoxicity, 90-day studies in rats, mice and dogs, a 1-year study in dogs, a carcinogenicity study in rats and mice, a three-generation study in rats, and developmental study in rabbits) with narasin produced by *Streptomyces* sp. NRRL 8092 (the strain from which the current production strain was obtained). The FEEDAP Panel concluded that the use of Monteban G100® in chickens for fattening at the maximum use level without applying a withdrawal period is safe for the consumer, and that the MRLs already in force (50 μg narasin/kg tissue) protect the consumers (EFSA FEEDAP Panel, 2018a).

Based on the equivalence from the toxicological viewpoint of the strains *Streptomyces* sp. NRRL 8092 and *Streptomyces* sp. NRRL B-67771, these conclusions are valid for the product obtained with the new production strain (see Section 3.2.1).

Consequently, the FEEDAP Panel concludes that Monteban® G100 is safe for the consumers of tissues obtained from chickens for fattening fed the additive under the proposed conditions of use without a withdrawal period. The existing MRLs for poultry tissues (50 μg narasin/kg) ensure consumer safety.

3.2.4 | Safety for the user

In its previous opinion, the FEEDAP Panel concluded that 'Monteban® G100 is irritant to the eyes but not to the skin. It has the potential to induce skin sensitisation. The acute systemic toxicity following dermal application is low. On the basis of the available information, inhalation exposure would pose a risk to persons handling the additive'.

No new information has been submitted in the current dossier regarding user safety. The Panel considers that the change in the production strain would not modify the previous conclusions.

3.2.5 | Safety for the environment

In its previous opinion, (EFSA FEEDAP Panel, 2018a) the FEEDAP Panel concluded that: 'Narasin, when used as a feed additive for chickens for fattening at 70 mg/kg feed, is not expected to pose a risk to the environment. The risk for sediment compartment could not be assessed. Narasin is not considered to have a bioaccumulation potential'. For the present assessment, the applicant addressed the data gap highlighted in the previous opinion and submitted an updated environmental risk assessment, including new studies, performed according to the FEEDAP guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

The environmental risk assessment of Monteban® as a feed additive for chickens for fattening is updated as follows.

3.2.5.1 | *Phase I*

Physico-chemical properties of narasin

The physico-chemical properties of narasin are summarised in Table 3.

TABLE 3 Physico-chemical properties of narasin.

Property	Value	Unit
Octanol/water partition coefficient (log K_{ow} 25°C)[a]	4.79 (pH 5) 4.85 (pH 7) 5.06 (pH 9)	
Water solubility[b]	102 (pH 7) 681 (pH 9)	mg/L
Vapour pressure[c]	–	Pa
Dissociation constant (pKa)[d]	7.9 (in 66% dimethylformamide)	–

[a]Technical dossier/Supplementary information January 2023/Annex III.4_05.
[b]Technical dossier/ Supplementary information January 2023/Annex III.4_04.
[c]Narasin is a high molecular weight solid and vapour pressure would be negligible.
[d]Technical dossier/Supplementary information January 2023/Annex III.4_06.

Fate and behaviour

For the current evaluation, the applicant submitted the same studies already evaluated by EFSA FEEDAP Panel (2018a). The FEEDAP Panel re-assessed available studies in the light of the principles set in the updated guidance to evaluate the safety of the additives for the environment (EFSA FEEDAP Panel, 2019); the outcome of the evaluation is reported below.

Fate in soil

Adsorption/desorption in soil

The adsorption and desorption behaviour of narasin was determined in five soils using five test concentrations following OECD 106.[20] The pH of the soils ranged from 5.2 to 7.7, and the soil organic carbon content ranged from 0.7% to 5.0%. Correlation coefficients indicated that the isotherms followed well the Freundlich equation. The adsorption or desorption coefficient corrected for soil organic carbon content (K_{oc}) values ranged from 873 to 2576, with a mean value of 1357 L/kg. The lowest K_{oc} value (873 L/kg) used in the 2018 evaluation is used in the present assessment for further calculations, as a worst case.

