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Safety of natural mixture of illite, montmorillonite and kaolinite (Argile Verte du Velay) for all animal species

EFSA Panel on Additives and Products or Substances used in Animal Feed
(EFSA FEEDAP Panel),

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Abstract

The additive is a natural mixture mainly composed of illite (~ 53%), montmorillonite (~ 16%) and kaolinite (~ 17%), referred as MIMK. In 2016 and in 2017, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) delivered two opinions on the safety and efficacy of the additive. In these opinions, the Panel concluded that the additive is safe for piglets, pigs for fattening and cattle for fattening and minor growing ruminants at a maximum concentration of 50,000 mg/kg. No conclusions could be drawn on the safety for poultry or any other species/categories. Following these opinions, the European Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment on the safety for all animal species. The applicant submitted a new tolerance study with chickens for fattening showing no adverse effect of the additive MIMK up to 100,000 mg/kg complete feed (twofold the highest recommended use level). The FEEDAP Panel therefore concludes that 50,000 mg MIMK/kg complete feed is safe for chickens for fattening. MIMK was already considered safe, at the same dietary concentration, for cattle for fattening with a margin of safety of two and for piglets but without a margin of safety. Therefore, extrapolation to all animal species is not possible for the concentration of 50,000 mg MIMK/kg complete feed. The Panel notes that the concentration of 20,000 mg MIMK/kg feed was tested in all the tolerance studies assessed and shown to be safe, with a margin of safety of at least 2.5. The Panel concludes that the additive MIMK is safe at 50,000 mg/kg complete feed for chickens for fattening and minor growing poultry species, for cattle for fattening and minor growing ruminant species and growing pigs; and at 20,000 mg/kg complete feed for all other animal species and categories.

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Table of contents

Abstract.....	1
1. Introduction.....	4
1.1. Background and Terms of Reference as provided by the requestor.....	4
1.2. Additional information.....	4
1.3. Interpretation of the terms of reference.....	4
2. Data and methodologies.....	5
2.1. Data.....	5
2.2. Methodologies.....	5
3. Assessment.....	5
3.1. Safety for the target species.....	5
3.1.1. Safety for chickens for fattening.....	5
3.1.2. Discussion on the safety for all animal species.....	6
4. Conclusions.....	6
Documentation provided to EFSA.....	7
Chronology.....	7
References.....	7
Abbreviations.....	7

1. Introduction

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

Regulation (EC) No 1831/2003¹ 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, Argile du Velay - Arvel, is seeking a Community authorisation of a natural mixture of illite, montmorillonite and kaolinite (Arvel), as a feed additive to be used as a binder and an anticaking agent for all animal species (Table 1).

Table 1: Description of the substances

Category of additive	Technological additives
Functional group of additive	Binders, Anticaking agents
Description	Natural mixture of illite, montmorillonite and kaolinite (Arvel)
Target animal category	All animal species
Applicant	Argile du Velay - Arvel.
Type of request	New opinion

On 5 July 2017, 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 in the safety of a natural mixture of illite, montmorillonite and kaolinite (Arvel) as a feed additive for all animal species.

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. The new data have been received on 16 February 2018.

In view of the above, the Commission asks the Authority to deliver a new opinion on a natural mixture of illite, montmorillonite and kaolinite (Arvel) as a feed additive for all animal species based on the additional data submitted by the applicant.

1.2. Additional information

The FEEDAP Panel, in 2016, delivered an opinion on the safety and efficacy of a natural mixture of illite, montmorillonite and kaolinite (referred as MIMK, Argile Verte du Velay) as a feed additive for all animal species (EFSA FEEDAP Panel, 2016). In this opinion, the Panel concluded that the additive is safe for the consumer, the user and the environment. The additive was also considered effective as an anticaking agent and as a binder at an inclusion level of 50,000 mg/kg feed. However, regarding the safety for the target animals, the Panel concluded that the additive is safe in complete feed for cattle for fattening at a maximum concentration of 50,000 mg/kg (with a margin of safety of 2) and at a maximum concentration of 20,000 mg/kg for piglets and pigs for fattening (with a margin of safety of 2.5), but no conclusions could be drawn concerning the safety for poultry or any other species/categories.

