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Efficacy of the feed additive consisting of decoquinate (Deccox®) for use in chickens for fattening (Zoetis Belgium SA)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Jürgen Gropp, Guido Rychen, Orsolya Holczknecht and Maria Vittoria Vettori

Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the efficacy of decoquinate (Deccox®) for chickens for fattening. In a former opinion adopted by the FEEDAP Panel, the potential of decoquinate to prevent coccidiosis in chickens for fattening could not be established due to insufficient evidence. In the present assessment, the applicant submitted new efficacy studies in chickens for fattening to address the data gaps identified in the previous opinion. In addition, the applicant proposed to increase the minimum of the dose range from 20 mg decoquinate/kg complete feed to 30 mg/kg. The coccidiostatic efficacy of decoquinate from Deccox® in chickens for fattening was shown in three floor pen studies at a level of 30 mg decoquinate/kg complete feed. Considering the results of three anticoccidial sensitivity tests (ASTs) with 30 mg decoquinate/kg complete feed for chickens for fattening already described and assessed in a previous FEEDAP opinion and taking into account the newly submitted floor pen data with 30 mg decoquinate/kg complete feed, the FEEDAP Panel concludes that decoquinate from Deccox® is effective in controlling coccidiosis in chickens for fattening at a minimum dose of 30 mg/kg complete feed.

Keywords: Deccox®, decoquinate, coccidiostats, chickens for fattening, efficacy

Requestor: European Commission

Question number: EFSA-Q-2020-00324

Correspondence: feedap@efsa.europa.eu

Panel members: Giovanna Azimonti, Vasileios Bampidis Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa and Ruud Woutersen.

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1. Introduction

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

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition and, in particular Article 9 defines the terms of the authorisation by the Commission.

The applicant, Zoetis Belgium SA, is seeking a Community authorisation for Deccox (E756) as a feed additive to be used as a coccidiostat for chickens for fattening (Table 1).

Table 1: Description of the substances

Category of additive	Coccidiostats and histomonostats
Functional group of additive	Coccidiostats
Description	Deccox (E756)
Target animal category	Chickens for fattening
Applicant	ZOETIS Belgium SA
Type of request	New opinion

On 29 November 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 anticoccidial efficacy of Deccox (E756) as coccidiostat. After the discussion with the Member States on the Standing Committee, it was suggested to check for the possibility to demonstrate the efficacy for Deccox (E756).

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 has been received on 27 February 2020. The relevant data have been sent by the applicant directly to EFSA.

In view of the above, the Commission asks the Authority to deliver a new opinion on Deccox (E756) as a feed additive for chickens for fattening based on the additional data submitted by the applicant.

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]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the efficacy of Deccox® (decoquinate) is in line with the principles laid down in Regulation (EC) No 429/2008[4] and the relevant guidance document: Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

3. Assessment

Deccox®, containing decoquinate as the active substance, is a feed additive intended to be used for the prevention of coccidiosis in chickens for fattening at a dose range of 20 to 40 mg/kg complete feed. In the current application, the increase of the minimum dose from 20 to 30 mg decoquinate/kg complete feed is also requested.

In 2018, the FEEDAP Panel adopted an opinion on the re-evaluation of Deccox® for chickens for fattening (EFSA FEEDAP Panel, 2019) and concluded that the additive is safe for the target species, consumers, users and the environment. No conclusions on the efficacy could be made. In particular,

[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] FEED dossier reference: FAD-2020-0018.
[3] FEED dossier reference: FAD-2013-0034.
[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.

the anticoccidial efficacy was demonstrated in three anticoccidial sensitivity tests (ASTs) conducted with 30 mg decoquinate/kg complete feed by an improvement of all endpoints related to this kind of test, while the three floor pen studies conducted with 20 mg decoquinate/kg complete feed did not show evidence of efficacy.

The proposal to increase the maximum dose level does not affect the safety of the additive already established at the maximum proposed dose of 40 mg decoquinate/kg feed. Therefore, the present assessment addresses only the efficacy. In the current assessment, the applicant submitted three new floor pen studies conducted at a dose of 30 mg decoquinate/kg complete feed which is in line with the newly proposed minimum dose.