Biodegradation in soil

The aerobic degradation of [^{14}C]-narasin was evaluated in three soils (sandy loam, a silt loam and a clay loam).[21] For the present evaluation, the DT_{50} values were re-calculated according single first-order kinetics (SFO). The time to degradation of 50% of original concentration of the compound in the tested soils (DT_{50}) values for sandy loam, silt loam and clay loam were 28, 50, and 14 days, respectively. The time to degradation of 90% of original concentration of the compound in the tested soils (DT_{90}) values were 85, 167 and 45 days, respectively. Considering that just three values for DT_{50} are available, the worst case DT_{50} of 50 days is considered for further assessment. This value, adjusted to a temperature of 12°C using the Arrhenius equation,[22] corresponds to a DT_{50} value of 106 days.

Fate in manure

The aerobic mineralisation and transformation of narasin in chicken manure was evaluated in a study following OECD guideline 307.[23] The conclusion reached in 2018 that 50% of the narasin can be degraded in chicken manure is still considered valid and used as a refinement in risk assessment below.

Conclusion on fate and behaviour

The following values will be used for the assessment: K_{oc} of 873 L/kg and a DT_{50} of 106 days (at 12°C).

Predicted environmental concentrations (PECs)

Based on the proposed use of 70 mg narasin/kg feed for chickens for fattening the calculated PEC_{soil} (1058 µg/kg) and $PEC_{groundwater}$ (15 µg/L) exceeded the trigger values of 10 µg/kg and 0.1 µg/L, respectively, as indicated in the FEEDAP Guidance of the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019). Therefore, the environmental risk assessment of narasin requires a Phase II assessment.

3.2.5.2 | *Phase II*

Exposure assessment

PECs calculation refined in Phase II

In its previous opinions (EFSA FEEDAP Panel, 2018a), the FEEDAP Panel considered that the metabolism data on narasin indicated that only 5% of the administered dose was excreted as parent compound and 30% was excreted as metabolites having not more than 20% of the ionophoric activity (as a worst-case assumption). In addition, 50% of the 5% parent compound is degraded in manure rapidly, leaving only 2.5% parent compound and 2.5% degradation products. Considering the data on degradation of narasin in manure, a further refinement of the amount of environmentally relevant ionophoric activity resulted to be 9% of the administered dose $(2.5 + (30 + 2.5) \times 0.20)$.

[20]Technical dossier/Supplementary information January 2023/Annex III.4_03.

[21]Technical dossier/Supplementary information January 2023/Annex III.4_07.

[22]The temperature correction was performed according to the scientific opinion of the Panel on Plant Protection Products and their Residues on a request from EFSA related to the default Q10 value used to describe the temperature effect on transformation rates of pesticides in soil (EFSA, 2008).

[23]Technical dossier/Supplementary information January 2023/Annex III.4_08.

According to EFSA guidance (EFSA FEEDAP Panel, 2019), if a high persistence in soil is anticipated (DT_{50} > 60 days at 12°C), the potential for residues to accumulate in soil should be considered. This is the case for narasin, having a DT_{50} at 12°C of 106 days.

Considering the degradation of narasin in manure and assuming that the ionophoric activity of narasin and its metabolites in chicken excreta would not exceed in total 9% of the orally administered dose, the refined dose used for PEC calculations was 6.3 mg/kg feed. The PEC_{soil}, $PEC_{surface\ water}$ and $PEC_{sediment}$ are reported in Table 4.

TABLE 4 Predicted environmental concentrations of narasin in soil (μg/kg), groundwater (μg/L), surface water (μg/L) and sediment (μg/kg dry weight) refined for metabolism and degradation.

