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Safety of ethyl ester of β-apo-8′-carotenoic acid as a feed additive for poultry for fattening and poultry for laying

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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 additional data submitted for ethyl ester of β-apo-8-carotenic acid (β-apo-8-ester) when used as a feed additive for poultry for fattening and poultry for laying. The proposed maximum content for β-apo-8-ester of 40 mg/kg complete feed is safe for laying hens with a margin of safety of at least two. The following dietary concentrations are considered safe for the adult consumers, including the age classes adults, elderly and very elderly: 15 mg β-apo-8-ester/kg complete feed for chickens for fattening, 5 mg β-apo-8-ester/kg complete feed for laying hens and 40 mg β-apo-8-ester/kg complete feed for laying hens only intended to the production of liquid eggs which will be only used by the pasta industry for the production of egg pasta. Concerns would arise for the age classes infants, toddlers, other children and adolescents in those countries where dietary surveys showed higher consumption of egg and egg-derived products (Bulgaria, Spain, the UK, the Netherlands, Greece, the Czech Republic and Italy) and higher consumption of egg pasta (Bulgaria, Spain, the UK, the Netherlands, Germany, Denmark, Greece, Austria, the Czech Republic, France, Latvia, Sweden and Italy) assuming that the egg pasta is manufactured with liquid eggs from laying hens treated with 40 mg β-apo-8-ester/kg complete feed.

Keywords: ethyl ester of β-apo-8′-carotenoic acid, safety, poultry, colourant

Requestor: European Commission

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Table of contents

Abstract 1
1. Introduction 4
1.1. Background and Terms of Reference as provided by the European Commission 4
1.2. Additional information 4
2. Data and methodologies 4
2.1. Data 4
2.2. Methodologies 5
3. Assessment 5
3.1. Characterisation 5
3.2. Safety 5
3.2.1. Safety for the target species 5
3.2.1.1. Conclusions on safety for the target species 7
3.2.2. Safety for the consumer 7
3.2.2.1. Conclusions on safety for the consumer 9
4. Conclusions 9
5. Documentation provided to EFSA and Chronology 10
References 10
Abbreviations 10
Appendix A – Calculation of consumer exposure with FACE model 11

1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

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, DSM Nutritional Products represented by DSM Nutritional products SP.Z.o.o., is seeking a Community authorisation for ethyl ester of β-apo-8′-carotenoic acid as a feed additive to be used as a a) colourants: ii-substances which, when fed to animals, add colours to food of animal origin for poultry for fattening an poultry for laying (Table 1).

Table 1: Description of the substances

Category of additive	Sensory additive
Functional group of additive	a) Colourants: ii-substances which, when fed to animals, add colours to food of animal origin
Description	ethyl ester of β-apo-8′-carotenoic acid
Target animal category	poultry for fattening and poultry for laying
Applicant	DSM Nutritional Products represented by DSM Nutritional products SP.Z.o.o.
Type of request	New opinion

On 08 March 2016, 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 ethyl ester of β-apo-8′-carotenoic acid as feed additive for poultry for fattening and poultry for laying.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and allow a revision of Authority's opinion. The new data have been received on 13 March 2018.

In view of the above, the Commission asks the authority to deliver a new opinion on ethyl ester of β-apo-8′-carotenoic acid as a feed additive for poultry for fattening and poultry for laying based on the additional data submitted by the applicant.

1.2. Additional information

In 2016, the FEEDAP Panel re-evaluated the use of β-apo-8-ester for poultry for fattening, poultry for laying (table eggs) and poultry for laying (liquid eggs for processed food) (EFSA FEEDAP Panel, 2016). In that opinion, 8 mg β-apo-8-ester/kg complete feed for laying hens and 15 mg β-apo-8-ester/kg complete feed for chickens for fattening was considered safe for the target animals. No safety conclusion could be made for 80 mg β-apo-8-ester/kg complete feed for laying hens producing eggs for use as liquid eggs in manufacturing of certain food items.

Regarding the safety for the consumer, the FEEDAP Panel noted that the exposure of consumers to residues from β-apo-8-ester in eggs and chicken tissues exceeded the acceptable daily intake (ADI) of 0.015 mg β-apo-8-ester/kg body weight (bw) at concentrations of 8 mg/kg for laying hens and 15 mg/kg for chickens for fattening.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of additional information[1] to a previous application on the same product.[2]

[1] FAD-2018-0008.
[2] FAD-2010-0224.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety of ethyl ester of β-apo-8-carotenic acid is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017a) and Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017b).

3. Assessment

Ethyl ester of β-apo-8′-carotenoic acid is a sensory feed additive (colourant) used to add colours to food of animal origin in poultry for fattening and poultry for laying (for the production of table eggs and liquid eggs for processed food).