3.1. Efficacy

3.1.1. Floor pen studies

The three trials submitted followed a similar design (Table 2).[5] The first two studies were conducted at the same time, in the same poultry house with the same feed.[6] In each trial, 1-day-old chickens (Ross 308; male and female) were penned and distributed into the experimental groups. The experimental groups were as follows: an uninfected untreated control (UUC) group, an infected untreated control (IUC) group and an infected and decoquinate-treated (IT) group. The IT group received feed containing 30 mg decoquinate/kg feed. The intended dietary levels were analytically confirmed (see Table 2). The experimental diets, based on wheat, maize and soybean meal, were fed for 35 days. In the infected groups, all birds were inoculated orally via a syringe at day 14 with recent field isolates of pathogenic *Eimeria* species.[7] Animal health status and mortality were monitored daily. Feed intake and body weight of the animals were measured, and feed to gain ratio was calculated. Samples of excreta, collected on days 20, 21, 22, 27, 28, 29 and 35, were analysed for oocyst excretion. Pen samples from days 20-21-22 and from days 27-28-29 were pooled. Randomly selected birds (five birds per pen) were necropsied for gut lesion scoring on days 21, 28 and 35 following the method of Johnson and Reid (1970) (0 = no lesion, 1 = very mild, 2 = mild, 3 = moderate and 4 = severe).

The data were analysed with a general linear mixed model, which included the effect of the treatment, sex and their interaction. The pen was the experimental unit for statistical purposes. All hypothesis tests were conducted at the 0.05 level of significance using two-sided tests and group means were compared with pairwise comparisons when a significant effect was found.

[5] Technical dossier/Section IV/Annex IV.01-03.

[6] Coccidiostats act on *Eimeria* spp. irrespectively of the composition of the feed and are not considered to modulate feed utilisation. Consequently, the inoculum with sporulated oocysts is considered the most critical factor in studies with artificial infection. In these studies, efficacy of the coccidiostat should be assessed by comparing the effect of *Eimeria* inocula observed in the IT group against the IUC group. Floor pen studies should also simulate the different use conditions (EFSA FEEDAP Panel, 2018). However, husbandry of chickens for fattening is EU wide standardised at a high degree. Taking into account the above, and the fact that in the two studies inocula with different geographical origin were used, the Panel considers that the two trials could be used to assess independently the effect of the additive against different *Eimeria* inocula. Therefore, the two studies could be considered as separate studies.

[7] The inocula used in floor pen trials were tested for its virulence in dose-titration studies. The doses selected (see Table 2) for trial 1 resulted in lesion scores of 1.5 (*E. acervulina*), 3.0 (*E. maxima*) and 3.5 (*E. tenella*) at day 7 post-inoculation (PI) and a weight gain reduction of 3%, no mortality was observed; for trial 2 resulted in mean lesion scores of 1.8 (*E. acervulina*), 1.6 (*E. maxima*) and 3.0 (*E. tenella*) at day 7 post-inoculation (PI) and a weight gain reduction of 30%, no mortality was observed; for trial 3 resulted in mean lesion scores of 2.0 (*E. acervulina*), 1.6 (*E. brunetti*) and 1.8 (*E. tenella*) at day 7 post-inoculation (PI) and a weight gain reduction of 23%, no mortality was observed.

Table 2: Experimental design of floor pen studies with chickens for fattening fed decoquinate (30 mg/kg feed) from Deccox®

Trial No (study start)	Replicates per treatment (birds per replicate)	Inoculum characteristics				Feed analysis decoquinate (mg/kg feed) starter/ grower[4]
		Date and country of isolation	Intended dose (number of oocysts) and strain per bird		Day and mode of inoculation	
1 (9/2019)	10 (30)[1]	1/2019, Belgium	17,200 34,800 29,600 2,800	*E. acervulina* *E. tenella* *E. maxima* *E. mitis*	Day 14 via syringe	28.7/28.3
2 (9/2019)	10 (30)[2]	12/2018, Greece	171,000 81,000 45,000 3,000	*E. acervulina* *E. tenella* *E. maxima* *E. mitis*	Day 14 vi syringe	28.7/28.3
3 (12/2019)	10 (30)[3]	7/2019, Italy	35,000 37,000 28,000	*E. acervulina* *E. brunetti* *E. tenella*	Day 14 via syringe	29.2/30.2 and 27.3[5]

(1): Five replicates with 30 males and five replicates with 30 females, except UUC of which one pen contained 26 male birds and another 22 female birds, reducing the total number of birds from 900 to 888.
(2): Five replicates with 30 males and five replicates with 30 females. One pen foreseen for IUC was removed from the study prior to inoculation due to an *E. acervulina* contamination reducing the total number of birds from 900 to 870.
(3): Each replicate contained 30 birds of mixed gender.
(4): Birds received starter diet from day 0 to 13, grower diet from day 13 to 35.
(5): The grower diet was prepared in two batches.