Input	Value
Dose (mg narasin/kg feed)	6.3
Molecular weight (narasin)	756
VP (Pa)	6E-24
Solubility (mg/L)	102
K_{oc} (L/kg)	873
DT_{50} at 12°C (days)	106
Output	
$PEC_{soil\ plateau}$ (μg/kg)	105
$PEC_{groundwater}$ (μg/L)	1.49
$PEC_{surfacewater}$ (μg/L)	0.50
$PEC_{sediment}$ (μg/kg)	45

Abbreviations: PEC, predicted environmental concentration; VP, vapour pressure.

Considering the highest DT_{50} value of 50 days at 20°C and the lowest K_{oc} value of 873 L/kg, the metamodel reported in the EFSA guidance (2019) identifies no risk for groundwater, even with these worst-case assumptions.[24] This conclusion is confirmed by the FOCUS modelling.[25]

Ecotoxicity studies

Toxicity to terrestrial compartment

Effects on plants

In a study performed in accordance with guideline OECD 208 and already evaluated by the FEEDAP Panel in 2018, the effects of soil incorporated narasin on the emergence and growth of three species of plants was determined.[26] Winter oats, radish and mung bean were exposed to 0, 0.375, 3.381 or 29.26 mg narasin/kg soil (nominal levels of 0, 0.35, 3.5 or 35 mg/kg). The results indicate that across all three species the lowest EC_{50} is 6.18 mg/kg (radish, growth) and the lowest no observed effect concentration (NOEC) is < 0.375 mg/kg (mung bean, emergence/growth).

An additional study was conducted to determine the effects of soil incorporated narasin on the emergence and growth of six species of higher plants (3 monocots and 3 dicots) in accordance with OECD 208.[27] Corn, pea, sunflower, tomato, wheat and ryegrass were exposed to nominal concentrations of 0, 0.1, 1.0, 10, 100 and 1000 mg narasin/kg soil. Dose verification from the stock solution was used to determine test item dosing concentrations. As the dose verification for the dosing solution was within ±20% tolerance the nominal dosing values were used for all analysis of results. Observations were made 14–21 days after 50% of the seedlings had emerged in the control group. Assessment of effects on percent seedling emergence and growth (fresh shoot weight and shoot height) were conducted in comparison with a control treatment.

A detrimental effect caused by narasin was seen across all species of plants at the 1000 mg/kg treatment group. Statistical analysis was performed for emergence (Dunnett's multiple comparison test), plant height and biomass (Dunnett's multiple comparison test followed by regression analysis). Significant effects on growth (height as well as the biomass) were recorded at the lowest narasin concentration tested (0.1 mg/kg) in case of three out of six test species: tomato, wheat and ryegrass.

Across all six species the lowest EC_{50} is 408 mg/kg (biomass for tomato) and the lowest NOEC is < 0.1 mg/kg (biomass for tomato, wheat and ryegrass).

Based on the results of the above two studies and considering all available data for all the species tested, the lowest EC_{50} is 6.18 mg/kg (radish, growth) while the lowest NOEC is < 0.1 mg/kg (biomass for tomato, wheat and ryegrass).

[24]Technical dossier/Section III/Annex_3.4_ERA_Appendix IV.

[25]Technical dossier/Supplementary information January 2023/Annex III.4.

[26]Technical dossier/Supplementary information January 2023/Annex III.4_13.

[27]Technical dossier/Supplementary information January 2023/Annex III.4_14.

In order to refine the predicted no effect concentration (PNEC) for terrestrial plants, a higher tier approach based on species sensitivity distribution (SSD) was applied.[28] To generate SSD, only five toxicity values, three from dicotyledonous plants (radish *Raphanus sativa*; sunflower *Helianthus annus* and pea *Pisum sativa*) and two from monocotyledonous plant species (winter oat *Avena sativa* and corn *Zea mays*) were used. The toxicity endpoint was based on plant growth (shoot weight) and the NOEC from each plant species (from the two studies evaluated above). The ETX 2.3 software program was used to generate the SSD, calculate the 5th percentile hazard concentration (HC_5) and assess normality.

