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SCIENTIFIC OPINION

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Efficacy of Availa®Cr (chromium chelate of DL-methionine) as a feed additive for dairy cows (Zinpro Animal Nutrition (Europe), Inc)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the efficacy of Availa®Cr (active compound: chromium chelate of DL-methionine) as a feed additive for dairy cows. In a previous opinion, the FEEDAP Panel concluded that Availa®Cr at a maximum recommended use level of 0.5 mg Cr(III) (8 mg Cr from Availa®Cr/cow per day) was safe for dairy cows and the consumers. Additionally, the FEEDAP Panel considered that the additives posed a risk to the user by inhalation, it was not irritant to skin and eyes, and it should be considered a skin sensitiser. The Panel could not conclude on the efficacy of the additive at the proposed conditions of use. Since the new information provided in the current application is lacking sufficient evidence, the FEEDAP Panel is still not in the position to conclude on the efficacy of chromium DL-methionine from Availa®Cr.

KEYWORDS

Availa®Cr, chromium chelate of DL-methionine, efficacy, zootechnical additives, other 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 and, in particular, Article 9 defines the terms of the authorisation by the Commission.

The applicant, Zinpro Animal Nutrition (Europe),[2] Inc, is seeking a Community authorisation of chromium chelate of DL-methionine as a feed additive to be used as other zootechnical additives for dairy cows for milk production (Table 1).

TABLE 1 Description of the additive.

Category of additive	Zootechnical additives
Functional group of additive	Other zootechnical additives
Description	Chromium chelate of DL-methionine
Target animal category	Dairy cows for milk production
Applicant	Zinpro Animal Nutrition (Europe), Inc
Type of request	New Opinion

On 30 January 2020, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) of the European Food Safety Authority (EFSA), in its opinion on the safety and efficacy of the product, could not conclude on the efficacy and analytical method in compound feed.

The Commission gave the possibility to the applicant to submit supplementary information and data in order to complete the assessment and to allow a revision of the EFSA's opinion. The new data have been received on the 13 February 2023 and the applicant has been requested to transmit to EFSA as well.[3]

In view of the above, the Commission asks EFSA to deliver a new opinion on chromium chelate of DL-methionine as a feed additive for dairy cows for milk production based on the additional data submitted by the applicant, in accordance with Article 29(1) of Regulation (EC) No 178/2002.

1.2 | Additional information

The additive, Availa®Cr (chromium chelate of DL-methionine), is intended for use as a zootechnical feed additive (functional group: other zootechnical additives) in dairy cows for milk production. This feed additive is not authorised in the European Union (EU).

In the past years, the FEEDAP Panel delivered two scientific opinions on the safety and efficacy of this product when used in feed for dairy cows (EFSA, 2009; EFSA FEEDAP Panel, 2020).

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of supplementary information[4] to a previous application on the same product.[5] The dossier was received on 22 February 2023 and the general information and supporting documentation available on Open.EFSA at https://open.efsa.europa.eu/questions/EFSA-Q-2023-00089.

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' (elicitation) knowledge, to deliver the present output.

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of chromium chelate of DL-methionine as a feed additive (Availa®Cr) is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

[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. 5831 PJ. Boxmeer. The Netherlands.
[3]No information on the analytical method for the test article has been made available.
[4]Dossier reference: EFSA-Q-2023-00089.
[5]Dossier reference: FAD-2018-0021.
[6]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.

3 | ASSESSMENT

The feed additive containing chromium chelate of DL-methionine (brand name: Availa® Cr) is intended to be used as a zootechnical feed additive (functional group: other zootechnical additives) for dairy cows to increase milk yield. Unless otherwise indicated, chromium in the opinion refers to chromium (III). It is specified to contain at least 1000 mg Cr/kg additive.

The additive was fully characterised in the previous opinion of the FEEDAP Panel (EFSA FEEDAP Panel, 2020). The additive is intended to be used in feed for dairy cows at a minimum supplementation rate of 0.3 mg Cr/kg complete feed, up to a maximum of 0.5 mg Cr/kg complete feed (with 88% DM), corresponding to 300 and 500 mg Availa®Cr/kg complete feed, respectively.[7] The additive is expected to be predominantly incorporated in complementary feed for dairy cows. Therefore, the applicant recommends a daily dose of 8 mg Cr from Availa®Cr/cow (derived from 0.06 mg Cr/kg metabolic weight ($bw^{0.75}$), approximately 7.3 mg Cr per 600 kg cow and 8.2 mg Cr per 700 kg cow).[8] The FEEDAP Panel notes that the proposed chromium supplementation rate from Availa®Cr is close to the background content of complete feeds (0.3–1.6 mg total Cr/kg complete feed; EFSA, 2009).

