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SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of chromium chelate of DL-methionine (Availa® Cr) for salmonids (Zinpro Animal Nutrition Europe, Inc.)

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The declarations of interest of all scientific experts active in EFSA's work are available at https://open.efsa.europa.eu/experts

Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of a feed additive consisting of chromium chelate of DL-methionine (Availa® Cr) for salmonids. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the additive is safe for salmonids at the maximum recommended of 600 mg additive/kg complete feed (corresponding to 0.6 mg Cr/kg complete feed). The use of the additive in animal feed is considered safe for the consumers and the environment. The additive is not an eye nor skin irritant. Due to the presence of nickel, the additive is considered a skin and respiratory sensitiser. Inhalation and dermal exposure are considered a risk. The FEEDAP Panel concludes that the additive may have the potential to be efficacious in improving the performance of salmonids at 200 mg additive/kg complete feed (0.2 mg Cr/kg complete feed).

KEYWORDS

chromium, efficacy, fish, safety, salmonids, zootechnical additives

CONTENTS

1 | INTRODUCTION

1.1 | Background and Terms of Reference

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 from Zinpro Animal Nutrition (Europe), Inc.[2] for the authorisation of the additive consisting of chromium chelate of DL-methionine (Availa® Cr), when used as a feed additive for salmonids (category: zootechnical additives; functional group: other zootechnical additives).

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 dossier was received on 30 June 2023, and the general information and supporting documentation are available at https://open.efsa.europa.eu/questions/EFSA-Q-2023-00453. The particulars and documents in support of the application were considered valid by EFSA as of 12 September 2023.

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 feed additive consisting of chromium chelate of DL-methionine (Availa® Cr), when used under the proposed conditions of use (see Section 3.1.2).

1.2 | Additional information

Chromium chelate of DL-methionine (Availa® Cr) is not currently authorised as a feed additive in the EU.

The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) adopted three opinions on the safety and/or efficacy of this product (EFSA, 2009; EFSA FEEDAP Panel, 2020, 2023b).

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[3] in support of the authorisation request for the use of chromium chelate of DL-methionine (Availa® Cr) as a feed additive.

The confidential version of the technical dossier was subject to a target consultation of the interested Member States from 12 September 2023 to 12 December 2023, for which the received comments were considered for the assessment.

According to Article 32c(2) of Regulation (EC) No 178/2002 and to the Decision of EFSA's Executive Director laying down the practical arrangements on pre-submission phase and public consultations, EFSA carried out a public consultation on the non-confidential version of the technical dossier from 13 March to 03 April 2024 for which no comments were received.

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, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

The European Union Reference Laboratory (EURL) considers that the conclusions and recommendations reached in the previous assessment regarding the methods used for the control of the active substance in animal feed are valid and applicable for the current application.[4]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and efficacy of chromium chelate of DL-methionine (Availa® Cr) is in line with the principles laid down in Regulation (EC) No 429/2008[5] and the relevant guidance documents: Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017a), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017b), Guidance on the assessment

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

[2]Zinpro Animal Nutrition (Europe), Inc. Akkerdistel 2E Boxmeer – Netherlands.

[3]Dossier reference: FEED-2023-16773.

[4]Evaluation report available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en.

[5]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.

of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019), Guidance on the assessment of the safety of feed additives for the users (EFSA FEEDAP Panel, 2023a).

3 | ASSESSMENT

Chromium chelate of DL-methionine (Availa® Cr) is intended to be used as a zootechnical additive (functional group: other zootechnical additives) in feed for salmonids to improve their growth performance. Unless otherwise indicated, chromium in the opinion refers to chromium(III).

3.1 | Characterisation

3.1.1 | Characterisation of the additive

The active substance chromium chelate of DL-methionine and the additive were characterised in previous assessments (EFSA, 2009; EFSA FEEDAP Panel, 2020). According to the applicant, the manufacturing process of chromium chelate of DL-methionine has not been changed since the previous evaluation (EFSA FEEDAP Panel, 2020). In the evaluation report on the analytical methods proposed for official control purposes linked to that opinion, the EURL could not recommend any method for the quantification of the added chromium content in feedingstuffs. To allow the EURL to complete the evaluation, the applicant made available information in the presence of a microtracer in the final additive (Availa®Cr) (see Appendix A). In the context of the current application, no new information was provided the physico-chemical characteristics of the additive, its stability and homogeneity. Considering that the manufacturing process has not been changed, the data previously assessed are considered to apply for the current assessment. New data have been submitted for batch-to-batch variation and impurities that are described below.