In its re-evaluation (EFSA FEEDAP Panel, 2016), the FEEDAP Panel could not conclude on the safety for the use of ethyl ester of β-apo-8-carotenic acid (β-apo-8-ester) at a dose of 80 mg β-apo-8-ester/kg complete feed for laying hens producing eggs for use as liquid eggs in manufacturing of certain food items, while 8 mg β-apo-8-ester/kg complete feed for laying hens and of 15 mg β-apo-8-ester/kg complete feed for chickens for fattening was considered safe for the target animals.

Moreover, in its assessment of consumer safety, the Panel noted that the exposure of consumers to residues from β-apo-8-ester in eggs and chicken tissues exceeded the ADI of 0.015 mg β-apo-8-ester/kg bw at feed concentrations of 8 mg/kg for laying hens and 15 mg/kg for chickens for fattening.

The present opinion is based on the assessment of the additional data submitted by the applicant on the safety of the additive for the target species and on the safety for the consumer considering the updated conditions of use proposed (see Section 3.1).

In particular, the applicant submitted (i) an updated proposal of the conditions of use based on data collected on actual concentrations of β-apo-8-ester in pasta and fine bakery products, (ii) a tolerance study in laying hens to demonstrate the safety of the dose of 40 mg/kg complete feed for the target species and (iii) an updated consumer exposure calculation according to the model previously used by FEEDAP in 2016 (EFSA FEEDAP Panel, 2016).

3.1. Characterisation

The active substance and the additive have been fully characterised by the FEEDAP Panel in 2016 (EFSA FEEDAP Panel, 2016). Following the previous opinion, the applicant has updated to conditions of use with regard the maximum contents as follow:

- 15 mg β-apo-8-ester/kg complete feed for chickens for fattening and minor poultry species for fattening,
- 5 mg β-apo-8-ester/kg complete feed for laying hens and minor poultry for laying for the production of table eggs,
- 5 mg β-apo-8-ester/kg complete feed for laying hens for the production of liquid eggs for bakery products and
- 40 mg β-apo-8-ester/kg complete feed for laying hens for the production of liquid eggs for pasta products.

3.2. Safety

3.2.1. Safety for the target species

In its opinion of 2016 (EFSA FEEDAP Panel, 2016), the FEEDAP Panel concluded that the 100-fold of the maximum proposed dietary concentration of β-apo-8-ester did not affect zootechnical parameters in chickens for fattening and in laying hens for an appropriate time period. It was concluded that the proposed maximum use levels of 15 mg β-apo-8-ester/kg complete feed for chickens for fattening and 8 mg β-apo-8-ester/kg complete feed for laying hens are safe for these target animals. No conclusion could be made on a feed concentration of 80 mg/kg complete feed as applied for hens used for liquid egg production because the tolerance study available was performed at 10 times the intended use concentration and no investigations on haematology and routine blood chemistry were performed.

In the supplementary information, the applicant submitted a literature search carried out to identify more recent studies related to the safety of β-apo-8-ester and a new tolerance study performed with the additive under assessment. The search of the databases[3] resulted in no new information relevant to the safety of the target species.[4] The new tolerance study is described below.[5]

A total of 84 Lohmann Brown hens (21 weeks old, 1,654 g body weight) were individually housed in enriched battery cages for 56 days. The hens were fed the same basal diet in mash form, consisting mainly of wheat, rice and soybean meal and low in yellow carotenoids (xanthophylls < 5 mg/kg). The diet was calculated to contain 16.3% crude protein (CP), 0.86% digestible methionine + cysteine and 11.8 MJ metabolisable energy (ME)/kg. Four groups of 21 replicates each were given the basal diet supplemented with 0, 40 (use level), 80 (2 ×) and 240 (6 ×) mg β-apo-8-ester/kg (analytically confirmed). Health status of the birds was recorded daily. At the end of the experiment, blood samples were collected from all animals for haematology and routine blood chemistry.[6] Gross pathology examination was conducted on ten preselected hens per treatment, with particular focus on liver, kidney, spleen, caecal tonsils and muscle tissue. Body weight of each hen was recorded at the beginning and at the end of the trial. Feed consumption was recorded at the end of the experimental period; average daily feed intake (in g/day) was calculated thereafter. Feed conversion ratio (FCR) per replicate was calculated dividing the total feed consumed by the total weight of eggs produced (g feed/g eggs). Eggs were collected daily from week 1 to week 8 and the number of broken eggs was noted for each replicate. Once a week, the collected eggs were weighed per replicate. Total egg production, egg weight and rate of broken eggs were calculated (n = 21 per treatment).

