FORM FOR THE SUBMISSION OF SUBSTANCES TO BE EVALUATED BY JECFA

In completing this form, only brief information is required. The form may be retyped if more space is needed under any one heading provided that the general format is maintained.

Name of Substance(s):	**Anionic Methacrylate Copolymer**
Question(s) to be answered by JECFA *(Provide a brief justification of the request in case of re-evaluations)*	Safety evaluation and establishment of specification when used as glazing / coating agent.

1. Proposal for inclusion submitted by:

Bundesministerium für Ernährung und Landwirtschaft (BMEL)
Federal Ministry of Food and Agriculture
Referat 311
(German Codex Contact Point)
Wilhelmstr. 54
10117 Berlin
Germany
Phone: +49-(0)30-18529-3515
E-Mail: codex.germany@bmel.bund.de

2. Name of substance; trade name(s); chemical name(s):

Name of substance: Anionic Methacrylate Copolymer, INS 1207

Trade names: Eudraguard® biotic

Chemical names: Poly (methyl acrylate-co-methylmethacrylate-co-methacrylic acid) 7:3:1, CAS number 26936-24-3

3. Names and addresses of basic producers:

Manufacturer:

Evonik Röhm GmbH
Kirschenallee
64293 Darmstadt
Germany

Marketer:

Evonik Nutrition & Care GmbH
Kirschenallee
64293 Darmstadt
Germany

4. Has the manufacturer made a commitment to provide data?

Evonik Nutrition & Care GmbH commits to provide data to support the proposal for inclusion of Anionic Methacrylate Copolymer in the list of substances to be evaluated by JECFA.

5. Identification of the manufacturer that will be providing data (Please indicate contact person):

Evonik Nutrition & Care GmbH
Kirschenallee
64293 Darmstadt
Germany

Attn.: Dr. Uta Deiting, Regulatory Affairs Specialist Food

uta.deiting@evonik.com +49 2407-5569960

6. Justification for use:

Quotation from EFSA opinion (p. 7, „*Background as provided by The European Commission*“):

“Enteric coating in the production of formulations of solid food supplements. The enteric properties of glazing agents protect the stomach against irritating nutraceutical ingredients. On the other hand, sensitive nutrients are protected against disintegration by the stomach acid. (…) The consumer can benefit from the better compatibility of the nutraceutical ingredients; the compliance with the intake recommendations can be facilitated, the amount of nutrient can be better managed and the safety of the food supplement can be improved.”

7. Food products and food categories within the GSFA in which the substance is used as a food additive or as an ingredient, including use level(s):

Food category: 13.6, food supplements
Max. use level: 100,000 mg/kg (10%)

8. Is the substance currently used in food that is legally traded in more than one country? (Please identify the countries); or, has the substance been approved for use in food in one or more country? (Please identify the country(ies))

EU: EU food additive list, (Reg. (EC) No. 1333/2008), Annex II: E 1207 (amendment for E 1207 by Reg. (EC) No 816/2013). EFSA opinion attached.

US: GRAS status in preparation

Other countries: product registration in progress / in preparation

9. List of data available (please check, if available)

Toxicological data

Anionic methacrylate copolymer is very poorly absorbed from the gastrointestinal tract. It is predominantly excreted via the feces following transit through the gastrointestinal tract. From the data using radiolabelled anionic methacrylate copolymer it can be concluded that the polymer is essentially not absorbed and that the very low amounts of absorbed radioactivity are not retained in the tissues. – The EFSA opinion on Anionic Methacrylate Copolymer provide details on the toxicological assessment.

(i) Metabolic and pharmacokinetic studies

See EFSA opinion, chapter 3.1. Quotation:

„The petitioner provided data of an ADME study performed according to Good Laboratory Practices. The ADME study was performed with male and female rats (CD Sprague-Dawley strain). (…)

„The study shows that, following ingestion, anionic methacrylate copolymer is very poorly absorbed from the gastrointestinal tract. It is predominantly excreted via the feces following transit through the gastro-

intestinal tract (Jolly, 1999). The petitioner argues that the very low level of absorption prevents the investigation of the kinetics of absorption/elimination and the determination of possible metabolism. However, the Panel does not preclude the existence of gastrointestinal metabolism."

(ii) Short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity, and developmental toxicity studies in animals and genotoxicity studies

See EFSA opinion, chapter 3.2.2 – 3.2.5. Selected quotations:

- Short term toxicity:

„The petitioner provided data from a 28-day study in the dog. The Panel noted that the study was performed according to GLP. (…) The authors concluded the No-Observed-Adverse-Effect Level (NOAEL) to be 400 mg/kg bw/day, the highest dose tested (Eileraas, 2004). The Panel agrees with this NOAEL."

- Sub-chronic toxicity:

„The petitioner provided data from a 26-week oral toxicity study in the rat. The Panel noted that the study was performed according to GLP. (…) The authors derived a NOAEL of 1500 mg/kg bw/day, the highest dose tested (Venturella, 2000). The Panel agrees with this NOAEL."

- Genotoxicity:

„Based on negative results derived from the in vitro Ames and mammalian cell mutation assays and the micronucleus assay in vivo, the Panel considers that anionic methacrylate copolymer does not raise concern with respect to genotoxicity."