The FEEDAP Panel noted that the SSD approach presented showed major limitations and the outcome of the exercise is not reliable for the refinement of the PNEC for terrestrial plants. In particular, the construction of SSD does not follow the EMA (2017) guideline in terms of data requirements and quality criteria for using SSD, particularly in respect the minimum number of plants (instead of required eight, SSD has been constructed using the endpoints for only five species); the goodness-of-fit was tested using the Anderson–Darling test showing a computed p-value from the Anderson–Darling test which was higher than 0.05, indicating that the data cannot be used for the SSD (EMA, 2017). Overall, the outcome of the exercise is not reliable for risk assessment due to low number of datapoints, non-normal data distribution and high uncertainty around HC_5 value.

In conclusion, the lowest EC_{50} of 6.18 mg/kg (radish, growth) and the lowest NOEC is < 0.1 mg/kg (biomass for tomato, wheat and ryegrass) will be used for PNEC derivation and risk characterisation (Table 5).

Effects on terrestrial invertebrates

The acute toxicity of nominal concentrations of 5, 40, 80, 160 and 320 mg/kg of narasin to the earthworm *Eisenia foetida* was assessed in a study conducted in accordance with OECD 207.[29] The study was already assessed in 2018 by the FEEDAP Panel (EFSA FEEDAP Panel, 2018a) and indicated that LC_{50} at 14 days was 46.4 mg/kg.

A chronic earthworm *Eisenia foetida* study conducted in line with guidelines OECD 222, already evaluated by the FEEDAP Panel in 2018, assessed the effects of nominal narasin levels of 3.1, 6.3, 13, 25 and 50 mg/kg narasin on reproduction.[30] The re-consideration of the study indicated that, no significant reduction of reproduction in 25 mg/kg treatment vs control was noted and that the 56-day $NOEC_{reproduction}$ is established as 25 mg/kg. Due to the high adult mortality in the highest tested concentration, the 50 mg/kg treatment was excluded from the analysis.

A collembolan reproduction and growth study was conducted with narasin according to OECD Guidance 232.[31] Ten juvenile *Folsomia candida* (9–12 days old) were exposed to eight narasin soil levels of 0, 17.1, 30.9, 55.6, 100, 180, 324, 583.2 and 1000 mg/kg soil. No mortality was observed at the 1000 mg/kg (the highest level tested). The reproduction rates were significantly different compared to the control at the three highest concentrations tested (Dunnett's t-test, $\alpha = 0.05$, one-sided smaller). The NOEC for reproduction of *F. candida* was determined to be 180 mg/kg.

Overall, the $NOEC_{reproduction}$ of 25 mg/kg from the chronic earthworm test will be used for the risk characterisation for the terrestrial compartment (Table 5).

Effects on soil microorganisms

The potential effects of narasin on the rate of microbial respiration and on the nitrification and nitrogen-mineralisation capacity of soil microflora under aerobic conditions were investigated in a study conducted according to OECD guidelines 216.[32] The study, already assessed in 2018 by the FEEDAP Panel (EFSA FEEDAP Panel, 2018a), show that exposure to nominal narasin, concentrations of 3.5 or 17.5 mg/kg (3.3 or 17.3 mg/kg exposure level) does not affect the microbial respiration, mineralisation of organic nitrogen or nitrification activity associated with the soil microflora.

Toxicity to aquatic organisms

Effects on algae

The toxicity of narasin on green algae (*Raphidocelis subcapitata*, formerly known as *Selenastrum capricornutum* and *Pseudokirchneriella subcapitata*) was investigated in a study conducted according to OECD guideline 201[33] The study, already assessed in 2018 by the FEEDAP Panel (EFSA FEEDAP Panel, 2018a), showed that the effect on growth rate resulted in the 72-h E_rC_{50} of 2.92 mg/L; this value is confirmed in the present evaluation and will be used for risk assessment (Table 6).