The performance parameters were assessed by a non-inferiority test, the biological endpoints by an equivalence test. Setting a type-one error of 5%, a power of 80% and for the non-inferiority test a margin of 20%, for the equivalence test boundaries of +/− 20%, the group size was calculated to be 21 replicates. With this sample size and the above assumptions, the trial was powered to show non-inferiority at a non-inferiority-margin of 20% for all performance parameters. It was also sufficiently powered to show equivalence for uric acid, albumin and aspartate aminotransferase.

Mean body weight of the hens (all treatment groups) at the end of the study was 1,782 g. For the control group, a laying rate of 97% was recorded over the whole experimental period (56 days); an average egg weight of 54 g, and a feed to egg mass ratio of 2.0 was calculated. All zootechnical parameters were non-inferior to the control group for the use-level group, for the groups with 2 × and 6 × overdoses. However, egg weight of the 6 × overdose group (52 g) was different ($p < 0.011$) to the control group.

Although a slight numerical decrease of red blood cells and haematocrit was noticed for the high dose group compared to the control group (1.64×10^6 to 1.76×10^6; 26.5 to 27.1%), and the mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) also tended to slightly numerically increase with the inclusion level of the additive (MCV: 157.7, 157.8, 163.5 and 165.9 per fL; MCH 51.5, 51.8, 54.9 and 55.5 pg), those differences were minor and were not statistically different among the treated groups and the control group.

Except for the plasma albumin and total protein concentrations, there was no influence of the treatments on the activity or concentration of the other determined biochemical blood parameters. Plasma albumin was statistically higher in treatment 2 × (2.18 g/dL) when compared to the control (2.06 g/dL), while hens of the high dose group showed similar albumin concentration as the control group. This incidental finding was not dose related and is considered of no toxicological relevance. Total protein concentration was statistically lower in treatment 6 × (47.4 g/L) in comparison to the control group (51.0 g/dL). In the absence of a decreased albumin level and other significant pathological findings either in the liver (appearance and weight) or in other plasma markers of liver toxicity (AST, ALT, GGT), the biological relevance of this finding is questionable.

Disregarding a change in kidney and liver colour in the intermediate and the high dose group, linked to the exposure of overdoses of β-apo-8-ester, there were no macroscopic findings indicating

[3] Database searched: SCOPUS, PubMed, Google Scholar and ToxNet; keywords: name of the additive and its synonyms; Time span: 2015–2017.
[4] Technical dossier/Annex III.2.
[5] Technical dossier/Annex III.3.
[6] Haematological parameters included: red blood cells, haemoglobin, haematocrit, mean corpuscular haemoglobin concentration (MCHC), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), total number of white blood cells. Blood chemistry parameters included: total protein, albumin, glucose, uric acid, total cholesterol, creatinine, total bilirubin. Blood enzyme measurements included: alanine transaminase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), amylase and creatine phosphokinase.

organ toxicity. Relative liver and spleen weight (average 2.25% and 0.12%, respectively) were not different between treatments. The relative weight of caecal tonsils was significantly higher in the 2 × overdose group (0.027%) than in the control group (0.024%). Reactional caecal tonsils were observed in all groups. 50% of the sacrificed animals in the control and in the use level and the 6 × overdose groups and in 100% of the sacrificed animals in the 2 × group showed reactional caecal tonsils. This is reflected in caecal tonsil weight. The absence of dose response for both incidence and severity and the high incidence and severity in the control treatment do not indicate a treatment-related effect. In the absence of treatment-related macroscopic lesions, microscopic examination was not considered necessary.

3.2.1.1. Conclusions on safety for the target species

The applied use level of 40 mg β-apo-8-ester/kg complete feed is safe for laying hens with a margin of safety of at least two.

3.2.2. Safety for the consumer

In 2016, the FEEDAP Panel established an ADI of 0.015 mg β-apo-8-ester/kg bw by applying a safety factor of 200 to the lowest no observed adverse effect level (NOAEL) of 3 mg/kg bw per day from the subchronic toxicity study in rats based on the absence of lymphoid hyperplasia and granulomas in the mesenteric lymph nodes (EFSA FEEDAP Panel, 2016). The same ADI will be used in the present assessment to evaluate the safety for the consumer.

In 2016, the exposure of consumers to residues from β-apo-8-ester in eggs and chicken tissues was calculated with the food basket given by the former FEEDAP guidance on consumer safety (EFSA FEEDAP Panel, 2012). The Panel noted that compliance of the consumer exposure[7] with the ADI could be reached at maximum concentration of 5 mg/kg feed for layers and 15 mg/kg feed for chickens for fattening (See Appendix B, Table 9, EFSA FEEDAP Panel, 2016). Furthermore, concerns were raised regarding the exposure to residues from the consumption of fine bakery and pasta products prepared with liquid eggs coming from hens fed 80 mg β-apo-8-ester/complete feed, as consumer exposure considerably exceeded the ADI (See Appendix B, Table 10, EFSA FEEDAP Panel, 2016).