- Chronic toxicity and carcinogenicity:

No data were provided.

- Reproduction and developmental toxicity:

„The petitioner did not provide data from one or two generation reproductive toxicity studies. – The petitioner provided data from a study assessing the effects of anionic methacrylate copolymer (AMC) on the survival and development of the unborn fetuses when administered during the organogenesis phase of gestation and until the completion of fetal development in the pregnant rats (Schmidt, 2003). The study was conducted in accordance with OECD guideline for the testing of chemicals No. 414. (…) The NOAEL for both dams and fetuses is 1000 mg/kg bw/day."

(iii) Epidemiological and/or clinical studies and special considerations

See EFSA opinion, chapter 3.2.6. Quotation:

„The petitioner states that no human volunteer studies have been undertaken with anionic methacrylate copolymer. The material has a limited history of use as a pharmaceutical excipient although analogous copolymers have an extensive history of such use with no reported adverse effects."

(iv) Other data

None.

Technological data

(i) Specifications for the identity and purity of the listed substances (specifications applied during development and toxicological studies; proposed specifications for commerce)

See EFSA opinion, chapters 2.1, Identity of substance, and 2.2., Specification, and commercial specification.

The product conforms to the specification as listed in Reg. (EU) No. 231/2012.

(ii) Technological and nutritional considerations relating to the manufacture and use of the listed substance

See below, intake assessment data.

Intake assessment data

(i) Levels of the listed substance used in food or expected to be used in food based on technological function and the range of foods in which they are used

See EFSA opinion, chapter 2.6., Case of need and proposed uses. Quotation:

„Anionic methacrylate copolymer is intended to be used as a glazing agent/coating agent in solid food supplements. The use is therefore restricted to products in dosage form, namely forms such as capsules, pastilles, tablets, pills and other similar forms like pellets, and powders. The petitioner states that anionic methacrylate copolymer will be specifically used for its 'enteric' properties, i.e. to protect the stomach against irritating ingredients (e.g. iron ions) or to protect sensitive nutrients against disintegration by the gastric acid."

„The petitioner indicated that only low use levels for coating are needed since the enteric properties can be obtained with a coating level of 5 mg/cm2, equivalent to 30 mg/tablet (tablet weight: 1000 mg). For special applications, higher coating levels are necessary. The highest coating level is estimated to be 100 mg/ tablet."

(ii) Estimation of dietary intakes based on food consumption data for foods in which the substance may be used.

See EFSA opinion, chapter 2.8.. Quotation from chapter 4., Discussion:

„As regards exposure, the Panel based its estimate on the worst case combined exposure by heavy users (assuming a coating level of 100 mg/tablet) to anionic methacrylate copolymer from both its proposed use in food supplements and from its approved use in pharmaceuticals, estimated to be equal to 23.4 mg/kg bw/day for a 60 kg adult, and 16 mg/kg bw/day for children (4-18 years), whereas the petitioner estimated this exposure to be 20 mg/kg bw/day and 16 mg/kg bw/day respectively. The Panel estimated the combined exposure to anionic methacrylate copolymer for heavy users assuming the normal maximum coating level of 30 mg/tablet, from both its proposed use in food supplements and from its approved use in pharmaceuticals to be 7 mg/kg bw/day for a 60 kg adult, and 4.8 mg/kg bw/day for a child. The respective estimates by the petitioner for these user groups are 6 mg/kg bw/day and 4.8 mg/kg bw/day. If anionic methacrylate is used solely in food supplements at the normal coating level of 30 mg/tablet, the estimated exposure by heavy users would be 3.5 mg/kg bw/day for adults and 2.4 mg/kg bw/day for children. Using the worst case exposure, the calculated exposure to the residual monomers (methacrylic acid, methyl

acrylate and methyl methacrylate) present in the substance would be less than 0.76 µg/kg bw/day (expressed as methacrylic acid) for adults, and less than 0.54 µg/kg bw/day (expressed as methacrylic acid) for children. The Panel noted that these figures are far below the group Tolerable Daily Intake (TDI) of 0.1 mg/kg bw/day (expressed as methacrylic acid) for these monomers as established by the SCF."

„The NOAELs derived from the available studies are: 1000 mg/kg bw/day from a developmental study in the rat (single dose level tested) and 1500 mg/kg bw/day from a 26-week feeding study in the rat (highest dose tested). Using this range of NOAELs and assuming the highest coating level (100 mg/tablet) and a combined exposure from food supplements and pharmaceuticals of 23.4 mg/kg bw/day for a 60 kg adult, and 16 mg/kg bw/day for children (4-18 years), the Panel calculates a margin of safety (MOS) for heavy users varying from at least 43 to 64 for adults and from 63 to 94 for children. If only the exposure from food supplements is considered, the MOS ranges from 85 to 128 for adults and from 125 to 188 for children. Given the high molecular weight of the substance, its lack of absorption, the fact that the MOS values are based on NOAELs that were the highest dose levels tested and that the exposures estimates were worst case, the Panel considers these MOS values sufficient.

Other information (as necessary/identified)

None

10. Date on which data could be submitted to JECFA

As soon as necessary.

Attachments:

1. AMC_Commercial specification_Eudraguard biotic.pdf
2. AMC_EFSA opinion.pdf