FEED UNIT

SCIENTIFIC PANEL ON ADDITIVES AND PRODUCTS OR SUBSTANCES USED IN ANIMAL FEED

MINUTES OF THE 153rd FEEDAP PLENARY MEETING

Webconference, 17-18 March 2021

(Agreed by written procedure on 26 March 2021)

Participants

- **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.

- **Hearing Experts:**

  Not applicable

- **European Commission**

  Not applicable

- **EFSA:**

  Feed Unit: Angelica Amaduzzi, Montserrat Anguita, Rosella Brozzi, Jaume Galobart, Lucilla Gregoretti, Davide Guerra, Matteo Lorenzo Innocenti, Gloria López-Gálvez, Elisa Pettenati, Paola Manini, Jordi Ortuño, Fabiola Pizzo, Joana Revez, Jordi Tarrés-Call, Frank Verdonck and Maria Vittoria Vettori.

- **Others:**

  Not applicable

1. Welcome and apologies for absence

The Chair welcomed the participants. No apologies were received. Jordi Ortuño was introduced to the Panel as a new Scientific Officer in the FEED Unit.

2. Adoption of agenda

The agenda was adopted without modifications.

European Food Safety Authority
Via Carlo Magno 1A – 43126 Parma, Italy
Tel. +39 0521 036 111
info@efsa.europa.eu | www.efsa.europa.eu

3. Declarations of Interest of Panel members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Panel members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

4. Report on written procedures since the 152nd FEEDAP Plenary meeting

The minutes of the 152nd FEEDAP Plenary meeting were agreed by written procedure on 16 February 2021[3].

5. Scientific topics for discussion

5.1. Botanically defined flavourings from Botanical Group 12 - Gentianales for all animal species and categories: gentian tincture (EFSA-Q-2011-00182)

This question refers to the authorisation under Article 4 and re-evaluation under Article 10 of Regulation (EC) No 1831/2003 of Botanically defined flavourings from Botanical Group 12 – Gentianales: gentian tincture as a sensory additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.2. *Bacillus amyloliquefaciens* DSM 25840 for all animal species (EFSA-Q-2017-00722)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of *Bacillus amyloliquefaciens* DSM 25840 as a technological additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.3. Bafasal® (preparation of four bacteriophages infecting *Salmonella enterica* ser. Gallinarum 1) for all avian species (EFSA-Q-2017-00724)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of Bafasal® (preparation of four bacteriophages infecting *Salmonella enterica* ser. Gallinarum 1) as a zootechnical additive for all avian species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.4. *Bacillus subtilis* DSM 32324 for all animal species (EFSA-Q-2017-00744)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of *Bacillus subtilis* DSM 32324 as a technological additive for all animal species.

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1 Policy on Independence
2 Competing Interest Management
3 https://www.efsa.europa.eu/sites/default/files/2021-02/152nd-plenary-meeting-feedap-panel-minutes.pdf

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.5. *Bacillus subtilis* DSM 32325 for all animal species (EFSA-Q-2017-00745)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of *Bacillus subtilis* DSM 32325 as a technological additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.6. *Ginkgo biloba* L. extract for cats and dogs (EFSA-Q-2018-00318)

This question refers to the re-evaluation under Article 10 of Regulation (EC) No 1831/2003 of *Ginkgo biloba* L. extract as a sensory additive for cats and dogs.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.7. *Panax ginseng* C.A. Mey. for cats and dogs (EFSA-Q-2018-00320)

This question refers to the re-evaluation under Article 10 of Regulation (EC) No 1831/2003 of *Panax ginseng* C.A. Mey. as a sensory additive for cats and dogs.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.8. *Arctium lappa* extract for cats and dogs (EFSA-Q-2018-00439)

This question refers to the re-evaluation under Article 10 of Regulation (EC) No 1831/2003 of *Arctium lappa* extract as a sensory additive for cats and dogs.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.9. Iron chelate of ethylenediamine for all animal species (EFSA-Q-2018-01016)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of Iron chelate of ethylenediamine as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.10. Danisco Xylanase 40000 G/Danisco Xylanase 40000 L (endo-1,4-β-xylanase) for all ducks, all other poultry species (except breeders), piglets (weaned, suckling), pigs for fattening and minor growing porcine species (EFSA-Q-2018-01039)