In the present submission, the applicant proposes as maximum concentration 5 mg β-apo-8-ester/kg feed for layers (for table eggs) and 15 mg β-apo-8-ester/kg feed for chickens for fattening, previously considered as safe for the consumer by the FEEDAP Panel, (EFSA FEEDAP Panel, 2016). In addition, with regard the production of liquid eggs, the applicant proposes the reduction of the maximum dose to:

- 5 mg β-apo-8-ester/kg complete feed for laying hens for the production of liquid eggs for bakery products;
- 40 mg β-apo-8-ester/kg complete feed for laying hens for the production of liquid eggs for pasta.

Concerning the application rate of 5 mg β-apo-8-ester/kg complete feed for laying hens, it should be noted that no distinction can be made between the production of table eggs and liquid eggs for processed food.

Concerning the application rate of 40 mg β-apo-8-ester/kg complete feed for laying hens, it is acknowledged that such a dose will be administered only to laying hens intended to the production of liquid eggs which will be only used by the pasta industry for the production of egg pasta.

For the current assessment, the exposure of consumers has been re-calculated (Table 3) following the methodology described in the most recent Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017b) (for further details see Appendix A), using the residue data reported in 2016 (Table 2).

[7] Two food items with highest values were taken using consumption values of 60 g/day liver and 70 g/day whole egg as indicated in the FEEDAP guidance on consumer safety (EFSA FEEDAP Panel, 2011).

Table 2: Residue data derived from the use of 5 mg β-apo-8-ester/kg feed in layers and of 15 mg β-apo-8-ester/kg feed in poultry for fattening[(1)]

Source	Tissue/product concentration of β-apo-8-ester (mg/kg) Mean + 2SD
Liver	7.87
Kidney	2.14
Muscle[(2)]	0.40
Skin/fat[(2)]	2.49
Egg yolk	20.49[(3)]

SD: standard deviation.
(1): EFSA FEEDAP Panel (2016).
(2): The residue concentration in muscle and skin/fat will be applied to the intake of meat at the following proportions: 90% muscle and 10% skin/fat (EFSA FEEDAP Panel, 2017b). This corresponds to 0.609 mg/kg.
(3): Corresponding to 5.53 mg/kg whole egg containing 27% of yolk.

Table 3: Chronic dietary exposure of consumers to β-apo-8-ester residues in tissues and products of poultry fed 5 mg β-apo-8-ester/kg complete feed (laying hens) and 15 mg β-apo-8-ester/kg complete feed (chickens for fattening) – Summary statistics across European dietary surveys

Population class	Number of surveys	Highest exposure estimate (mg/kg bw per day)	% ADI[(1)]
Infants	6	0.0206	137%
Toddlers	10	0.0238	159%
Other children	18	0.0240	160%
Adolescents	17	0.0156	104%
Adults	17	0.0092	61%
Elderly	14	0.0079	53%
Very elderly	12	0.0093	62%

(1): ADI: 0.015 mg β-apo-8-ester/kg bw.

The results showed that the chronic exposure is below the ADI for the age classes adults, elderly and very elderly confirming the outcome of the former assessment. However, exposure for the other age classes (infants, toddlers, other children and adolescents) is above the ADI. From the detailed results per population class, country and survey (Appendix A, Table A.1), it is noted that the ADI is exceeded in 13 surveys from a total of 51 surveys available in these age classes (Bulgaria, Spain, the UK, the Netherlands, Greece, the Czech Republic and Italy).

This exposure scenario includes only residues coming from the consumption of tissues, table eggs and processed food containing liquid egg yolk (e.g. bakery products) of laying hens fed 5 mg β-apo-8-ester/kg and of chickens fed 15 mg β-apo-8-ester/kg complete feed. In order to take into consideration the contribution to the exposure of residues coming from the consumption of egg pasta prepared with liquid egg of laying hens fed 40 mg β-apo-8-ester/kg, the Comprehensive European Food Consumption Database has been used to quantify the % contribution of egg pasta to the total egg consumption. Results indicated that the egg pasta consumption varies among the different countries from 1.7% to 20.1% (See Appendix A, Table A.2). Therefore, an estimate of 10% of egg pasta consumption has been assumed for the European population.

As no data on residues in eggs are available from the use of 40 mg β-apo-8-ester/kg feed, the β-apo-8-ester concentration of egg yolk can be derived from the regression equations ($y_{yolk} = 3.8 \times -0.1$, and $y_{yolk} = 3.227 \times -0.8816$, EFSA FEEDAP Panel, 2016). The mean of the two equations results in 140.05 mg β-apo-8-ester/kg yolk. Assuming a standard deviation of 10% (worst-case scenario, same approach as EFSA FEEDAP Panel, 2016), the residue would be 168 mg β-apo-8-ester/kg yolk (mean + 2SD) when laying hens are fed 40 mg/kg β-apo-8-ester. This corresponds to 45.4 mg β-apo-8-ester/kg whole egg.