The additive contains chromium chelate of DL-methionine at 2%, vegetable oil at 1%, calcium carbonate at 96% and [redacted] Zinpro® F-Yellow #5 Lake at [redacted].

The additive is specified to contain a minimum of 1000 mg Cr/kg of additive.

Analytical data to confirm the specifications were provided for five batches of the additive, showing the average values for chromium of 1084 mg/kg additive (1052–1146 mg Cr/kg). The same batches were analysed for the content of methionine, which was on average 1.41% (1.35%–1.48%).[6]

Three batches of the additive were analysed for impurities and showed the following average values: lead, 0.53 mg/kg (0.51–0.55 mg/kg); cadmium, 0.11 mg/kg (< 0.1–0.11 mg/kg); arsenic, 1.21 mg/kg (1.14–1.29 mg/kg); mercury, 0.016 mg/kg (< 0.01–0.03 mg/kg); nickel, 1.25 mg/kg (1.25–1.33 mg/kg); and fluoride, 8.68 mg/kg (4.1–12.03 mg/kg).[7]

Dioxins and dioxin-like PCBs' concentrations/levels were 0.15 ng/kg and 0.05 ng/kg, respectively; non-dioxin-like PCBs ranged from 0.01 to 0.02 µg/kg additive.

Dioxins and the sum of dioxins plus dioxin-like PCB concentrations/levels were 0.15 ng WHO-PCDD/F-TEQ/kg and 0.05 ng WHO-PCDD/F-PCB-TEQ/kg; non-dioxin-like PCBs ranged from 0.01 to 0.02 µg/kg additive.[8]

The same batches were also analysed to detect mycotoxins including aflatoxin B1 and ochratoxin A that showed values below the LOQ.[9]

Also, microbiological contamination was analysed in the same batches, resulting in concentrations of *Escherichia coli* < 10 CFU/g, *Salmonella* spp. (no detection in 25 g) and *Enterobacteriaceae* < 10 CFU/g.

The FEEDAP Panel considers that the microbial contamination and the amounts of the detected impurities do not raise safety concerns (except for nickel, see Section 3.2.3).

The additive is a solid preparation. The water solubility was determined according to OECD Testing Guideline (TG) 105 (flask method) and was 183 g/L.[10]

The characterisation of the microtracer is found in Appendix A.

3.1.2 | Conditions of use

The additive is intended for use in feed for salmonids at a proposed minimum content of 200 mg additive/kg complete feed (corresponding to 0.2 mg Cr/kg complete feed) and a maximum content of 600 mg additive/kg complete feed (corresponding to 0.6 mg Cr/kg complete feed).

[6]Annex II.2.7 Availa Cr 1000 Batch-to-batch_conf.pdf.

[7]Annex II.2.7 Availa Cr 1000 Batch-to-batch_conf.pdf.

[8]Annex II.2.7 Availa Cr 1000 Batch-to-batch_conf.pdf.

[9]LOQ: < 5 µg/kg.

[10]II.2.6. OECD 105 Solublity Chromium-DL-methionine_conf.

3.2 | Safety

The safety of the additive Availa® Cr is assessed below, and a detailed assessment of the [redacted] Zinpro® F-Yellow #5 Lake is summarised in Appendix A.

3.2.1 | Safety for the target species

The applicant provided one combined tolerance –efficacy study conducted with the additive under assessment in rainbow trout (*Oncorhynchus mykiss*) to support the safety for the target animals.