This question refers to the authorisation under Article 4, the modification of the conditions of the authorisation under Article 13 and the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of Danisco Xylanase 40000 G/Danisco Xylanase 40000 L (endo-1,4-β-xylanase) as a zootechnical additive for all ducks, all other poultry species (except breeders), piglets (weaned, suckling), pigs for fattening and minor growing porcine species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.11. Copper chelate of ethylenediamine for all animal species (EFSA-Q-2019-00059)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of copper chelate of ethylenediamine as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.12. ECONASE® XT (endo-1,4-β-xylanase) for piglets (weaned), pigs for fattening, chickens for fattening, chickens reared for laying, laying hens, turkeys for fattening, turkeys reared for breeding and minor poultry species (EFSA-Q-2019-00330)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of ECONASE® XT (endo-1,4-β-xylanase) as a zootechnical additive for piglets (weaned), pigs for fattening, chickens for fattening, chickens reared for laying, laying hens, turkeys for fattening, turkeys reared for breeding and minor poultry species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.13. L-Lysine monohydrochloride/Concentrated liquid L-Lysine produced by fermentation with *Corynebacterium glutamicum* KCCM 80183 for all animal species (EFSA-Q-2019-00411)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of L-Lysine monohydrochloride/Concentrated liquid L-Lysine produced by fermentation with *Corynebacterium glutamicum* KCCM 80183 as nutritional additives for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additives. The Panel unanimously adopted the opinion.

5.14. Enviva® PRO 202 GT (*Bacillus amyloliquefaciens* PTA-6507, *Bacillus amyloliquefaciens* NRRL B-50013 and *Bacillus amyloliquefaciens* NRRL B-50104) for turkeys for fattening (EFSA-Q-2019-00457)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of Enviva® PRO 202 GT (*Bacillus amyloliquefaciens* PTA-6507, *Bacillus amyloliquefaciens* NRRL B-50013 and *Bacillus amyloliquefaciens* NRRL B-50104) as a zootechnical additive for turkeys for fattening.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.15. KemTRACE™ Chromium (chromium propionate) (EFSA-Q-2019-00804)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of KemTRACE™ Chromium (chromium propionate) as a zootechnical additive for all growing poultry species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.16. Vitamin E/all-rac-α-tocopherol acetate for all animal species (EFSA-Q-2020-00005)

This question refers to the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of Vitamin E/all-rac-α-tocopherol acetate as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.17. Vitamin E/all-rac-α-tocopheryl acetate for all animal species (EFSA-Q-2020-00136)

This question refers to the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of Vitamin E/all-rac-α-tocopheryl acetate as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.18. Vitamin K_1 (phytomenadione) for horses (EFSA-Q-2020-00142)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of Vitamin K_1 (phytomenadione) as a nutritional additive for horses.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.19. Vitamin E/all-rac-α-tocopheryl acetate (3a700) for all animal species (EFSA-Q-2020-00146)

This question refers to the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of Vitamin E/all-rac-α-tocopheryl acetate as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.20. Vitamin E/all-rac-α-tocopheryl acetate for all animal species (EFSA-Q-2020-00148)

This question refers to the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of Vitamin E/all-rac-α-tocopheryl acetate as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.21. RRR-α-tocopherol acetate for all animal species (EFSA-Q-2020-00156)

This question refers to the renewal of the authorisation under Article 14 of Regulation (EC) No 1831/2003 of RRR-α-tocopherol acetate as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.22. Plexomin® L-Fe (ferrous lysinate sulfate) for all animal species (EFSA-Q-2020-00169)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of Plexomin® L-Fe (Ferrous lysinate sulfate) as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.23. L-lysine monohydrochloride and L-lysine sulphate from *Corynebacterium glutamicum* CCTCC M 2015595 for all animal species (EFSA-Q-2020-00265)

EFSA was requested to deliver an opinion on the safety of L-lysine monohydrochloride and L-lysine sulphate from *Corynebacterium glutamicum* CCTCC M 2015595 as nutritional additives for all animal species based on the additional information provided by the applicant.

The draft opinion was discussed focusing on the characterisation and safety of the additives. The Panel unanimously adopted the opinion.

5.24. L-valine for all animal species (EFSA-Q-2020-00375)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of L-valine as a nutritional additive for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.25. AVIMATRIX® Z (preparation of benzoic acid, calcium formate and fumaric acid) for all avian species other than laying birds (EFSA-Q-2020-00546)

This question refers to the authorisation under Article 4 of Regulation (EC) No 1831/2003 of AVIMATRIX® Z (preparation of benzoic acid, calcium formate and fumaric acid) as a zootechnical additive for all avian species other than laying birds.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additive. The Panel unanimously adopted the opinion.