Considering 10% of contribution of egg pasta to the total egg consumption, this residue value can be reduced to 4.54 mg β-apo-8-ester/kg whole egg. The remaining 90%, derived from the consumption of table eggs and processed food containing liquid egg yolk (e.g. bakery products) would result in 4.977 mg (5.53 × 0.9) β-apo-8-ester/kg whole egg. This weighed residue value of 9.517 mg/kg (4.54 + 4.977) can be used in the consumer exposure calculation of which results are shown in Table 4.

Table 4: Chronic dietary exposure of consumers to β-apo-8-ester residues in tissues and products of poultry fed 40 mg β-apo-8-ester/kg complete feed (laying hens destinated for liquid egg production for pasta), 5 mg β-apo-8-ester/kg complete feed (laying hens) and 15 mg β-apo-8-ester/kg complete feed (chickens for fattening) – Summary statistics across European dietary surveys

Population class	Number of surveys	Highest exposure estimate (mg/kg bw per day)	%ADI(1)
Infants	6	0.0344	229%
Toddlers	10	0.0385	257%
Other children	18	0.0405	270%
Adolescents	17	0.0262	175%
Adults	17	0.0144	96%
Elderly	14	0.0126	84%
Very elderly	12	0.0158	105%

(1): ADI: 0.015 mg β-apo-8-ester/kg bw.

The results showed that the chronic exposure is below the ADI for the age classes adults, elderly and slightly above the ADI for very elderly. However, exposure of the other age classes (infants, toddlers, other children and adolescents) were above the ADI. From the detailed results per age class, country and survey (Appendix A, Table A.3.), it is noted that the ADI is exceeded in 34 surveys from a total of 51 surveys available in these age classes (Bulgaria, Spain, the UK, the Netherlands, Germany, Denmark, Greece, Austria, the Czech Republic, France, Latvia, Sweden and Italy).

3.2.2.1. Conclusions on safety for the consumer

The following dietary concentrations are considered safe for the adult consumers, including the age classes adults, elderly and very elderly: 15 mg β-apo-8-ester/kg complete feed for chickens for fattening, 5 mg β-apo-8-ester/kg complete feed for laying hens and 40 mg β-apo-8-ester/kg complete feed for laying hens only intended to the production of liquid eggs which will be only used by the pasta industry for the production of egg pasta.

Concerns would arise for the age classes infants, toddlers, other children and adolescents in those countries where dietary surveys showed higher consumption of egg and egg-derived products (Bulgaria, Spain, the UK, the Netherlands, Greece, the Czech Republic and Italy) and higher consumption of egg pasta (Bulgaria, Spain, the UK, the Netherlands, Germany, Denmark, Greece, Austria, the Czech Republic, France, Latvia, Sweden and Italy) assuming that the egg pasta is manufactured with liquid eggs from laying hens treated with 40 mg β-apo-8-ester/kg complete feed.

4. Conclusions

The proposed maximum content for ethyl ester of β-apo-8-carotenic acid (β-apo-8-ester) of 40 mg/kg complete feed is safe for laying hens with a margin of safety of at least two.

The following dietary concentrations are considered safe for the adult consumers, including the age classes adults, elderly and very elderly: 15 mg β-apo-8-ester/kg complete feed for chickens for fattening, 5 mg β-apo-8-ester/kg complete feed for laying hens and 40 mg β-apo-8-ester/kg complete feed for laying hens only intended to the production of liquid eggs which will be only used by the pasta industry for the production of egg pasta.

Concerns would arise for the age classes infants, toddlers, other children and adolescents in those countries where dietary surveys showed higher consumption of egg and egg-derived products (Bulgaria, Spain, the UK, the Netherlands, Greece, the Czech Republic and Italy) and higher consumption of egg pasta (Bulgaria, Spain, the UK, the Netherlands, Germany, Denmark, Greece, Austria, the Czech Republic, France, Latvia, Sweden and Italy) assuming that the egg pasta is manufactured with liquid eggs from laying hens treated with 40 mg β-apo-8-ester/kg complete feed.