In 2017, the FEEDAP Panel was requested to assess additional information submitted by the applicant. In its opinion (EFSA FEEDAP Panel, 2017), the Panel assessed an additional study in piglets and an analysis that the applicant made of the previous EFSA opinion regarding poultry and milk-producing animals. The Panel concluded that the additive is safe for piglets and pigs for fattening at 50,000 mg/kg without a margin of safety. The Panel also concluded that the safe level (50,000 mg/kg) identified in its previous opinion for cattle for fattening could be extrapolated to minor growing ruminants, but that conclusion could not be extrapolated to dairy cows and minor ruminant species for milk production. The Panel also concluded that, in the absence of any new data 'no reason to modify its former position that no safe concentration of MIMK in feed for chickens for fattening could be identified'.

1.3. Interpretation of the terms of reference

In the view of the above, the current opinion will focus on the assessment of the safety of the additive for the target species.

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

2. Data and methodologies

2.1. Data

The present assessment is based on the data submitted by the applicant in the form of additional information² following two previous applications on the same product.³

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety of illite, montmorillonite and kaolinite (Argile Verte du Velay) for all animal species is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Guidance on technological additives (EFSA FEEDAP Panel, 2012) and the Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011).

3. Assessment

The product under assessment is a natural mixture mainly composed of illite (~ 53%), montmorillonite (~ 16%), and kaolinite (~ 17%), subsequently referred to as MIMK. It was described and properly characterised in a previous opinion (EFSA FEEDAP Panel, 2016).

The additive is intended to be used as a technological additive (functional groups: (i) anticaking agents and (g) binders) in premixtures and feedingstuffs for all animal species and categories, with no minimum and maximum content. The applicant proposed use levels in premixtures and feedingstuffs of 20,000–50,000 mg/kg complete feed.

The FEEDAP Panel delivered two opinions on the additive under assessment (EFSA FEEDAP Panel, 2016, 2017). In the current application, the applicant submitted a new tolerance study in chickens for fattening to support the safety of the additive for all animal species.

3.1. Safety for the target species

In its first opinion (EFSA FEEDAP Panel, 2016), the Panel concluded that the additive is safe for piglets and pigs for fattening at a maximum concentration of 20,000 mg/kg, and for cattle for fattening at a maximum concentration of 50,000 mg/kg complete feed. In the same opinion, the Panel concluded that MIMK in chickens for fattening up to 50,000 mg/kg feed did not influence the absorption of nutrients/micronutrients and monensin sodium. However, the safety for chickens for fattening could not be shown, because the data indicated a worsening effect on feed to gain ratio in all the treated groups. In the second opinion (EFSA FEEDAP Panel, 2017), the Panel assessed an additional study in piglets and an analysis of the previous EFSA opinion regarding poultry and milk-producing animals. The Panel concluded that additive is safe for piglets and pigs for fattening at 50,000 mg/kg without a margin of safety. The Panel also concluded that the safe level (50,000 mg/kg) identified in its previous opinion for cattle for fattening could be extrapolated to minor growing ruminants but not to dairy cows and minor ruminant species for milk production owing to the insufficient magnitude of the margin of safety. In order to complete the assessment of the safety for all animal species, the applicant submitted a new tolerance study in chickens for fattening.

3.1.1. Safety for chickens for fattening

A total of 1,200 one-day-old male chickens (Ross 308) was fed pelleted diets supplemented with 0, 20,000 (0.4× the highest recommended use level), 50,000 (1×), 75,000 (1.5×) or 100,000 (2×) mg MIMK/kg complete feed for 35 days.⁴ Group size was six replicates with 40 birds each. The diets (starter, from day 0 to day 21; grower, from day 22 to day 35) consisting mainly of maize and soybean meal, were isonitrogenous (starter: about 21.7% crude protein (CP); grower: about 18.7% CP) and isocaloric (starter: about 12.4 MJ ME/kg; grower: about 12.8 MJ/kg, by an increase of soy oil and full fat extruded soybeans with increasing content of the additive). The intended concentrations of the additive were analytically confirmed (by analysis of aluminium). The diets contained 100 mg monensin sodium/kg. Body weight and feed intake were recorded at days 21 and 35. Feed to gain ratio was

² Dossier reference: FAD-2018-0006.

³ Dossier reference: FAD-2012-0025 and FAD-2016-0080.

⁴ Technical dossier/Annex 3A, Annex 3B, Annex 3C, Annex 3D and Annex 3E.

calculated for the corresponding periods. At the end of the experiment, blood samples were taken from one chicken per pen for haematology⁵ and clinical chemistry.⁶ An analysis of variance (ANOVA) was done with the data considering the treatment and the block (location of the pen) in the model and using the pen as the experimental unit. Group means were compared with the Tukey's test.

Overall mortality was low (total mortality 1.3%, no differences among groups). No differences were observed on the performance parameters among the groups for the overall study period (control group: final body weight 2.31 kg, average daily feed intake 92.3 g and feed to gain ratio 1.43).