A total of 960 fish with an initial body weight of 16.3 ± 0.6 g were distributed in 24 tanks (350 L, 11.2 ± 1.1°C, 40 fish/tank), which were randomly allocated into six experimental groups (four replicates per group).[11] A pelleted extruded feed (fishmeal 10%, animal by-products and vegetable protein sources) was either not supplemented (control) or supplemented with Availa® Cr at 200 (minimum use level), 400 (0.67× maximum use level), 600 (1×), 4000 (6.7×) or 6000 (10×) mg/kg complete feed to add 0.2, 0.4, 0.6, 4 or 6 mg Cr/kg complete feed (confirmed by analysis).[12] The experimental feeds were offered to visual satiety for 90 days.

Fish health was monitored daily. Feed intake and tank body weight were measured at days 30, 59 and 90. The specific growth rate, feed-to-gain ratio, relative daily feed intake and protein efficiency ratio were calculated. At the end of the trial, a macroscopic evaluation of potential abnormalities was performed, and blood samples from three fish per tank were taken for haematology[13] and biochemistry[14] analysis (12 fish per group). In addition, three fish per tank were used to measure liver weight, viscera weight and fillet weight to allow the calculation of hepatosomatic index, viscerosomatic index, carcass yield and fillet yield.

Data were analysed statistically with a one-way analysis of variance (ANOVA), and group means were compared with a Student–Newman–Keuls test, if appropriate, using the tank as the experimental unit. Body weight and specific growth rate were also treated by regression analysis in relation to either dietary chromium levels or chromium intake. Statistical significance was set at 0.05.

No mortality was observed during the trial. While the final body weight, specific growth rate, feed-to-gain ratio and protein efficiency ratio were improved up to 4000 mg Availa® Cr/kg complete feed, the dietary supplementation with the additive at 6000 (10×) mg/kg complete feed resulted in a significantly lower final body weight (209.9 vs. 221.3 g) and specific growth rate (2.84 vs. 2.90%), and a worse feed-to-gain ratio (0.80 vs. 0.79) and protein efficiency ratio (3.07 vs. 3.14), when compared with the control group. Haematological, blood biochemistry, somatic indexes, carcass and fillet yields were not significantly affected by any of the dietary treatments. The gross pathology evaluation of the fish sampled showed an overall low incidence of abnormalities (11 out of 192 analysed fish) not related to the dietary supplementation with the additive.

Overall, no adverse effects were observed in the performance of fish when fed with Availa® Cr supplemented up to 4000 mg/kg complete feed (6.7× maximum proposed use level).

3.2.1.1 | *Conclusions on safety for the target species*

Considering the results of the tolerance study in rainbow trout in which the additive was tolerated at 6.7× the maximum proposed use level, the FEEDAP Panel concludes that the use of Availa® Cr in feed for salmonids up to 600 mg/kg complete feed is safe.

3.2.2 | Safety for the consumer

3.2.2.1 | *Absorption, distribution, metabolism, excretion and residues (ADMER)*

No specific data on absorption, distribution, metabolism and excretion (ADME) of the additive under assessment in the target species were submitted in the current application. In the previous assessments, limited information was provided on ADME in humans, rodents and dairy cows (EFSA FEEDAP Panel, 2020).

No residue studies conducted in accordance with the requirements of the FEEDAP Panel Guidance were submitted by the applicant (EFSA FEEDAP Panel, 2017a). However, some data on the deposition of chromium in fish fed with the additive under assessment were provided.

Fish muscle samples were collected from one efficacy trial (Trial 2, see Section 3.3). The study was conducted in rainbow trout and included four dietary treatments with 0, 0.2, 0.4, and 0.8 mg Cr/kg complete feed, given to the animals for 90 days.

[11] III.1.1 Efficacy and tolerance Availa Cr rainbow trout.

[12] Total Cr: 3.12, 3.34, 3.57, 3.73, 7.04 and 9.30 mg Cr/kg complete feed, respectively.

[13] Haematocrit, haemoglobin, red and white blood cells counts, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration.

[14] Total protein, albumin, urea, creatinine, glucose, triglycerides, total bilirubin, total cholesterol, amylase, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, gamma-glutamyl transferase, creatine kinase, alkaline phosphatase, sodium, potassium, chloride, calcium, inorganic phosphate and magnesium.