5. Documentation provided to EFSA and Chronology

Date	Event
27/02/2018	Dossier received by EFSA; Ethyl ester of β-apo-8′-carotenoic acid. February 2018. Submitted by DSM Nutritional Products Spz.o.o.
21/03/2018	Reception mandate from the European Commission
20/04/2018	Acknowledgement of the mandate to EC. Start of the Scientific assessment
12/11/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ADI	acceptable daily intake
bw	body weight
CP	crude protein
FCR	Feed conversion ratio
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
HRP	highest reliable percentile
ME	metabolisable energy
NOAEL	no observed adverse effect level
RAC	raw agricultural commodities

Appendix A – Calculation of consumer exposure with FACE model

Methodology

As described in the Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017b), consumption data of edible tissues and products as derived from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) will be used to assess exposure to residues from the use of feed additives in different EU countries, age classes[8] and special population groups. For each EU country and age class, only the latest survey available in the Comprehensive Database will be used.

While the residue data reported for feed additives refer to organs and tissues (raw agricultural commodities (RAC)), the Comprehensive Database includes consumption data for foods as consumed. In order to match those consumption data with the available residue data for feed additives, the consumption data reported in the Comprehensive Database have been converted into RAC equivalents. For assessing the exposure to coccidiostats from their use in (non-reproductive) poultry, the following list of commodities is considered: meat, fat, liver, other offals (including kidney).

Depending on the nature of the health-based guidance derived, either a chronic or acute exposure assessment may be required.

For chronic exposure assessments, the total relevant residues will be combined for each individual with the average daily consumptions of the corresponding food commodities, and the resulting exposures per food will be summed in order to obtain total chronic exposure at individual level (standardised by using the individual body weight). The mean and the higher percentile (usually the 95th percentile) of the individual exposures will be subsequently calculated for each dietary survey (country) and each age class separately.

As opposed to the chronic exposure assessments, acute exposure calculation will be carried out for each RAC value separately. The higher percentile (usually the 95th percentile) exposures based on the consuming days only will be calculated for each food commodity, dietary survey and age class separately.

Detailed results on chronic exposure calculation

Table A.1: Chronic dietary exposure per population class, country and survey (mg/kg bw per day) of consumers to β-apo-8-ester residues in tissues and products of poultry fed 5 mg β-apo-8-ester/kg complete feed (laying hens) and 15 mg β-apo-8-ester/kg complete feed (chickens for fattening) (in yellow marked those exceeding ADI)

Population class	Survey's country	Number of subjects	HRP[(1)]	HRP description
Infants	Bulgaria	523	0.0206	95th
Infants	Germany	142	0.0055	95th
Infants	Denmark	799	0.0049	95th
Infants	Finland	427	0.0018	95th
Infants	United Kingdom	1,251	0.0125	95th
Infants	Italy	9	0.0000	50th
Toddlers	Belgium	36	0.0119	90th
Toddlers	Bulgaria	428	0.0238	95th
Toddlers	Germany	348	0.0143	95th
Toddlers	Denmark	917	0.0098	95th
Toddlers	Spain	17	0.0177	75th
Toddlers	Finland	500	0.0081	95th
Toddlers	United Kingdom	1,314	0.0175	95th
Toddlers	United Kingdom	185	0.0151	95th
Toddlers	Italy	36	0.0123	90th
Toddlers	Netherlands	322	0.0162	95th

[8] Infants: < 12 months old, toddlers: ≥ 12 months to < 36 months old, other children: ≥ 36 months to < 10 years old, adolescents: ≥ 10 years to < 18 years old, adults: ≥ 18 years to < 65 years old, elderly: ≥ 65 years to < 75 years old, and very elderly: ≥ 75 years old.

Population class	Survey's country	Number of subjects	HRP(1)	HRP description
Other children	Austria	128	0.0142	95th
Other children	Belgium	625	0.0122	95th
Other children	Bulgaria	433	0.0235	95th
Other children	Czech Republic	389	0.0151	95th
Other children	Germany	293	0.0142	95th
Other children	Germany	835	0.0145	95th
Other children	Denmark	298	0.0097	95th
Other children	Spain	399	0.0173	95th
Other children	Spain	156	0.0240	95th
Other children	Finland	750	0.0112	95th
Other children	France	482	0.0139	95th
Other children	United Kingdom	651	0.0120	95th
Other children	Greece	838	0.0206	95th
Other children	Italy	193	0.0168	95th
Other children	Latvia	187	0.0124	95th
Other children	Netherlands	957	0.0144	95th
Other children	Netherlands	447	0.0128	95th
Other children	Sweden	1,473	0.0103	95th
Adolescents	Austria	237	0.0086	95th
Adolescents	Belgium	576	0.0067	95th
Adolescents	Cyprus	303	0.0062	95th
Adolescents	Czech Republic	298	0.0096	95th
Adolescents	Germany	393	0.0118	95th
Adolescents	Germany	1,011	0.0060	95th
Adolescents	Denmark	377	0.0047	95th
Adolescents	Spain	651	0.0121	95th
Adolescents	Spain	209	0.0156	95th
Adolescents	Spain	86	0.0072	95th
Adolescents	Finland	306	0.0042	95th
Adolescents	France	973	0.0079	95th
Adolescents	United Kingdom	666	0.0069	95th
Adolescents	Italy	247	0.0095	95th
Adolescents	Latvia	453	0.0096	95th
Adolescents	Netherlands	1,142	0.0079	95th
Adolescents	Sweden	1,018	0.0066	95th
Adults	Austria	308	0.0053	95th
Adults	Belgium	1,292	0.0055	95th
Adults	Czech Republic	1,666	0.0062	95th
Adults	Germany	10,419	0.0058	95th
Adults	Denmark	1,739	0.0039	95th
Adults	Spain	981	0.0072	95th
Adults	Spain	410	0.0072	95th
Adults	Finland	1,295	0.0061	95th
Adults	France	2,276	0.0054	95th
Adults	United Kingdom	1,265	0.0055	95th
Adults	Hungary	1,074	0.0077	95th
Adults	Ireland	1,274	0.0055	95th
Adults	Italy	2,313	0.0065	95th
Adults	Latvia	1,271	0.0085	95th