[28]Technical dossier/Supplementary information June 2023/Monteban Elanco Suppl Data 2.
[29]Technical dossier/Supplementary information January 2023/Annex III.4_15.
[30]Technical dossier/Supplementary information January 2023/Annex III.4_16.
[31]Technical dossier/Supplementary information January 2023/Annex III.4_17.
[32]Technical dossier/Supplementary information January 2023/Annex III.4_12.
[33]Technical dossier/Supplementary information January 2023/Annex III.4_18.

Effects on crustaceans

The toxicity of narasin to *Daphnia magna* was investigated in a 48-h static test.[34] The study, already assessed in 2018 by the FEEDAP Panel (EFSA FEEDAP Panel, 2018a), indicated a 48-h EC_{50} of 20.6 mg/L; this value is confirmed in the present evaluation and will be used for risk assessment (Table 6).

Effects on fish

The toxicity of narasin to fish was investigated in a 96-h static test.[35] The study, already assessed in 2018 by the FEEDAP Panel (EFSA FEEDAP Panel, 2018a), indicated a 96-h LC_{50} of 2.23 mg/L; this value is confirmed in the present evaluation and will be used for risk assessment (Table 6).

The toxicity of narasin to fish has been investigated in another 96-h static test.[36] Juvenile bluegill (*Lepomis macrochirus)* were exposed to narasin with measured narasin concentrations of 0.88, 1.66, 2.80, 4.68, 6.00, 6.74, 7.80, 8.70 and 9.55 mg/L. No physical signs of toxicity were observed in the control populations. Fish treated at concentrations between 3.0 and 10.0 mg/L exhibited exposure-related signs of toxicity ranging from hypoactivity to immobilisation. No mortalities or behavioural signs of toxicity were found at measured concentrations ≤1.66 mg/L. The 96 hr LC_{50} was 5.02 mg/L (Table 6).

Effects on sediment-dwelling invertebrates

For the current assessment the applicant submitted a new study performed according to OECD guideline 218.[37] The study performed in 2019 investigated the effects of narasin (purity: 97.6% w/w) on the survival and development of the sediment dwelling larvae of the midge *Chironomus riparius*. For this purpose, first instar larvae of *C. riparius* were exposed for 28 days in a sediment-water system to concentrations of 100, 50, 25, 12.5, 6.25 and 3.125 mg test item/kg dry weight (plus a control), corresponding to the following geometric mean measured concentrations: 87.1, 40.1, 20.1, 10.0, 4.68 and 2.51 mg test item/kg dry weight. The validity criteria of the study were met. The total number of adults emerged (emergence rate) and the time to emergence (development rate) were recorded. The test item concentrations were not stable during the run of the test. Therefore, all reported results refer to geometric mean measured concentrations, calculated from the recovery rates of the two examined treatment levels (100 and 6.25 mg test item/kg dry weight) and of the control. The 28-day NOEC, lowest observed effect concentration (LOEC), EC_{10} for the emergence rate were 4.68, 10.0, and 9.09 mg test item/kg dry weight (dw), respectively. The NOEC for the development rate was determined to be 10.0 mg test item/kg dw, with associated LOEC and EC_{10} values of 20.1 and 18.3 mg test item/kg dw. The EC_{50} for the emergence rate was calculated to be 16.1 mg test item/kg dw and determined to be > 87.1 mg test item/kg dw for development rate. NOEC for the emergence rate of 4.68 mg test item/kg dw was used in risk assessment.

Risk characterisation (PEC/PNEC ratio)

The risk characterisation ratios for terrestrial, freshwater and sediment compartments are reported in Tables 5, 6 and 7, respectively.

TABLE 5 Risk characterisation (PEC/PNEC ratio) for terrestrial compartment.

Taxa	PEC_{soil} (μg/kg)	$NOEC/EC_{50}$ (mg/kg)	AF	PNEC (μg/kg)	PEC/PNEC
Earthworm	105	25[a]	10	2500	0.042
Plants		< 0.1[b]	10	< 10	> 10.5
		6.18[c]	100	61.8	1.70

Abbreviation: AF, assessment factor.