The study is fully described in Section 3.3. Chromium concentration in fish muscle was only analysed in the control group and in the group supplemented with the highest concentration of the additive (800 mg additive/kg complete feed corresponding to 0.8 mg Cr/kg complete feed). The latter is a higher concentration compared to the maximum proposed use level (0.6 mg Cr/kg complete feed). The analysis of the samples indicated that there is no statistical difference ($p > 0.05$) in the deposition of Cr in the muscle of rainbow trout, between the control group and the highest dose administered (73 vs. 70 µg Cr/kg tissue, in the control and treated group, respectively).[15] However, the FEEDAP Panel noted some limitations in the analysis performed which cast doubts on the reliability of the results: Only four fish per group were analysed, and the Cr background level in the control diet amounted to fivefold the intended supplementation level.

A second set of deposition data was provided by the applicant.[16] Muscle samples (12 fish per group) collected from the control group and the group with 0.8 mg Cr/kg complete feed of the efficacy study mentioned above were analysed for Cr content. The data showed that the highest dose of the additive did not increase Cr content of trout flesh compared to the control (80 vs. 72 µg Cr/kg tissue, in the treated and control group, respectively). However, the FEEDAP Panel noted that the Cr background level was still high in the control group (5-fold the intended supplementation level) and considered that this would limit the use of these data in the assessment of the consumer exposure.

Even in the absence of kinetic data in fish, the deposition results described above are in line with those obtained in other species (dairy cows and cattle for fattening) (EFSA FEEDAP Panel, 2009, 2020).

3.2.2.2 | *Toxicological studies*

The FEEDAP Panel already assessed the toxicological profile of the additive in the previous assessments (EFSA, 2009; EFSA FEEDAP Panel, 2020). The Panel concluded that, based on the toxicological dataset provided, although the additive showed a genotoxic activity in vitro, this is not expressed in vivo after systemic exposure. Although no data on genotoxicity at the site of contact were available, the Panel noted that Cr(III) is not carcinogenic and concluded that the additive is unlikely to pose a carcinogenic risk at levels occurring in the diet. The Panel also identified the no observed adverse effects levels (NOAELs) of 630 and 715 mg/kg body weight (bw) per day for males and females, respectively, corresponding to 34 and 39 mg Cr (III)/kg bw per day, based on a subchronic oral toxicity study in rats. No new data were provided by the applicant. The FEEDAP Panel reiterates the previous conclusions.

3.2.2.3 | *Consumer exposure*

For the assessment of consumer exposure to chromium from the use of the additive, the FEEDAP Panel considered the following: (i) the deposition data submitted presented some limitations but would support the lack of deposition of supplemental Cr in fish flesh; (ii) the results obtained (Section 3.2.2.1) would represent the worst-case scenario considering that the animals were exposed to the additive at a concentration higher than the proposed conditions of use.

Based on the above, the FEEDAP Panel concludes that the use of the additive in feed for salmonids up to the maximum proposed use level of 0.6 mg Cr/kg complete feed would not significantly increase consumer exposure to chromium.

3.2.2.4 | *Conclusions on safety for the consumer*

The FEEDAP Panel considers that the use of the additive in salmonids at the maximum proposed use level of 600 mg additive/kg complete feed (corresponding to 0.6 mg Cr/kg complete feed) is safe for the consumer.

3.2.3 | Safety for the user

In the previous assessment, the FEEDAP Panel concluded that the additive poses a risk to users by inhalation and that it is not an irritant for skin and eyes but should be considered a skin sensitiser (EFSA FEEDAP Panel, 2020).

In the current assessment, no additional studies were provided; however, updated analytical data on the content of nickel in the additive were submitted.

The highest dusting potential measured was 5.57 g/m^3 (EFSA FEEDAP Panel, 2020). Therefore, the FEEDAP Panel considers that exposure through inhalation is likely.

The FEEDAP Panel notes that the additive contains nickel (1.25–1.33 mg/kg). The European Directive 2022/431[17] set an occupational exposure limit (OEL) of 0.01 and 0.05 mg/m^3 for both respirable and inhalable fractions, respectively, as nickel meets the criteria for classification as carcinogenic (category 1A). Therefore, to reduce the risk, the FEEDAP Panel considers that the exposure of the users should be minimised.