5.26. Botanically defined flavourings from Botanical Group 08 - Sapindales for all animal species and categories: expressed lemon oil and its fractions and lime oil (EFSA-Q-2021-00126)

This question refers to the authorisation under Article 4 and re-evaluation under Article 10 of Regulation (EC) No 1831/2003 of Botanically defined flavourings from Botanical Group 08 - Sapindales: expressed lemon oil and its fractions and lime oil as sensory additives for all animal species.

The draft opinion was discussed focusing on the characterisation, safety and efficacy of the additives. The Panel unanimously adopted the opinion.

6. New mandates

6.1. New Applications under Regulation (EC) 1831/2003 since the previous meeting

The Commission has forwarded to EFSA the following new applications of feed additives seeking authorisation under Regulation (EC) No 1831/2003 since the last Plenary meeting. These applications were presented to the Panel:

EFSA-Q-Number	Subject
EFSA-Q-2021-00074	Coxidin (monensin sodium (carrier Perlite, calcium carbonate)) for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding
EFSA-Q-2021-00075	Natupulse® TS/Natupulse® TS L (endo-1,4-beta-D-mannanase) for chickens for fattening, turkeys for fattening, minor growing poultry species, other poultry for fattening (e.g. ducks, geese, pheasants, quail, guinea fowl, ostrich), ornamental birds
EFSA-Q-2021-00076	*Lactiplantibacillus plantarum* E-98 NCIMB 30236 for all animal species
EFSA-Q-2021-00082	*Lactococcus lactis* NCIMB 30160 for all animal species
EFSA-Q-2021-00084	IMP (disodium 5'-inosinate) produced by fermentation with *Corynebacterium stationis* KCCM 80235 for all animal species
EFSA-Q-2021-00086	L-lysine sulphate produced by *E. coli* CGMCC 7.398 for all animal species
EFSA-Q-2021-00095	Plexomin® L-Mn (manganese lysinate sulfate) for all animal species
EFSA-Q-2021-00097	PB6 (*Bacillus velezensis* ATCC PTA-6737) for turkeys for fattening, turkeys reared for breeding, piglets (weaned), weaned minor porcine species, laying hens, minor poultry species for laying, sows in order to have benefits in piglets
EFSA-Q-2021-00098	Xygest™ HT (endo-1,4-beta-xylanase (EC 3.2.1.8)) for poultry
EFSA-Q-2021-00099	NS AH007 (*Bacillus velezensis* (deposited as *B. amyloliquefaciens*; NRRL-B-50910), *Pediococcus acidilactici* (NRRL-B-50959) and *Pediococcus acidilactici* (NRRL-B-50964)) for chickens for fattening, chickens reared for laying
EFSA-Q-2021-00101	Ammonium chloride AF animal feed grade (ammonium chloride) for cats, dogs and ruminants
EFSA-Q-2021-00102	KDF preservative (potassium diformate) for all animal species

6.2. Valid applications under Regulation (EC) No 1831/2003 since the previous meeting

Applications considered valid for the start of the assessment:

EFSA-Q-Number	Subject	Valid on
EFSA-Q-2020-00462	Protural Granular, Protural Powder (sodium benzoate) for weaned piglets and other growing suidae	12/02/2021
EFSA-Q-2020-00598	Blend of grape (*Vitis vinifera* L.) and wild blueberry (*Vaccinium angustifolium* A.) extracts (FLAMORE)	17/02/2021
EFSA-Q-2020-00708	L-lysine sulphate produced by *C. glutamicum* KCCM 80227 (DK257RN) for all animal species	19/02/2021
EFSA-Q-2020-00728	Rosemary extract for cats and dogs	11/03/2021
EFSA-Q-2020-00767	Axtra® PHY GOLD 30 L, Axtra® PHY GOLD 30 T, Axtra® PHY GOLD 65 G (6- phytase) for all pigs, all poultry species	08/03/2021
EFSA-Q-2020-00807	AveMix XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) for piglets (suckling and weaned piglets)	03/03/2021
EFSA-Q-2020-00809	Butylated hydroxyanisole (BHA) for cats	26/02/2021
EFSA-Q-2020-00814	*Pediococcus acidilactici* DSM 16243 for all animal species	17/02/2021
EFSA-Q-2020-00815	Amoklor™ (ammonium chloride) for all ruminants, sows for urinary health, cats and dogs	17/02/2021
EFSA-Q-2020-00835	Biomin® DC-P (Preparation of carvacrol, thymol, D-carvone, methyl salicylate and L-mentho) for all avian species	08/03/2021
EFSA-Q-2020-00841	Vitamin E/all-rac-α-tocopheryl acetate for all animal species	17/02/2021
EFSA-Q-2020-00843	CI-FER (ferric citrate chelate) for chickens for fattening, chickens reared for laying, turkeys reared for breeding, turkeys for fattening, all minor poultry species for rearing (up to slaughter or point of lay)	17/02/2021
EFSA-Q-2020-00845	*Pediococcus pentosaceus* DSM 12834 for all animal species	09/03/2021
EFSA-Q-2020-00847	*Lactobacillus acidophilus* D2/CSL (CECT 4529) for all poultry species and categories and all ornamental birds	09/03/2021
EFSA-Q-2021-00074	Coxidin (Monensin sodium (carrier Perlite, Calcium carbonate)) for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding	08/02/2021
EFSA-Q-2021-00075	Natupulse® TS / Natupulse® TS L (endo-1,4-beta-D-mannanase) for chickens for fattening, turkeys for fattening, minor growing poultry species, other poultry for fattening (e.g. ducks, geese, pheasants, quail, guinea fowl, ostrich), ornamental birds	01/03/2021
EFSA-Q-2021-00082	*Lactococcus lactis* NCIMB 30160 for all animal species	02/03/2021
EFSA-Q-2021-00086	L-Lysine sulphate produced by *E. coli* CGMCC 7.398 for all animal species	16/02/2021

EFSA-Q-Number	Subject	Valid on
EFSA-Q-2021-00101	Ammonium chloride AF animal feed grade (Ammonium chloride) for cats, dogs and ruminants	02/03/2021
EFSA-Q-2011-00188	Botanically defined flavourings from Botanical Group 16 - Rosales: Hawthorne tincture, Dropwort tincture, Hop tincture, Tormentill tincture, Rose tincture, Black berry tincture, Common nettle extract (sb), Common nettle extract (wb), Dwarf nettle tincture	09/03/2021

These applications were assigned to the respective working groups, where relevant.

6.3. New questions under Regulation (EC) No 178/2002 since the previous meeting

EFSA-Q-Number	Subject
EFSA-Q-2020-00644	Iron Oxide Red, Black & Yellow for all animal species
EFSA-Q-2021-00103	Coxar® (nicarbazin) for turkeys for fattening
EFSA-Q-2021-00104	Coxar® (Nicarbazin) for turkeys for fattening
EFSA-Q-2021-00109	Acetic acid for all animal species

These questions were assigned to the respective working groups, where relevant.

7. Feedback from Scientific Committee/Scientific Panels, EFSA or the European Commission

7.1. Scientific Committee/Scientific Panels

a) The SubWG on Growth Promotion of the WG on maximum levels of cross-contamination for 24 antimicrobial active substances in non-target feed provided an update of the work and presented the first draft assessments for two antimicrobials. These will be tabled for possible endorsement in the next plenary meeting.

7.2. EFSA

a) Update on the implementation of Transparency Regulation

The Head of Unit provided details on the practical implementation of the Transparency Regulation, including the general pre-submission advice, the pre-submission advice for renewals, notification of studies and proactive publication of data.

7.3. European Commission

Not discussed.

8. Other scientific topics for information/or discussion

a) Criteria for the assessment of efficacy for additives belonging to the functional group "hygiene condition enhancers"

The Panel discussed a proposal for the assessment of the efficacy of additives belonging to the functional group "hygiene condition enhancers" within the category of technological additives. The Panel agreed on the criteria, which are included in Annex 1. The FEEDAP Panel may review the approach above in view of the experience gained in the assessment of these additives. This material will also be used in a future update of the guidance on the assessment of the efficacy of feed additives.

b) General approach to assess the safety for the target species of botanical preparations which contain compounds that are genotoxic and/or carcinogenic

In the frame of the assessment of some botanical preparations intended to be used as feed additives, the Panel identified that some of these contain substances that are genotoxic and/or carcinogenic. These substances are naturally present in plants and their presence in low concentrations in botanical preparations intended for use as feed additives cannot be fully avoided. The Panel discussed on how to consider them in the assessment of the safety of the target animals. The Panel agreed on the methodology described in Annex 2. The Panel will apply this approach on a case by case basis and may review it in view of the experience gained in the assessment of these additives.