[a]NOEC reproduction.

[b]NOEC biomass.

[c]EC_{50}.

[34]Technical dossier/Supplementary information January 2023/Annex III.4_19.

[35]Technical dossier/Supplementary information January 2023/Annex III.4_20.

[36]Technical dossier/Supplementary information January 2023/Annex III.4_21.

[37]Technical dossier/Supplementary information January 2023/Annex III.4_22.

TABLE 6 Risk characterisation (PEC/PNEC ratio) for freshwater compartment.

Taxa	$PEC_{surfacewater}$ (μg/L)	$ErC_{50}/EC_{50}/LC_{50}$ (mg/L)	AF	PNEC (μg/L)	PEC/PNEC
Algae *Raphidocelis subcapitata*		2.92[a]			
Aquatic invertebrates *Daphnia magna*	0.50	20.6[b]	1000	2.2	0.23
Fish *Oncorhynchus mykiss* *Lepomis macrochiru*		2.2[c] 5.02[c]			

Abbreviation: AF, assessment factor.
[a]72-h E_rC_{50}.
[b]48-h EC_{50}.
[c]96-h LC_{50}.

TABLE 7 Risk characterisation (PEC/PNEC ratio) for sediment.

Taxa	$PEC_{sediment}$ (μg/L)	NOEC (mg/kg dry weight)	AF	PNEC (μg/L)	PEC/PNEC
Chironomus riparius	45	4.68	100	46.8	0.96

Abbreviation: AF, assessment factor.

3.2.5.3 | *Bioaccumulation and risk for secondary poisoning*

Based on the log K_{ow} of 4.79–5.06, narasin has the potential to bioaccumulate and the risk of secondary poisoning has to be assessed for this substance. The applicant submitted an assessment of the risk for secondary poisoning.[38]

To assess the risk of secondary poisoning for worm/fish-eating birds and mammals via the food web chain the method proposed in the relevant Guidance from the European Medicines Agency (EMA) has been considered (EMA, 2016). A log K_{ow} of 4.85 at pH 7 was used for the assessment.

Since there were no bioaccumulation data available for fish or terrestrial organisms, the FEEDAP Panel assessed secondary poisoning of narasin for the aquatic and terrestrial food chains. Based on the lowest NOAEL for dogs of 0.5 mg/kg body weight (bw) per day, derived from a 1-year dog oral toxicity study, a NOEC value of 20 mg/kg feed was calculated using a conversion factor of 40 for dogs. By applying an assessment factor of 30, the corresponding $PNEC_{oral}$ was determined to be 0.67 mg/kg feed. The estimated concentration in fish, based on a PEC_{sw} of 0.50 μg/L is 2.65 mg/kg and the estimated concentration in earthworms, based on a PEC_{gw} < 0.5 μg/L and a PEC_{soil} of 105 μg/kg is 0.087 mg/kg. The risk of secondary poisoning cannot be excluded for fish-eating birds and mammals, while it can be excluded for worm-eating birds and mammals. The PEC/PNEC ratios for exposure through the aquatic and terrestrial food chains are given in Table 8.

TABLE 8 The risk assessment for secondary poisoning for narasin through the aquatic and terrestrial food chains based on the 100% of the proposed recommended dose.

	PEC_{fish}[a] (mg/kg)	PEC_{worm}[b] (mg/kg)	$PNEC_{oral}$ (mg/kg)	$PEC_{fish}/PNEC_{oral}$	$PEC_{worm}/PNEC_{oral}$
Narasin	2.65	0.087	0.67	3.97	0.13

[a]$PEC_{fish\ (oral,\ predator)}$.
[b]$PEC_{earthworm\ (oral,\ predator)}$.

Conclusions on environmental risk assessment

Narasin, when used as a feed additive for chickens for fattening at 70 mg/kg feed, is not expected to pose a risk to the aquatic compartment and to sediment, while a risk for the terrestrial compartment cannot be excluded. No risk for groundwater is expected.