In a previous opinion (EFSA FEEDAP Panel, 2020), the FEEDAP Panel concluded that Availa®Cr is safe for the target species, for consumers of products derived from animals fed the additive and for the environment. With regard to user safety, the Panel concluded that the additive poses a risk to users by inhalation, it is not an irritant to skin and eyes but should be considered a skin sensitiser. However, the Panel was not in the position to conclude on the efficacy of Availa®Cr for dairy cows.

The applicant has provided supplementary information to support the efficacy of the feed additive on dairy cows.

3.1 | Efficacy

The additive is intended to improve milk production in dairy cows. In the previous opinion (EFSA FEEDAP Panel, 2020), three efficacy studies were assessed by the Panel. However, the Panel could not conclude on the efficacy of chromium DL-methionine from Availa®Cr for dairy cows, as positive results on milk production were observed in only one study, while the other two studies were not considered in the assessment due to limitations in the design.

In the current submission, the applicant provided three additional studies in dairy cows (Studies 1, 2 and 3) and a statistical pooled analyses of two of them (Studies 2 and 3), which are described below. The main details of the design of the studies are described in Table 2.

The experimental design followed in Studies 1[12] and 2[13] was similar. Multiparous cows were randomly distributed over two experimental groups (control and Availa®Cr). The two studies were set up following a randomised complete block

TABLE 2 Experimental design of the efficacy trials performed in dairy cows.

Study	Total no of animals (animals × replicate) Replicates × treatment	Breed (duration)	Composition feed (form)[a]	Cr content from Availa® in feed (mg Cr/kg complete feed)	
				Intended	Calculated[b]
1[9]	60 (1) 30	Holstein (111 days)	PMR[c] *ad libitum* – 400 g barley/cow per day	0.30	0.30
2[10]	50 (1) 25	Holstein (111 days)	PMR[d] *ad libitum* – 400 g barley/cow per day	0.30	0.35
3[11]	54 (1) 27	Holstein-Friesian (118 days)	PMR[e] *ad libitum* – 600 g concentrates/cow per day	0.30	0.29

[a]Feed additive was supplemented via the concentrates/barley provided separately to the partial mixed ration (PMR).

[b]Values provided were calculated based on the average feed intake recorded during the study and averaged and expressed per cow and day.

[c]Rations were composed mainly as follows, (1) PMR pre-partum: rye grass hay, fescue hay, straw, soya bean meal; (2) PMR post-partum: rye grass hay, fescue hay, wheat silage, maize, soya bean meal, corn silage, alfalfa hay and soy hulls.

[d]PMR: rye grass hay, fescue hay, wheat silage, maize, wheat, soya bean meal, corn silage, alfalfa hay, barely straw and soy hulls.

[e]PMR: grass silage, maize silage, straw (only during the dry-period), soybean meal and barley (only during the lactation period) and the concentrates mixture contained soybean meal, wheat, beet pulp and palm oil.

[7]FEED dossier reference: FAD-2018-0021.Technical dossier/Supplementary information/April 2019)

[8]Metabolic body weight. $700^{0.75} = 136$; 136 (kg metabolic bw) × 0.06 (recommended Cr in mg/kg metabolic bw per day) = 8.2 mg Cr per 700 kg cow and day. Considering the default values from the FEEDAP Guidance of safety for target species for body weight and feed intake of dairy cows, 8 mg per cow and day would correspond to 0.4 mg Cr/kg complete feed [= 8 mg Cr/cow and day/(20 kg feed dry matter/0.88 (for 12% moisture))].

[9]Blanca Study Report 2022_conf.

[10]2. Blanca 2 Study_conf.

[11]WLR Study Report 2021_conf.

[12]Blanca Study Report 2022_conf.

[13]2. Blanca 2 Study_conf.

design in which cows were blocked by parity number and expected calving date. There were no significant differences between both experimental groups in the milk production during the previous lactation. The administration of the feed additive started 21 days before the expected calving date and was maintained during the first 90 days of lactation. All cows were fed the same partial mixed ration (PMR) on *ad libitum* basis. Besides, 400 g of pelleted barley was offered daily to each cow either not supplemented (control) or supplemented with 8 g Availa®Cr (equivalent to 0.3 mg Cr/kg complete feed) in head lock feeders (before calving) or at the milking parlour (after calving). Cows were milked twice daily. The analytical contents of Cr in the PMR and the supplemented barley were confirmed by analysis.[14] During the 90 days of lactation, health status of the animals, individual feed intake, body weight, milk yield and milk quality were determined daily. The energy-corrected milk yield[15] and the feed efficiency were calculated for the whole lactation period.