Due to the presence of nickel, the additive should be considered a respiratory and dermal sensitiser.

[15] III.2.6 CoA Eurofins 2023_conf.pdf; III.2.7 Statistical Output 2024.pdf.

[16] III.2.8 CoAs Zinpro_conf.pdf.

[17] DIRECTIVE (EU) 2022/431 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 9 March 2022 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work. OJ L 88/2, 16.3.2022, 14 pp.

3.2.3.1 | *Conclusions on safety for the user*

The additive is not an eye or skin irritant. The additive is considered a skin and respiratory sensitiser. Inhalation and dermal exposure are considered a risk.

3.2.4 | Safety for the environment

Considering a maximum use level of 0.6 mg Cr/kg complete feed, the calculated predicted environmental concentration (PEC) in marine sediment is 1323 μg/kg sediment dry weight. From a data set of the European Marine Observation and Data Network (EMODnet), involving 313 samples of European marine sediment, the background concentration for Cr corresponds to 131,000 μg/kg sediment dry weight.[18] Since 10% of the background concentration (13,100 μg/kg sediment dry weight) is well above the calculated PEC for marine sediment, no risk is expected for this compartment from the use of the additive in marine aquaculture when supplemented according to the conditions of use.

Considering a maximum use level of 0.6 mg Cr/kg complete feed, the PEC in surface water for land-based aquaculture (raceway, ponds, tanks) is 0.001 μg/L. This value is well below 10% of the background concentration (0.14 μg/L) of Cr in water reported in the FOREGS database (2005). Furthermore, this value is also well below the trigger value of Phase I for aquaculture in land-based systems. Consequently, no risk is expected for surface water from the use of the additive in land-based aquaculture when supplemented according to the conditions of use.

3.3 | Efficacy

The applicant provided three trials (two in rainbow trout and one in Atlantic salmon) to demonstrate the efficacy of the additive. One of the two studies in trout (trial 1) was a combined tolerance –efficacy study and is described above in Section 3.2.1.

In the second study with rainbow trout, a total of 480 fish with an initial body weight of about 33 g were distributed to 16 tanks of 30 fish each (145 L; 15°C), which were randomly distributed into four groups (four replicates per group).[19] A pelleted extruded feed (fishmeal 13%, animal by-products and vegetable protein sources) was either not supplemented (control) or supplemented with Availa® Cr at 200 (minimum proposed use level), 400 or 800 mg/kg complete feed to provide 0.2, 0.4 and 0.8 mg Cr/kg complete feed (confirmed by analysis; see Table 1). The experimental feeds were offered to visual satiety for 84 days.

The third trial was performed with 400 Atlantic salmon (*Salmo salar*) with an initial body weight of 57.1 ± 3.2 g, distributed in 16 tanks of 25 fish each (1000 L; 14.6 ± 0.4°C), which were randomly allocated into four groups (four replicates per group).[20] A pelleted extruded feed (fishmeal 20%, krill meal and vegetable protein sources) was either not supplemented (control) or supplemented with the additive at 200 (minimum proposed use level), 400 or 600 mg/kg complete feed to provide 0.2, 0.4 and 0.6 mg Cr/kg complete feed (confirmed by analysis; see Table 1). Four tanks (replicates) of 25 fish/tank were assigned to each treatment group. Feed was offered to visual satiety for 95 days.

For both trials, fish health was monitored daily. Feed intake was measured daily. Tank body weight was measured on days 28 and 56 (trial 2), and days 31, 61 and 95 (trial 3). Specific growth rate, feed to gain ratio, relative daily feed intake and protein efficiency ratio were calculated.

At the beginning and at the end of Trial 2, fish were sampled for whole-body composition to allow determining the chromium retention. At the end of each trial, a macroscopic evaluation of potential abnormalities was performed. In addition, three fish per replicate tank were used to measure liver weight, viscera weight and fillet weight to allow the calculation of hepatosomatic index, viscerosomatic index, carcass yield and fillet yield.