Population class	Survey's country	Number of subjects	HRP[(1)]	HRP description
Adults	Netherlands	2,055	0.0062	95th
Adults	Romania	1,254	0.0092	95th
Adults	Sweden	1,430	0.0079	95th
Elderly	Austria	67	0.0060	95th
Elderly	Belgium	511	0.0050	95th
Elderly	Germany	2,006	0.0052	95th
Elderly	Denmark	274	0.0044	95th
Elderly	Finland	413	0.0050	95th
Elderly	France	264	0.0048	95th
Elderly	United Kingdom	166	0.0049	95th
Elderly	Hungary	206	0.0060	95th
Elderly	Ireland	149	0.0059	95th
Elderly	Italy	289	0.0056	95th
Elderly	Netherlands	173	0.0054	95th
Elderly	Netherlands	289	0.0049	95th
Elderly	Romania	83	0.0079	95th
Elderly	Sweden	295	0.0072	95th
Very elderly	Austria	25	0.0037	75th
Very elderly	Belgium	704	0.0054	95th
Very elderly	Germany	490	0.0052	95th
Very elderly	Denmark	12	0.0032	75th
Very elderly	France	84	0.0050	95th
Very elderly	United Kingdom	139	0.0045	95th
Very elderly	Hungary	80	0.0063	95th
Very elderly	Ireland	77	0.0056	95th
Very elderly	Italy	228	0.0051	95th
Very elderly	Netherlands	450	0.0050	95th
Very elderly	Romania	45	0.0082	90th
Very elderly	Sweden	72	0.0093	95th

(1): HRP: highest reliable percentile, i.e. the highest percentile that is considered statistically robust for combinations of dietary survey, age class and possibly raw primary commodity, considering that a minimum of 5, 12, 30 and 61 observations are respectively required to derive 50th, 75th and 90th and 95th percentile estimates. Estimates with less than 5 observations were not included in this table.

Table A.2: Average contribution of egg pasta to the chronic egg consumption of the different surveys based on the Comprehensive European Food Consumption Database

Country	Highest_mean contribution (%)
Belgium	1.7
Latvia	2.7
Bulgaria	3.0
Netherlands	3.3
Sweden	3.4
Romania	3.5
Ireland	3.9
France	4.3
Italy	5.5
Czech Republic	5.7
Spain	5.9
Denmark	8.5
Cyprus	11.8

Country	Highest_mean contribution (%)
Austria	13.9
Finland	14.1
Greece	14.2
Germany	15.3
United Kingdom	19.9
Hungary	20.1

Table A.3: Chronic dietary exposure per population class, country and survey (mg/kg bw per day) of consumers to β-apo-8-ester residues in tissues and products of poultry fed 40 mg β-apo-8-ester/kg complete feed (laying hens destinated for liquid egg production for pasta), 5 mg β-apo-8-ester/kg complete feed (laying hens) and 15 mg β-apo-8-ester/kg complete feed (chickens for fattening) (in yellow marked those exceeding ADI)