Mortality is reported in Table 3. In all trials, inoculation resulted in a moderate to high number of losses due to coccidiosis (17% in the IUC group). In all trials, coccidiosis-related mortality was significantly reduced by the treatment as seen by the comparison of the IT group vs IUC.

Table 3: Coccidiosis-related mortality and total mortality[1] in floor pen trials (n)

Trial No	Total number of birds per treatment[2]	Number of dead birds		
		UUC	IUC	IT
1	300	1^a (3)	50^b (56)	7^a (11)
2	300	2^a (6)	56^b (59)	4^a (10)
3	300	1^a (34)	15^b (45)	1^a (11)

a, b: means with different superscript letter in a row are significantly different ($p < 0.05$)
(1): Total mortality is indicated in brackets. It also includes birds culled or withdrawn due to yolk sac infection in trial 3. In trial 1, statistical analysis was done on the percent values.
(2): See also footnotes 1 and 2 of Table 2.

In each floor pen trial, lesions were separately recorded for three *Eimeria* species. Mean intestinal lesion scores (ILSs) due to *E. acervulina* and *E. tenella* species were significantly lower on day 21 (7 days after inoculation) in the IT group compared to IUC in all three trials; and ILSs due to *E. brunetti* were significantly lower at that day in trial 3. Lesion scores on day 28 (14 days post-inoculation) observed for *E. tenella* in trials 1 and 3, for *E. maxima* in trial 1 (only males) and for *E. acervulina* in trial 3 were significantly lower for IT compared to IUC (Table 4).

Table 4: Intestinal lesion scores for different *Eimeria* species at different study days in floor pen trials(1)

	***E. acervulina* lesion scores**			***E. maxima* (Trial 1 and 2) *and* *E. brunetti* (Trial 3) lesion scores**			***E. tenella* lesion scores**		
	Day 21	**Day 28**	**Day 35**	**Day 21**	**Day 28**	**Day 35**	**Day 21**	**Day 28**	**Day 35**
Trial 1(1)									
UUC	0.14^{a}	1.24^{b}	0.63^{b}	$0.40^{a}/0.72^{a}$	$1.24^{a}/0.80^{a}$	1.30	0.16^{a}	0.20^{a}	0.33
IUC	1.68^{b}	0.52^{a}	0.16^{a}	$1.16^{b}/0.92^{a}$	$1.00^{a}/1.80^{b}$	1.00	2.62^{c}	1.22^{b}	0.69
IT	0.30^{a}	1.88^{c}	1.16^{c}	$1.64^{b}/0.84^{a}$	$1.12^{a}/1.12^{a}$	1.26	1.24^{b}	0.40^{a}	0.30
Trial 2									
UUC	0.06^{a}	1.48^{b}	0.70^{b}	0.52^{a}	0.50	1.06	$0.08^{a}/0.12^{a}$	0.14^{a}	0.34
IUC	1.71^{b}	0.22^{a}	0.12^{b}	0.58^{a}	0.88	0.93	$2.44^{c}/2.60^{b}$	0.69^{b}	0.72
IT	0.18^{a}	1.56^{b}	0.62^{b}	1.44^{b}	0.66	1.38	$0.92^{b}/0.20^{a}$	1.60^{c}	0.36
Trial 3									
UUC	0.00^{a}	0.18^{a}	1.11^{b}	0.36^{a}	1.29	1.58	0.32^{a}	0.31^{a}	0.09
IUC	0.27^{b}	2.36^{c}	0.00^{a}	0.98^{b}	1.56	1.47	2.63^{b}	0.89^{b}	0.11
IT	0.02^{a}	1.58^{b}	0.18^{a}	0.22^{a}	1.36	1.52	0.18^{a}	0.46^{a}	0.14

a, b, c: means with different superscript letter in a column within a trial are significantly different ($p < 0.05$)
(1): For trial 1 (*E. maxima* day 21 and 28) and trial 2 (*E. tenella* day 21), values are female/male and superscripts indicate treatment differences within a sex.

Significantly lower oocysts per gram of excreta (OPG) values were found in the IT group in comparison to the IUC group for the composite samples of days 20-21-22 (in an average 7 days post-inoculation) in trials 2 and 3 (Table 5). A comparable significant effect was seen in trial 1 for *E. acervulina* (38,868 vs 4,362) and *E. tenella* (29,290 vs 458) oocysts, but not for total OPG. *E. maxima* oocysts excretion was not influenced by the treatment in trials 1 and 2. No OPG reduction was seen later on days 27-28-29 and 35 (about 14 and 21 days post-inoculation) in all trials. At the end of trials 1 and 3 significantly higher OPG values were found for the UUC compared to the IUC.