While there is no risk of secondary poisoning through the terrestrial food chain for narasin, the risk of secondary poisoning through the aquatic food chain cannot be excluded.

3.3 | Efficacy

In its former opinion (EFSA FEEDAP Panel, 2018a), the FEEDAP Panel concluded that the efficacy of Monteban® G100 was demonstrated in three floor pen studies and in two anticoccidial sensitivity tests (ASTs). Since three ASTs showing positive effects of the treatment with the coccidiostat under application are required, the FEEDAP Panel was not in the position to conclude on the efficacy of Monteban® G100 for chickens for fattening under EU farming conditions.

[38]Technical dossier/Supplementary information January 2023/Annex III.4_26 Risk Assessment Secondary Poisoning.

In the present submission, the applicant provided a new AST.[39] Three treatment groups were included in the experimental design: an uninfected untreated control (UUC), an infected untreated control (IUC) and an infected Monteban®-treated (IT); each group with 13 replicates of 5 birds.

The feed for the IT group was supplemented with narasin from Monteban® G100 at an intended concentration of 60 mg/kg feed (57 mg/kg analysed value). One-day-old chickens (Ross 308, male) were randomly allocated to the groups after an acclimatisation period of 12 days; the experimental diets were fed for 10 days. Two days after allocation, all birds of the IUC and IT treatment groups were orally inoculated with 169,500 sporulated oocysts/bird (1.5 mL of inoculum) from a recent field isolate (2019). The field strains originated from Norway and were composed by: *E. acervulina:* 107,000 oocysts/mL, *E. maxima:* 4000 oocysts/mL *and E. tenella:* 2000 oocysts/mL. The virulence of the inoculum was confirmed in a dose titration study. Birds of the UUC group were inoculated with a sham inoculum. Feed intake was measured throughout the study and body weight was measured at the beginning and the end of the study, feed to gain ratio was calculated. Animal health and mortality were monitored daily. The day before inoculation, excreta samples were examined to ensure animals were not shedding relevant amounts of oocysts. Oocyst excretion was analysed at Days 6 and 7 post-inoculation (PI). Intestinal lesions were scored following the method of Johnson and Reid (1970) (0 = no lesion, 1 = very mild, 2 = mild, 3 = moderate and 4 = severe) at Days 6 and 7 PI. The data were analysed using ANOVA linear models considering the treatment as the fixed effect, and the cage was the statistical unit. Group means were compared to the IUC group as reference (independent comparisons). The oocyst counts data were log-transformed prior to analysis. Statistical significance was assessed at $p \leq 0.05$.

During the entire study period, no post-challenge coccidiosis-related mortality was observed. Overall mortality was low (2 animals in the IT group).

The results of the parameters measured are summarised in Table 9. Intestinal lesion scores (ILS) in the middle intestinal region due to *Eimeria* spp. were significantly reduced in the IT group compared to IUC. Total oocyst count in excreta was also significantly lower in the IT group compared to IUC. Secondary parameters (body weight and daily weight gain) were also significantly improved in the IT birds when compared to IUC birds.

TABLE 9 Main results of the anticoccidial sensitivity test.[a]

Group	Lesion scores			Total oocysts per gram	Feed intake (g/day)	Final body weight (g)	Weight gain (g/day)	Feed to gain ratio
	Upper intestine	Middle intestine	Lower intestine					
UUC	0.39	0.47	0.07	3	95	916	63	1.50
IUC	2.70	1.43	0.03	1,664,123	89	850	55	1.62
IT	2.47	1.04*	0.09	560,916*	93	894*	60*	1.54

Abbreviations: IUC, infected untreated control; IT, infected treated group; UUC, uninfected untreated control.

*IT mean significantly differs from IUC mean ($p \leq 0.05$).