Data were analysed statistically with a one-way ANOVA, and group means were compared with Tukey (trial 2) or Student–Newman–Keuls test (trial 3), using the tank as the experimental unit. In trial 2, a regression analysis was applied to the body weight and specific growth rate data in relation to the dietary chromium levels and chromium intake. Statistical significance was set at 0.05.

The results are shown in Table 1. Final body weight and specific growth rate were significantly improved with the supplementation with Availa® Cr up to 400 (trial 3), 800 (trial 2) and 4000 (trial 1) mg/kg complete feed when compared to the control. Feed to gain ratio was also significantly improved up to 400 (trial 3) and 4000 (trial 1) mg Availa® Cr/kg complete feed, while no significant differences were observed for trial 2. No differences were observed for the calculated somatic indexes and the whole-body composition.

[18] Annex III.4.2 Chromium marine sediments.

[19] IV.2. Efficacy of chromium DL-methionine in Rainbow Trout.

[20] IV.1 Efficacy of Availa Cr in Atlantic salmon.

TABLE 1 Effects of the additive on the performance of salmonids.

Trial (species)	Supplemented Cr (III) from Availa® Cr (mg/kg complete feed)	Analysed Cr[1] (mg/kg complete feed)	Feed intake[2]	Final body weight (g)	Specific growth rate (% body weight/day)	Feed to gain ratio	Mortality (%)
1 (Trout)	0	3.12	1.52^{a}	221.3^{c}	2.90^{c}	0.79^{a}	0
	0.2	3.34	1.43^{b}	230.5^{a}	2.95^{a}	0.74^{b}	0
	0.4	3.57	1.44^{b}	229.0^{ab}	2.94^{ab}	0.75^{b}	0
	0.6	3.73	1.43^{b}	233.1^{a}	2.96^{a}	0.74^{b}	0
	4	7.04	1.45^{b}	225.5^{b}	2.92^{b}	0.75^{b}	0
	6	9.30	1.53^{a}	209.9^{d}	2.84^{d}	0.80^{a}	0
2 (Trout)	0	3.03	275^{b}	393^{b}	2.94^{b}	0.77	0
	0.2	3.17	280^{ab}	408^{ab}	2.99^{a}	0.75	0.8
	0.4	3.60	283^{a}	414^{a}	3.01^{a}	0.75	1.7
	0.8	3.78	284^{a}	412^{a}	3.00^{a}	0.75	0
3 (Salmon)	0	1.98	1.16^{a}	242.5^{b}	1.52^{b}	0.90^{b}	2
	0.2	2.23	1.13^{a}	253.6^{a}	1.57^{a}	0.84^{c}	2
	0.4	2.39	1.14^{a}	253.5^{a}	1.57^{a}	0.86^{c}	2
	0.6	2.59	1.22^{b}	239.6^{b}	1.51^{b}	0.95^{a}	0

[a,b,c]Mean values within a trial and within a column with a different superscript are significantly different, $p < 0.05$.

[1]Total Cr: Cr from Availa® Cr plus background Cr.

[2]Trials 1 and 3: % body weight/day; trial 2: g/fish.

The FEEDAP Panel notes that the proposed chromium supplementation from Availa® Cr is ≤ 10% of the background content of the complete feeds used in these studies.

The applicant provided 10 studies from publications retrieved from a literature search.[21] However, none of these studies could be considered as evidence of the efficacy of Availa® Cr for salmonids, as all of them showed limitations in the experimental design (different target species, short duration of the studies and/or the test item used was not representative of the one under assessment).

The Panel notes that the inclusion of the additive at the highest proposed use level in the feed for salmon (Trial 3) showed a worse feed to gain ratio compared to the control. This effect was not seen when similar levels were added to the feed for trout. Based on the results of the tolerance trial in trout, in which higher levels of Cr were tested and a more comprehensive set of analyses was performed, the Panel did not consider this adverse effect on the productivity as a safety issue for salmonids.

3.3.1 | Conclusions on efficacy

The FEEDAP Panel concludes that the additive may have the potential to be efficacious in improving the performance of salmonids at 200 mg additive/kg complete feed (0.2 mg Cr/kg complete feed).

