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# Safety and efficacy of ethyl ester of $\beta$ -apo-8'-carotenoic acid as a feed additive for poultry for fattening and poultry for laying

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

### Abstract

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid ( $\beta$ -apo-8-ester) at a concentration of 8 mg/kg complete feed for laying hens and of 15 mg/kg complete feed for chickens for fattening is safe for the target animals. No safety conclusion could be made for 80 mg  $\beta$ -apo-8-ester/kg complete feed for laying hens.  $\beta$ -Apo-8-ester was devoid of genotoxic potential. Repeat dose toxicity studies and the two-generation reproduction toxicity study showed toxicity of  $\beta$ -apo-8-ester by adverse effects on the liver, spleen and mesenteric lymph nodes. An acceptable daily intake (ADI) of 0.015 mg  $\beta$ -apo-8-ester/kg body weight (bw) was set 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 based on the absence of lymphoid hyperplasia and granulomas in the mesenteric lymph nodes. Compliance of consumers 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. Maximum residue levels (MRLs) were proposed: 20 mg  $\beta$ -apo-8-ester/kg egg yolk, 8 mg  $\beta$ -apo-8-ester/kg liver and 2.5 mg  $\beta$ -apo-8-ester/kg skin/fat.  $\beta$ -Apo-8-ester is not an irritant to skin and eyes, and not a dermal sensitiser. Owing to the absence of information, no conclusions could be made on the risk of users by inhalation. The use of  $\beta$ -apo-8-ester in poultry feed at a maximum of 80 mg/kg would not likely pose a risk to the environment.  $\beta$ -Apo-8-ester is effective as a yellow colourant for egg yolk, and skin and shank of broilers. The equally effective doses of  $\beta$ -apo-8-ester in water for drinking are half of those in feed. Conclusions on safety and efficacy for chickens were extended to minor poultry species and categories. No conclusion can be made for turkeys since no data were provided for this major animal species.

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**Keywords:** ethyl ester of  $\beta$ -apo-8'-carotenoic acid, safety, efficacy, poultry, colourant

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## Summary

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 safety and efficacy of ethyl ester of  $\beta$ -apo-8'-carotenoic acid for poultry for fattening, poultry for laying (table eggs) and poultry for laying (liquid eggs for processed food).

The proposed maximum contents for ethyl ester of  $\beta$ -apo-8-carotenoic acid ( $\beta$ -apo-8-ester) of 8 mg/kg complete feed for laying hens and of 15 mg/kg complete feed for chickens for fattening are safe for the target animals. No safety conclusion could be made for 80 mg  $\beta$ -apo-8-ester/kg complete feed for laying hens producing eggs for use as liquid eggs in manufacturing of certain food items. The FEEDAP Panel extended the conclusions on safe levels to all minor poultry for fattening (15 mg/kg complete feed) and for laying (8 mg/kg complete feed). No conclusion can be made for turkeys since no data were provided for this major animal species.

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid is absorbed to a considerable extent, undergoes very limited biotransformation and is eliminated slowly. Its metabolic fate is qualitatively similar in chickens and rats.  $\beta$ -Apo-8-ester is the marker residue. Highest concentrations were found in egg yolk, followed by liver, abdominal fat, skin, kidney and muscle tissue. There was a strong linear relation between feed concentration and deposition in tissue/products over a wide range of dietary concentrations.

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid was positive in several *in vitro* tests, while negative results were reported *in vivo* in two bone marrow micronucleus studies, in which, however, no evidence of target exposure was reported, and in an *in vitro* unscheduled DNA synthesis (UDS) assay in rat hepatocytes in the presence of measurable amounts of the test item in the liver. The FEEDAP Panel concluded that the positive outcomes reported *in vitro* were due to secondary oxidation products of the test item and that  $\beta$ -apo-8-ester is devoid of genotoxic potential.

Repeat dose toxicity studies and the two-generation reproduction toxicity study showed toxicity of  $\beta$ -apo-8-ester which was characterised by adverse effects on the liver, spleen and mesenteric lymph nodes. The lowest dose tested, 3 mg/kg body weight (bw) per day, was considered as the no observed adverse effect level (NOAEL) for the subchronic study. A two-generation reproduction toxicity study of  $\beta$ -apo-8-ester in rats and a developmental toxicity study in rabbits showed no reproductive toxicity in rats and no developmental toxicity in rats or rabbits at any dose tested. In the two-generation reprotoxicity study, BMDL<sub>10</sub> for the absence of granulomatous inflammation in the liver was 4.3 mg/kg bw per day.

An ADI of 0.015 mg  $\beta$ -apo-8-ester/kg bw was set by applying an uncertainty factor of 200 to the lowest NOAEL of 3 mg/kg bw per day from the subchronic toxicity study based on the absence of lymphoid hyperplasia and granulomas in the mesenteric lymph nodes.

The exposure of consumers to residues from  $\beta$ -apo-8-ester in eggs and chicken tissues exceeded the ADI at feed concentrations of 8 mg/kg for laying hens and 15 mg/kg for chickens for fattening. Compliance with the ADI could be reached if the maximum concentration in complete feed for laying hens was reduced to 5 mg/kg.

The FEEDAP Panel proposed the following maximum residue levels (MRLs): 20 mg  $\beta$ -apo-8-ester/kg egg yolk, 8 mg  $\beta$ -apo-8-ester/kg liver and 2.5 mg  $\beta$ -apo-8-ester/kg skin/fat.

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid is not an irritant to skin and eyes, and not a dermal sensitiser. Owing to the absence of information on the inhalation toxicity of  $\beta$ -apo-8-ester, the FEEDAP Panel could not conclude on the risk of users by inhalation.

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid, when excreted, will enter the pool of carotenoids naturally occurring in plants. Considering the oxidative susceptibility of carotenoids, the FEEDAP Panel considered it unlikely that the use of  $\beta$ -apo-8-ester in poultry feed at a maximum of 80 mg/kg would pose a risk to the environment.

Ethyl ester of  $\beta$ -apo-8'-carotenoic acid is effective as a yellow colourant of (i) egg yolk at a dietary concentration of 5 mg/kg complete feed for laying hens and (ii) skin and shanks at a dose of 15 mg/kg complete feed for chickens for fattening. The two oral administration routes (by feed or water for drinking) are bioequivalent, considering yolk and skin pigmentation. The equally effective

doses of  $\beta$ -apo-8-ester in water for drinking are half of those in feed. The conclusions on efficacy could be extended to minor poultry species for laying and for growing, respectively.

The FEEDAP Panel made some recommendations on (i) the maximum TPPO content in the additive and (ii) the maximum concentration of colourants when used together.