[a]Lesion scores and oocysts per gram: cumulative results for Days 6 and 7 post-inoculation. Zootechnical data: cumulative results for the time when the experimental diet was fed (10 days).

Conclusions on efficacy

Considering the results of three floor pen trials and two ASTs described and assessed in a previous EFSA opinion and taking into account the results of the newly submitted AST, the FEEDAP Panel concludes that narasin from Monteban® G100 is efficacious in controlling coccidiosis in chickens for fattening at a minimum concentration of 60 mg/kg feed.

3.4 | Post-market monitoring

Field monitoring of *Eimeria* spp. resistance to narasin should be undertaken, preferably during the latter part of the period of authorisation.

4 | CONCLUSIONS

The active substance narasin is produced by a non-genetically modified strain of *Streptomyces* spp. (NRRL B-67771). The data submitted to taxonomically identify the strain do not allow to assign NRRL B-67771 to any described microbial species. The production strain *Streptomyces* spp. NRRL B-67771 was shown to be free of genes of concern. No viable cells of the production organism were detected in the active substance, representative of the final additive. Therefore, the use of Monteban® G100 does not raise safety concerns as regards the production strain.

The FEEDAP Panel concludes that Monteban® G100 at the maximum use level of 70 mg narasin/kg complete feed is safe for chickens for fattening with a margin of safety of 1.4. The use of narasin as a feed additive in chickens for fattening is unlikely to increase shedding of *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Campylobacter jejuni*.

[39]Technical dossier/Annex IV_01, Annex IV_02, Annex IV_03.

The FEEDAP Panel concludes that the use of Monteban® G100 in chickens for fattening at the maximum concentration proposed, and without applying a withdrawal period, is safe for the consumer. MRLs of 50 µg narasin/kg of all wet tissues ensure consumer safety.

Monteban® G100 is irritant to the eyes but not to the skin. It has the potential to induce skin sensitisation. The acute systemic toxicity following dermal application is low. Inhalation exposure would pose a risk to persons handling the additive.

Narasin, when used as a feed additive for chickens for fattening at 70 mg/kg feed, is not expected to pose a risk to the aquatic compartment and to sediment. However, a risk for the terrestrial compartment cannot be excluded. No risk for groundwater is expected. There is no risk of secondary poisoning through the terrestrial food chain for narasin. However, the risk of secondary poisoning through the aquatic food chain cannot be excluded.

The FEEDAP Panel concludes that narasin from Monteban® G100 is efficacious in controlling coccidiosis in chickens for fattening at a minimum concentration of 60 mg/kg feed.

ABBREVIATIONS

AF	assessment factor
ALP	alkaline phosphatase
AMR	antimicrobial resistance
AST	anticoccidial sensitivity test
bw	body weight
CFU	colony forming unit
CLSI	Clinical and Laboratory Standards Institute
CP	crude protein
DT_{50}	time to degradation of 50% of original concentration of the compound in the tested soils
DT_{90}	time to degradation of 90% of original concentration of the compound in the tested soils
dw	dry weight
EC_{10}	the concentration of a test substance which results in 10% of the test organisms being adversely affected, i.e. both mortality and sublethal effects
EC_{50}	the concentration of a test substance which results in 50% of the test organisms being adversely affected, i.e. both mortality and sublethal effect
EMA	European Medicines Agency
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
FOCUS	FOrum for the Co-ordination of pesticide fate models and their USe
HC	hazard concentration
IFS	intestinal lesion score
KOC	adsorption or desorption coefficient corrected for soil organic carbon content
LC_{50}	lethal concentration, median
LOD	limit of detection
LOEC	lowest observed effect concentration
Log K_{ow}	logarithm of octanol–water partition coefficient
MIC	minimum inhibitory concentration
MRL	maximum residue limit
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentrations
PNEC	predicted no effect concentration
SEM	scanning electron microscopy
SFO	single first-order kinetics
SSD	species sensitivity distribution
VP	vapour pressure
WGS	whole genome sequence

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CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

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