Table 5: Oocyst excretion (OPG) at different study days in floor pen trials

	Day 20-21-22	**Day 27-28-29**	**Day 35**
Trial 1			
UUC	2^{a}	71,964	$37,989^{b}$
IUC	$144,276^{b}$	172,022	472^{a}
IT	$80,043^{b}$	79,590	$60,875^{b}$
Trial 2			
UUC	8^{a}	110,245	39,158
IUC	$322,243^{b}$	46,577	3,799
IT	$21,534^{c}$	106,399	22,141
Trial 3			
UUC	1^{a}	$4,419^{a}$	$129,261^{b}$
IUC	$214,124^{c}$	$184,744^{b}$	$2,913^{a}$
IT	53^{b}	$126,930^{b}$	$6,169^{a}$

a, b, c: Means with different superscript letter in a column per trial are significantly different ($p < 0.05$).

Table 6 shows the results of the performance parameters, considered as secondary for the assessment of the efficacy. In trial 1, the IT group showed a better feed to gain ratio in both sexes when compared to the IUC group. In trials 2 and 3, all parameters (feed intake, weight gain and feed to gain ratio) were significantly better in the IT group compared to the IUC group.

Table 6: Zootechnical parameters of chickens for fattening fed Deccox® in floor pen studies at day 35

	Feed Intake (g/day)	Weight Gain (g/day)	Feed to gain ratio(1)
Trial 1			
UUC	80	58[b]	1.47[a]/1.39[a]
IUC	71	53[a]	1.58[c]/1.59[c]
IT	77	55[a]	1.54[b]/1.51[b]
Trial 2			
UUC	82[c]	59[c]	1.48[a]
IUC	69[a]	52[a]	1.60[b]
IT	76[b]	55[b]	1.51[a]
Trial 3			
UUC	87[b]	65[b]	1.42[a]
IUC	82[a]	59[a]	1.51[b]
IT	87[b]	65[b]	1.42[a]

a, b, c: Means with different superscript letter in a column per trial are significantly different ($p < 0.05$).
(1): In trial 1, values are females/males and superscripts indicate treatment differences within sex.

3.1.2. Synopsis of floor pen trials

The individual inoculation of birds in the floor pen studies resulted in a clear response of the mortality showing that the inoculation was effective, and the strains used were virulent.

In all three trials, the treatment with 30 mg decoquinate/kg feed significantly reduced coccidiosis-related mortality, oocyst excretion and lesion scores due to the infection of different *Eimeria* species 7 days post-inoculation. The coccidiostatic effect of decoquinate was demonstrated by these primary endpoints. It is noted that reduction of intestinal lesions was not seen for *Eimeria maxima* in one trial.

The reduction of the coccidial challenge by decoquinate as described above was associated with a significant improvement of the performance parameters (weight gain, feed intake and feed to gain ratio) in two trials and of the feed to gain ratio in another trial.

3.1.3. Conclusions on floor pen trials

The coccidiostatic efficacy of decoquinate from Deccox® in chickens for fattening was shown in three floor pen studies at a level of 30 mg decoquinate/kg complete feed.

4. Conclusions

Considering the results of three AST with 30 mg decoquinate/kg complete feed for chickens for fattening already described and assessed in a previous FEEDAP opinion and taking into account the newly submitted floor pen data with 30 mg decoquinate/kg complete feed, the FEEDAP Panel concludes that decoquinate from Deccox® is efficacious in controlling coccidiosis in chickens for fattening at a minimum dose of 30 mg/kg complete feed.

5. Documentation as provided to EFSA/Chronology

Date	Event
28/02/2020	Dossier received by EFSA. Additional information on Deccox®. Submitted by Zoetis Belgium SA.
23/04/2020	Reception mandate from the European Commission
30/04/2020	Application validated by EFSA – Start of the scientific assessment
21/10/2020	Request of supplementary information to the applicant in line with Article 7(3) of Commission Regulation (EC) No 1304/2003 – Scientific assessment suspended. *Issues: efficacy*
18/11/2020	Reception of supplementary information from the applicant - Scientific assessment re-started
28/01/2021	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

AST	anticoccidial sensitivity test
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
ILS	intestinal lesion scores
IT	infected treated
IUC	infected untreated control
OPG	oocyst count per gram of excreta
PI	Post-inoculation
UUC	uninfected untreated control