9. Any other business

a) The Panel agreed on the dates of the plenaries for 2022: 25-27 January, 22-24 March, 3-5 May, 28-30 June, 27-29 September, 22-24 November.

Annex 1

Criteria for the assessment of efficacy of feed additives from the functional group of hygiene condition enhancers

Hygiene condition enhancers are defined by Regulation (EC) No 1831/2003 as "substances or, when applicable, microorganisms which favourably affect the hygienic characteristics of feed by reducing a specific microbiological contamination." These additives are intended to have an effect in feed by reducing the contamination with specific microorganism(s) relevant to feed safety (e.g., potential human or animal enteropathogens or harmful or potentially harmful bacteria) (EFSA FEEDAP Panel, 2018).

The target microorganism(s) against which the additive will exert its function should be specified, as well as the feeds where the additive should exert its function.

Evidence of the efficacy should be demonstrated using laboratory-based studies by means of appropriate criteria as reflected in recognised acceptable methods, under the intended practical conditions of use in comparison with appropriate control feed. The studies (at least three) should be designed to cover a representative range of feed matrices to which the additive will be applied. If the additive is intended for use in water for drinking, specific studies are required. For additives intended to be used in all feedingstuffs, efficacy should be demonstrated in feed matrices covering a range of approximately 10-80% dry matter (DM). The DM content and corresponding water activity of each matrix should be provided. The feeds may be naturally or artificially contaminated with the target microorganism(s). In case of artificially contaminated feed, the applicant should describe and justify the selection and inoculation levels of the microbial strain(s) used. Any pre-treatments not routinely used in the feed production/preparation and intended to reduce the background contamination of the experimental feed (e.g., sterilisation of the feeds, use of antimicrobial substances) or to stimulate the growth of the active agent(s) present in the additive (e.g., use of buffers and/or nutrient broths and incubation conditions optimal for the strain(s) but not relevant for the feed) should be avoided.

An appropriate number of replicates of the feed(s) should be stored in conditions mimicking practical use at EU farm level. Samples should be stored in the presence of oxygen (ambient) and at temperature(s) reflecting practical use conditions. Any deviations should be properly justified. Other practical use conditions should be reflected in the study design (e.g., constant mixing). The experimental design should include at least two groups: one group with the experimental feed contaminated with the target microorganism(s) (control) and the other with the same basal contaminated feed treated with the additive for which authorisation is sought at the minimum recommended inclusion level. Other groups with different levels of the additive may be included in the design, if appropriate. The microbial contamination with target microorganisms should be present in the feed at the time the additive is incorporated into it. Alternatively, in case of artificial contamination, both the target microorganism(s) and the additive should be added at the same time.

The duration of the study should cover the period for which an effect is claimed according to the proposed conditions of use (e.g., for reconstituted milk replacer, the study should last until time of feeding). Sampling times should reflect real use conditions, allow measurement of the persistence of the effect(s) and include at least measurements at time 0 (treatment with the additive) and at the end of the study. Feed samples should be monitored for the viable counts of the target microorganism(s) using cultivation-based methods. Changes below 0.5 log are considered in the normal variation of the methods and will not be taken as a proof of an effect. Other endpoints intended to monitor the microbial quality of the feed should be included (e.g., total aerobic bacteria,

Enterobacteriaceae, yeast and filamentous fungi counts). For target microorganisms producing toxic compounds, these compounds should also be analysed in the feed samples at the end of the study.

Reference

EFSA FEEDAP Panel (EFSA Panel on additives and products or substances used in animal feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, Lopez-Alonso M, Lopez Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J, Innocenti ML and Martino L, 2018. Guidance on the assessment of the efficacy of feed additives. EFSA Journal 2018;16 (5):5274, 25 pp. https://doi.org/10.2903/j.efsa.2018.5274

Annex 2

General approach to assess the safety for the target species of botanical preparations which contain compounds that are genotoxic and/or carcinogenic when used as feed additives

In the framework of the assessment of feed additives under Regulation (EC) No 1831/2003,[4] the European Commission requested EFSA to undertake a risk assessment of feed additives of botanical origin. Among these botanical preparations, the FEEDAP Panel has identified some additives which naturally contain substances that are genotoxic and/or carcinogenic.

The EFSA Scientific Committee indicated repeatedly that "substances which are both genotoxic and carcinogenic should not be approved for deliberate addition to foods or for use earlier in the food chain, if they leave residues which are both genotoxic and carcinogenic in food" (EFSA, 2005; EFSA SC, 2012).