Population class	Survey's country	Number of subjects	HRP[(1)]	HRP description
Infants	Bulgaria	523	0.0344	95th
Infants	Germany	142	0.0089	95th
Infants	Denmark	799	0.0080	95th
Infants	Finland	427	0.0019	95th
Infants	United Kingdom	1,251	0.0214	95th
Infants	Italy	9	0.0000	50th
Toddlers	Belgium	36	0.0192	90th
Toddlers	Bulgaria	428	0.0385	95th
Toddlers	Germany	348	0.0238	95th
Toddlers	Denmark	917	0.0166	95th
Toddlers	Spain	17	0.0300	75th
Toddlers	Finland	500	0.0130	95th
Toddlers	United Kingdom	1,314	0.0298	95th
Toddlers	United Kingdom	185	0.0258	95th
Toddlers	Italy	36	0.0213	90th
Toddlers	Netherlands	322	0.0271	95th
Other children	Austria	128	0.0238	95th
Other children	Belgium	625	0.0202	95th
Other children	Bulgaria	433	0.0364	95th
Other children	Czech Republic	389	0.0251	95th
Other children	Germany	293	0.0242	95th
Other children	Germany	835	0.0248	95th
Other children	Denmark	298	0.0162	95th
Other children	Spain	399	0.0286	95th
Other children	Spain	156	0.0405	95th
Other children	Finland	750	0.0186	95th
Other children	France	482	0.0234	95th
Other children	United Kingdom	651	0.0201	95th
Other children	Greece	838	0.0350	95th
Other children	Italy	193	0.0288	95th
Other children	Latvia	187	0.0211	95th
Other children	Netherlands	957	0.0242	95th
Other children	Netherlands	447	0.0216	95th
Other children	Sweden	1,473	0.0170	95th
Adolescents	Austria	237	0.0146	95th
Adolescents	Belgium	576	0.0116	95th

Population class	Survey's country	Number of subjects	HRP[(1)]	HRP description
Adolescents	Cyprus	303	0.0098	95th
Adolescents	Czech Republic	298	0.0150	95th
Adolescents	Germany	393	0.0198	95th
Adolescents	Germany	1,011	0.0102	95th
Adolescents	Denmark	377	0.0079	95th
Adolescents	Spain	651	0.0203	95th
Adolescents	Spain	209	0.0262	95th
Adolescents	Spain	86	0.0121	95th
Adolescents	Finland	306	0.0064	95th
Adolescents	France	973	0.0129	95th
Adolescents	United Kingdom	666	0.0115	95th
Adolescents	Italy	247	0.0162	95th
Adolescents	Latvia	453	0.0163	95th
Adolescents	Netherlands	1,142	0.0130	95th
Adolescents	Sweden	1,018	0.0110	95th
Adults	Austria	308	0.0088	95th
Adults	Belgium	1,292	0.0093	95th
Adults	Czech Republic	1,666	0.0105	95th
Adults	Germany	10,419	0.0097	95th
Adults	Denmark	1,739	0.0066	95th
Adults	Spain	981	0.0122	95th
Adults	Spain	410	0.0122	95th
Adults	Finland	1,295	0.0104	95th
Adults	France	2,276	0.0088	95th
Adults	United Kingdom	1,265	0.0093	95th
Adults	Hungary	1,074	0.0119	95th
Adults	Ireland	1,274	0.0089	95th
Adults	Italy	2,313	0.0110	95th
Adults	Latvia	1,271	0.0144	95th
Adults	Netherlands	2,055	0.0103	95th
Adults	Romania	1,254	0.0144	95th
Adults	Sweden	1,430	0.0135	95th
Elderly	Austria	67	0.0100	95th
Elderly	Belgium	511	0.0083	95th
Elderly	Germany	2,006	0.0088	95th
Elderly	Denmark	274	0.0075	95th
Elderly	Finland	413	0.0081	95th
Elderly	France	264	0.0078	95th
Elderly	United Kingdom	166	0.0083	95th
Elderly	Hungary	206	0.0098	95th
Elderly	Ireland	149	0.0098	95th
Elderly	Italy	289	0.0092	95th
Elderly	Netherlands	173	0.0088	95th
Elderly	Netherlands	289	0.0085	95th
Elderly	Romania	83	0.0126	95th
Elderly	Sweden	295	0.0123	95th
Very elderly	Austria	25	0.0064	75th
Very elderly	Belgium	704	0.0092	95th
Very elderly	Germany	490	0.0090	95th
Very elderly	Denmark	12	0.0053	75th

Population class	Survey's country	Number of subjects	HRP(1)	HRP description
Very elderly	France	84	0.0077	95th
Very elderly	United Kingdom	139	0.0076	95th
Very elderly	Hungary	80	0.0103	95th
Very elderly	Ireland	77	0.0096	95th
Very elderly	Italy	228	0.0087	95th
Very elderly	Netherlands	450	0.0083	95th
Very elderly	Romania	45	0.0131	90th
Very elderly	Sweden	72	0.0158	95th

(1): HRP: highest reliable percentile, i.e. the highest percentile that is considered statistically robust for combinations of dietary survey, age class and possibly raw primary commodity, considering that a minimum of 5, 12, 30 and 61 observations are respectively required to derive 50th, 75th and 90th and 95th percentile estimates. Estimates with less than 5 observations were not included in this table.