No differences were observed between treated and control animals in any of the haematological and clinical biochemistry parameters.

The results show that complete feed for chickens for fattening containing up to 100,000 mg MIMK/kg can be formulated and fed without causing adverse effects to chickens for fattening.

3.1.2. Discussion on the safety for all animal species

The results of the tolerance study with chickens for fattening indicate that 100,000 mg MIMK/kg is tolerated; the concentration of 50,000 mg MIMK/kg complete feed is therefore considered safe for chickens for fattening with a margin of safety of two. This conclusion is extrapolated to minor growing poultry species.

In a tolerance study in cattle for fattening, assessed in a previous opinion (EFSA FEEDAP Panel, 2016), MIMK was tested at concentrations of 20,000, 50,000 and 100,000 mg/kg complete feed. The additive was tolerated at the highest concentration tested, and the Panel concluded that 50,000 mg MIMK/kg complete feed is safe for cattle for fattening with a margin of safety of two. This conclusion was extrapolated to minor growing ruminants. In contrast, the Panel considered that the margin of safety of 2 derived from the cattle for fattening study was too low to be applied to dairy cows. Consequently, the conclusion was not extrapolated to dairy ruminants (EFSA FEEDAP Panel, 2017).

In a first tolerance study with piglets (EFSA FEEDAP Panel, 2016), MIMK was tested at concentrations of 20,000 and 100,000 mg/kg complete feed. The results indicated that 20,000 mg MIMK/kg feed was tolerated, but a margin of safety could not be identified, owing to a significant reduction of serum phosphate in the group fed the highest dose of the additive. In a second tolerance study with weaned piglets, MIMK was tested at concentrations of 20,000, 50,000, 70,000 and 100,000 mg/kg complete feed (EFSA FEEDAP Panel, 2017). The results showed that concentrations up to 50,000 mg MIMK/kg feed were tolerated, but without a margin of safety, since the two highest concentrations showed a significant detrimental effect on serum phosphate.

The use of MIMK at 50,000 mg MIMK/kg complete feed is considered safe chickens for fattening and for cattle for fattening with a margin of safety of 2 and for piglets, but without a margin of safety. In the absence of a comparable margin of safety in three major species, extrapolation to all animal species is not possible for a dietary level of 50,000 mg MIMK/kg complete feed.

The Panel notes that the MIMK concentration of 20,000 mg/kg feed was tested in all the tolerance studies assessed (two with weaned piglets, one with chickens for fattening and one with cattle for fattening). This concentration of MIMK was shown to be safe, with a margin of safety of 2.5 in the piglets study and five in cattle for fattening and chickens for fattening. Since the safety of MIMK at 20,000 mg/kg feed is demonstrated in three major species with a comparable margin of safety, the FEEDAP Panel concludes that the concentration of 20,000 MIMK mg/kg complete feed is safe for all animal species.

4. Conclusions

The additive MIMK is considered safe at 50,000 mg/kg complete feed for chickens for fattening and minor growing poultry species, for cattle for fattening and minor growing ruminant species and growing pigs; and at 20,000 mg/kg complete feed for all other animal species and categories.

⁵ Haemoglobin (Hb), red blood cell count (RBC), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), platelets, white blood cell count (WBC), white blood cell differentials (segmented neutrophils, banded neutrophils, lymphocytes, monocytes, eosinophils).

⁶ Alanine transaminase (ALT), alkaline phosphatase, aspartate aminotransferase (AST), creatine phosphokinase (CPK), gamma-glutamyl transpeptidase (GGT), glutamate dehydrogenase (GLDH), glutathione peroxidase (GSH-Px), lactate dehydrogenase (LDH), albumins, globulins, total protein, glucose, uric acid, phosphate.

Documentation provided to EFSA

- 1) Natural mixture of illite, montmorillonite and kaolinite (Argile Verte du Velay) for all animal species. February 2018. Submitted by ARGILE DU VELAY - ARVEL.

Chronology

Date	Event
02/05/2018	Reception mandate from the European Commission
22/05/2018	Acceptance of the mandate by EFSA. Start of the scientific assessment
05/07/2018	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

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- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017. Scientific Opinion on the safety and efficacy of natural mixture of illite, montmorillonite and kaolinite for all animal species. EFSA Journal 2017;15(7):4940, 8 pp. <https://doi.org/10.2903/j.efsa.2017.4940>

Abbreviations

ANOVA	analysis of variance
CP	crude protein
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
MIMK	Natural mixture of illite, montmorillonite and kaolinite