Since these substances are naturally present in plants, their presence in low concentrations in botanical preparations intended for use as feed additives cannot be fully avoided and therefore has to be addressed in the assessment of the safety of the target animals, the consumer and the user. In any case, manufacturing processes of botanical feed additives should avoid selective extraction and enrichment of genotoxic and/or carcinogenic substances and should aim at the reduction of these substances. The Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements" (EFSA SC, 2009) states that "In cases …where the botanical ingredient contains substances that are both genotoxic and carcinogenic, the "Margin of Exposure" (MOE) approach (EFSA, 2005) could be applied covering the botanical(s) under examination and any other dietary sources of exposure. The MOE approach compares toxic effect levels with human exposure levels. Alternatively, it could be evaluated whether the expected exposure to the genotoxic and carcinogenic ingredient is likely to be increased, compared to the intake from other sources."

Considering the above and in order to address the request of the European Commission, the FEEDAP Panel decided to extend the methodology based on the MOE approach developed by EFSA for human risk assessment of impurities which are both genotoxic and carcinogenic in substances added to food/feed (e.g. unavoidable contaminants or by-products resulting from a production, process) to animal risk assessment of botanical preparations intended for use as feed additives (EFSA SC, 2019a).[5]

The methodology applied to the assessment of the **safety for the target species** of botanical preparations containing substances that are both genotoxic and/or carcinogenic depends on the available dataset on carcinogenicity studies in rodents. Three scenarios are considered possible:

(i) for substances for which carcinogenicity studies in rodents are available, from which a $BMDL_{10}$ can be derived, the MOE approach (EFSA, 2005; EFSA SC, 2012) can be applied. Similarly, to human risk assessment, a combined (total) margin of exposure (MOET) with a magnitude of ≥ 10,000, when comparing estimated exposure to genotoxic and/or carcinogenic substances with a $BMDL_{10}$ from a rodent carcinogenicity study, would be indicative of a low concern for the target species (EFSA SC, 2019a)

(ii) when carcinogenicity studies in rodents are not available or would not allow the identification of a reference point to be used in the risk assessment, the threshold of toxicological concern (TTC) concept for genotoxic substances can be applied. Similarly, to human risk assessment, for substances that have the potential to be DNA-reactive mutagens and/or carcinogens based on the weight of evidence, (combined) estimated

[4] 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

[5] The proposed methodology was discussed in EFSA Scientific Committee in November 2020 and endorsed for further work strategy by the FEEDAP Panel https://www.efsa.europa.eu/sites/default/files/event/2020/101st-plenary-meeting-scientific-committee-minutes.pdf

exposures below the TTC value of 0.0025 µg/kg bw per day would be indicative of low probability of adverse effects (EFSA SC, 2019b)

(iii) when carcinogenicity studies are not available, it could be evaluated whether the exposure to these substances of concern is likely to be increased by the use of the feed additive compared to the intake from other dietary sources. For those animal species that are fed relevant plant materials as part of daily feed, a minimal increase[6] of the intake of these substances via the feed use of the additive of botanical origin would be indicative of low probability of additional risk

The FEEDAP Panel notes that genotoxicity and carcinogenicity are relevant endpoints for long-living animals (e.g. companion animals, racing horses, reproduction animals), whereas in the case of short-living animals (e.g. animals for fattening) the relevance of these endpoints could be negligible (EFSA SC, 2017). The short lifespan of animal species for fattening under farming conditions makes it very unlikely that these develop cancer as a result of the exposure to genotoxic and/or carcinogenic substances in the diet. Therefore, a comparison of the exposure to these substances with a reference point/threshold based on other (non-neoplastic) endpoints could be more appropriate to assess the safety of the target animals.

For fattening animals, a different magnitude of the MOE(T) (e.g. a MOE(T) > 100 when comparing estimated exposure with a reference point based on non-neoplastic endpoints) or the application of the TTC for non-genotoxic substances is considered more appropriate.

Precondition for the applicability of this approach is the availability of ADME/residue data for the food-producing animal species to consider possible carry-over of genotoxic and/or carcinogenic substances to the animal-derived food products in the assessment of consumer safety.

The FEEDAP Panel underlines that the methodology is applicable only to the risk assessment of additives of botanical origin and cannot be extended to individual compounds intended to be added to feed as such.

The Panel will apply this approach on a case by case basis and may review it in view of the experience gained in the assessment of these additives.

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[6] This will be considered on a case by case basis

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