3.4 | Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[22] and good manufacturing practice.

4 | CONCLUSIONS

The additive Availa® Cr is safe for salmonids at the maximum proposed use level of 600 mg additive/kg complete feed (corresponding to 0.6 mg supplemented Cr/kg complete feed).

The use of the feed additive in animal nutrition under the conditions of use proposed is of no concern for consumer safety and the environment.

The additive is not an eye or skin irritant but is considered a skin and respiratory sensitiser. Inhalation and dermal exposure are considered a risk.

[21]IV Efficacy.

[22]Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

The additive may have the potential to be efficacious in improving the performance of salmonids at the minimum content of 200 mg additive/kg complete feed (corresponding to 0.2 mg supplemented Cr/kg complete feed).

ABBREVIATIONS

ADME	absorption, distribution, metabolism and excretion
ANOVA	analysis of variance
BW	body weight
CAS	Chemical Abstracts Service
DM	dry matter
EMODnet	European Marine Observation and Data Network
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
IUPAC	International Union of Pure and Applied Chemistry
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LOD	limit of detection
LOQ	limit of quantification
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development

REQUESTOR

European Commission

QUESTION NUMBER

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APPENDIX A

Assessment of the [redacted] Zinpro F-Yellow #5 Lake

The additive Availa® Cr contains [redacted] of the [redacted] Zinpro® F-Yellow #5 Lake. The microtracer is characterised and its safety assessed below.

A.1 | CHARACTERISATION OF THE MICROTRACER

The [redacted] Zinpro® F-Yellow #5 Lake consists of a minimum of [redacted] iron grit, coated with FD&C Lake Food Coloring (tartrazine) ([redacted]) and shellac[23] ([redacted]).[24]

The applicant provided an analysis of five batches of the [redacted] Zinpro F-Yellow #5 Lake to demonstrate compliance with the proposed specifications, which showed the following average results: shellac [redacted] ([redacted]); FD&C Lake Food Coloring [redacted] ([redacted]).[25]

Particle size was measured by sieve analysis on the same five batches of the microtracer. On average, 96.4% (range: 95.09%–97.9%) of the particles were below 420 μm, 2.8% (range: 1.94%–3.72%) of the particles were below 149 μm, 0.5% (range: 0.07%–0.86%) of the particles were below 125 μm, 0.19% (range: 0.05%–0.3%) of the particles were below 105 μm and 0.05% (range: 0.03%–0.08%) of the particles were below 74 μm.[26]

The highest proposed use level of Availa® Cr, 600 mg additive/kg complete feed, corresponds to [redacted] mg microtracer/kg complete feed. Considering the respective specifications, the levels of tartrazine would be [redacted] μg/kg complete feed and those of shellac [redacted] μg/kg complete feed.

A.2 | SAFETY OF THE MICROTRACER

The available information regarding the safety of the microtracer and its components is presented below.

The analytical data submitted by the applicant concerning the particle size of the microtracer measured by sieving showed that up to 0.08% of the particles was smaller than 74 μm. The FEEDAP Panel notes that the highest size limit for intestinal absorption is 10 μm for Peyer's patches (paracellular mechanism) (O'Hagan, 1996). Due to the size of the particles, the microtracer is not expected to be absorbed in the gut of the target species; therefore, systemic exposure is not expected.

A.2.1 | Tartrazine lake

Tartrazine (2a102) is currently authorised for cats and dogs, grain-eating ornamental birds, small rodents and ornamental fish. Tartrazine has been previously evaluated by JECFA in 1966 and the SCF in 1975 and 1984. Both committees established an ADI of 0–7.5 mg/kg bw. In 2009, the ANS Panel re-evaluated tartrazine (E 102) and its aluminium lakes as food additives and confirmed the ADI of 7.5 mg/kg bw (EFSA ANS Panel, 2009). In 2016, JECFA withdrew the ADI of 0–7.5 mg/kg bw and replaced it with an ADI of 0–10 mg/kg bw on the basis of a NOAEL of 984 mg/kg bw per day (reduction in body weight in a chronic rat study) (JECFA, 2016).