In study 3, the administration of the feed additive started 28 days before the expected calving date and was maintained during the first 90 days of lactation.[16] Multiparous cows were distributed in two experimental groups (control and Availa®Cr). The study followed a randomised complete block design in which cows were blocked in pairs by parity number and expected calving date. All cows were fed *ad libitum* the same PMR. Every day, each animal received 600 g of a pelleted mix of concentrates which were either not supplemented (control) or supplemented with 8 g Availa®Cr (equivalent to 0.3 mg Cr/kg complete feed).[17] Both PMR and pelleted concentrates were provided via automatic feeding systems. Cows were milked twice daily. During the 90 days of lactation, the health status of the animals, individual feed intake, body weight, milk yield and milk composition (fat and protein contents) were recorded daily. The energy-corrected milk yield[15] and the feed efficiency were calculated for the whole lactation period.

For all three studies, the cow was the experimental unit and performance parameters were analysed using a general linear mixed model (GLMM) for repeated measures with cow as a random effect and treatment, week of lactation and their interaction as fixed effects. Significance was set at 0.10.

The main results of the three studies are summarised in Table 3.

TABLE 3 Effect of Availa®Cr on milk yield and cow's body weight (first 90 days of lactation).

Study	Groups	Final BW (kg)	Dry matter intake (kg DM/day)	Milk yield (kg/day)	ECM[a] (kg/day)	Feed[b] efficiency
1[18]	Control	679	25.1	42.0	44.0	1.78
	Availa®Cr	672	24.3	44.0	46.5*	1.95*
2[19]	Control	621	20.1	41.1	43.1	2.24
	Availa®Cr	646	21.6*	42.7	45.0	2.20
3[20]	Control	714	25.1	41.6	45.0	1.84
	Availa®Cr	699	24.8	42.2	45.9	1.88

[a]Studies 1 and 2 – ECM; energy-corrected milk = (0.3246 × kg of milk) + (12.86 × kg of fat) + (7.04 kg of protein) (NRC, 2001; Tyrrell & Reid, 1965). Study 3 - ECM; energy-corrected milk = (0.25 × kg of milk) + (12.2 × kg of fat) + (7.7 × kg of protein) (Sjaunja et al., 1990).

[b]Calculated as (kg ECM/day)/(kg DMI/day).

*Significantly different from control ($p \leq 0.10$)

Body weight at the end of the experimental period was not affected by treatment in any of the studies reported. In Study 1, feed efficiency was significantly improved, and energy-corrected milk yield was greater in cows supplemented with Availa®Cr compared to the control. In Study 2, a higher dry matter intake was observed in the Availa®Cr group relative to the control. In Study 3, no effects on performance parameters were identified. In all the three studies submitted, milk composition was unaffected by treatment.

A pooled analysis was also performed combining Studies 2 and 3. The differences between the control diet and that supplemented with Availa®Cr were not significant for any of the performance parameters evaluated except for ECM. This endpoint was increased in the Availa®Cr group compared to control. However, a significant difference ($p < 0.10$) in the study × treatment interaction was identified for ECM and, according to the Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), pooling of data from different studies is appropriate 'provided that the interaction treatment × study is not significant'. Therefore, the results of this pooled data analysis were not further considered.

[14]The additive was mixed at a rate of 20,000 mg of Availa®Cr/kg of barley (20 mg Cr/kg barley). The chromium contents in pelleted barley were 0.124 mg Cr/kg (control) and 15.7 mg Cr/kg in Study 1, and 0.295 mg Cr/kg (control) and 26.0 mg Cr/kg in Study 2. The background Cr content in the PMR was 1.2 mg and 1.89 Cr/kg DM for Study 1 and 2, respectively.

[15]ECM; energy corrected milk = (0.3246 × kg of milk) + (12.86 × kg of fat) + (7.04 kg of protein) (Tyrrell & Reid, 1965; NRC, 2001).

[16]WLR Study Report 2021_conf.

[17]Analysed concentrations of chromium in the additive and in the pellet concentrate mix were 1065 mg Cr/kg and 16 mg Cr/kg, respectively. The background Cr content in the PMR was 1.47 mg Cr/kg feed in the dry period and 1.46 mg Cr/kg in the lactation period, whereas the background Cr content in the pelleted concentrate mix was of 0.86 mg Cr/kg.

[18]Blanca Study Report 2022_conf.

[19]2. Blanca 2 Study_conf.

[20]WLR Study Report 2021_conf.

3.1.1 | Conclusions on efficacy

Considering all the data submitted in support of the efficacy of Availa®Cr in dairy cows, one study from a previous opinion and another one assessed herein showed a positive effect on milk production when cows received the additive. In the absence of further weight of evidence from a third study, the FEEDAP Panel is not in a position to conclude on the efficacy of chromium DL-methionine from Availa®Cr when used in feed for dairy cows.

ABBREVIATIONS

ADFI	average daily feed intake
ADG	average daily gain
BW	body weight
DM	dry matter
FCR	feed conversion ratio
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
GLMM	general linear mixed model
mbw	metabolic body weight
SCF	Scientific Committee on Food

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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