A.2.2 | Shellac

Shellac is currently authorised as a food additive, but not as a feed additive. JECFA evaluated shellac and, based on in vitro microbial assays, concluded that shellac (food grade regular bleached) is not mutagenic (JECFA, 1992).

In a 90-day study, female rats fed diets containing food-grade shellac (2%) showed caecal enlargement and swelling in the proximal region of the colon. There were no histopathological changes associated with the consumption of shellac; however, the JECFA Committee noted a failure of both experimental and control animals to grow during the latter part of the study. Another 90-day study (including an in utero exposure phase) produced no evidence of treatment-related toxic or pathological effects in rats (F0 or F1) fed diets containing up to 1% shellac (regular bleached; equal to 660 mg/kg bw per day for female rats) (JECFA, 1992).

The EFSA FAF Panel has recently re-evaluated the safety of the different types of shellac (E 904) for use as a food additive and derived an ADI of 4 mg/kg bw per day for wax-free shellac (E 904) produced by physical decolouring, based on a NOAEL of 400 mg/kg bw per day and applying an uncertainty factor of 100 (EFSA FAF Panel, 2024). For wax-free shellac (E 904) produced by chemical bleaching, the ADI of 4 mg/kg bw per day was considered temporary. This ADI is not applicable for wax-containing shellac as a food additive.

[23] ADR1 2024-02-22/ RFI October 2023.
[24] ADR1 2024-02-22/Annex 7.
[25] Tracer CoA_conf (4).pdf.
[26] Tracer CoA_conf.pdf.

A.2.3 | Safety for the target species

Due to the size of the particles, the microtracer is not expected to be absorbed in the gut of the target species; therefore, systemic exposure is not expected. In addition, the applicant provided a tolerance trial conducted in fish exposed to the additive (containing the microtracer at [redacted])[27] which did not highlight any adverse effects of the additive concentration up to 6.7× the maximum recommended level.

A.2.4 | Safety for the consumer

The microtracer is not expected to be absorbed in the gut of the target species; therefore, no exposure of the consumer is expected. The colouring used in the microtracer coating is authorised as food additives in the EU (Tartrazine (E102)) and shellac is authorised as a glazing agent in food (E904). Considering the above and the low inclusion level of these components, the use of the microtracer in the composition of the additive is considered safe for the consumer.

A.2.5 | Safety for the users

No specific data were submitted by the applicant on the safety for the user of the microtracer when added to the additive. The conclusions reached for the additive are taken to include also the microtracer.

A.2.6 | Safety for the environment

The applicant provided an environmental risk assessment of a microtracer containing [redacted] iron grit, [redacted] tartrazine lake and [redacted] shellac coating agent.[28]

Considering that the microtracer is [redacted] of the additive and that the additive will be used in feed for salmonids at a maximum content of 600 mg additive/kg complete feed, the following values are expected in feed: [redacted] mg iron grit/kg feed, [redacted] mg tartrazine lake/kg feed and [redacted] mg shellac/kg feed.

The above concentrations do not raise safety concerns for the environment when the additive is used in land-based aquaculture.

As regards marine sediment, the PEC of tartrazine is below the trigger value of 10 µg/kg sediment dry weight, while the PEC sediment for shellac is above the trigger value. The Panel reviewed the scientific literature provided by the applicant[29] and noted that shellac shows no toxicity and is a polymer of natural origin that has been shown to be (bio)degradable. Therefore, no risk is expected from the use of the microtracer in the additive in marine aquaculture when used according to the conditions of use.

Based on the above, the Panel concludes that no concerns for the environment are expected for the use of the microtracer under assessment.

A.3 | CONCLUSIONS ON THE SAFETY OF THE MICROTRACER

Based on the information available, the FEEDAP Panel concludes that the use of the [redacted] Zinpro® F-Yellow #5 Lake in the additive Availa® Cr at [redacted] is safe for the target species, the consumer and the environment. The use of the microtracer does not add any concerns to those already highlighted for the additive with regard to user safety.

[27]Composition statement_conf.pdf.

[28]III.4 Updated safety for the environment.

[29]III.4 Updated safety for environment_conf.pdf.