FEED INFO SESSION - 14th and 15th November 2019

Info session on applications for feed additives

Trusted science for safe food

efsa
European Food Safety Authority

Plenary session 1

Assessment of the efficacy of feed additives

Guidance on the assessment of the efficacy of feed additives

- Endorsed November 2017
- Public consultation December 2017-January 2018
- Adopted April 2018
- Implementation 1st September 2018

14 November 2019

European Food Safety Authority

FEEDAP Panel guidance on the assessment of the efficacy of feed additives

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Scientific Officer

Efficacy of feed additives

- **Simplification and harmonisation**
- **Reduction of animal testing**
- **End-points for all categories/functional groups**
- **More details on study designs/reporting**

Efficacy of feed additives

Simplification and harmonisation

- All requirements in one document
- General principles
- Exclusion criteria
- Requirements
- Harmonisation

rational for the assessment
means to provide evidence

each category/functional group

duration of the studies
number of studies

Efficacy of feed additives

Simplification and harmonisation

- General principles
  - additive(s) for which authorisation is sought
  - efficacy for each proposed use - at least one of the characteristics set out in Article 5(3) of Regulation (EC) No 1831/2003
  - evaluation of the efficacy of the additive according to common feed manufacturing, animal husbandry and farming practices in the EU

Efficacy of feed additives

Simplification and harmonisation

- General principles
  - additives for which efficacy is recognized: no further demonstration of efficacy
  - for others: the Panel may be able to conclude on the potential efficacy of the additive under EU farming conditions

Efficacy of feed additives

Simplification and harmonisation

- General principles
  - *in vitro* studies (effect on the characteristics of feed),
  - *in vivo* studies (effect on the animal/effect once ingested)
  - Published studies

    Active substance/agent
    - is identical to that under application
    - or would still allow conclusions on the additive under application to be made.

Efficacy of feed additives

Simplification and harmonisation

- Exclusion criteria
  - Technological additives
  - Sensory additives
- additive already authorised for use in food
- the intended use of the additive in feed is the same
- the effect seen when used in food could reasonably be expected to be seen when used in feed at the recommended concentration
- food and feed matrices are of comparable nature
- **No further demonstration of efficacy is generally necessary**

Efficacy of feed additives

Simplification and harmonisation

- Exclusion criteria
  - Nutritional additives

No evidence of efficacy is necessary for amino acids naturally occurring in proteins of plants and animals and their salts, urea and vitamins, pro-vitamins and compounds of trace elements

- amino acid analogues, new forms of compounds of trace elements, chemically well-defined substances having similar effect to vitamin, and urea derivatives
- other (novel) nutritional additives

One study in a single animal species or category including laboratory animals

Efficacy of feed additives

Simplification and harmonisation

- Requirements
  - For each category functional group:
    - *in vitro / in vitro + in vivo / in vivo*

    (e.g., technological, technological which exert their function in the animal, zootechnical additives)
    - long term or short term studies
  - Specific requirements for coccidiostats and histomonostats
    - Three floor pen/battery cage studies
    - Three anticoccidial sensitivity tests/field trials

Efficacy of feed additives

Simplification and harmonisation

- Duration of the studies
  - *In vitro vs in vivo*
  - *In vitro* – the conditions of use and intended effect
  - *In vivo* - Shorth term vs long term studies
  - Short term studies
    - Duration shorter than the one indicated for the respective species/categories for the long term studies

Efficacy of feed additives

Simplification and harmonisation

- Duration of the studies
  - Long term studies

Category	Definition of the animal category	Start	Minimum duration
Piglets (weaned)	Young animals having completed the suckling period	≤ 7 days after weaning	**42 days** **35 days if growth rate is ≥ 0.5 kg/day**
Pigs for fattening	Animals intended for meat production until day of transport to slaughterhouse	≤35 kg	**Until slaughter, but not less than 70 days**
Sows	Female animals having been inseminated/mated	Insemination/ mating	**For effects on reproduction: two cycles (from insemination/mating until weaning).** **For effects on piglets, preferably at least two weeks before parturition until weaning**

Efficacy of feed additives

Simplification and harmonisation

- Duration of the studies

Category	Definition of the animal category	Start	Minimum duration
Laying hens	Productive female birds held for egg production purposes	22-25 weeks of age	**84 days**
Turkeys for fattening	Birds raised for fattening	1 day of age	**84 days**
Calves	Calves which are reared for reproduction, veal production or beef production	1-4 weeks of age	**56 days**
Cattle	Bovine animals that have completed the weaning period	Full development of rumination but ≤ 6 months of age	**84 days**
Cows	Lactating cows	4-8 weeks after calving	**84 days**
Lambs/kids	Young animals reared for reproduction or meat production	1-4 weeks of age	**56 days**

Efficacy of feed additives

Simplification and harmonisation

Reduction of animal testing

- Number of studies
  - Generally a minimum of 3 studies is requested….
  - effect on the characteristics of feed:
  - **at least three *in vitro* studies**
  - effect on the animal/effect once ingested:
  - **at least three in *vivo* studies in each animal species/category**

Efficacy of feed additives

- Extrapolation to physiologically related species

Chickens for fattening	other poultry for fattening (e.g., turkeys, ducks, geese, pheasants, quail, guinea fowl, ostrich) and ornamental birds
Laying hens	other birds kept for egg production or breeding (e.g., turkeys ducks, geese, pheasants, quail, guinea fowl, ostrich)
Piglets or pigs for fattening	other growing Suidae
Sows	other reproductive Suidae
Calves or cattle for fattening	other growing ruminants (e.g., sheep, goat, buffalo) at the corresponding developmental stage
Dairy cows	other dairy ruminants (e.g., goat, sheep, buffalo)
Salmon or trout	ornamental fish
Horses	other Equidae
Rabbits	other Leporidae

Efficacy of feed additives

Reduction of animal testing

All Poultry

All Pigs

All ruminants

All fin fish

Efficacy of feed additives

- Multiple species/categories

All growing poultry species	3 in chickens for fattening
All poultry species	3 in chickens for fattening 3 in laying hens
All growing pigs	3 in weaned piglets 3 in pigs for fattening
All pigs	3 in weaned piglets 3 in sows
All growing ruminants	3 in calves 3 in cattle for fattening
All ruminants	3 in calves 3 in cows
All fin fish	3 in salmonids (salmon or trout) 3 in other species (1 in each)
Crustaceans	3 in shrimp/crustaceans
Rabbits (growing and reproductive)	3 (growing and reproductive)

Efficacy of feed additives

- Multiple species/categories

All growing poultry species	3 in chickens for fattening
All poultry species	3 in chickens for fattening 3 in laying hens
All growing pigs	3 in weaned piglets 3 in pigs for fattening
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Efficacy of feed additives

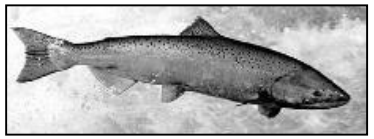
Reduction of animal testing

All Poultry

All Pigs

All ruminants

All fin fish



Pets/non food-producing animals

Efficacy of feed additives

End-points for all categories/functional groups

- Additive which require *in vitro* studies
  - End-points related to the expected effect

Functional group	Demonstration of efficacy
Preservatives	**Inhibition of the growth of spoilage microorganisms. Duration of the study should cover the period for which an effect is claimed. Test materials could be naturally or artificially contaminated.**
Antioxidants	**Protection against oxidative damage of key nutrients/components during feed processing and/or storage. The period for which a protective effect is claimed should be demonstrated.**
Emulsifiers	**Formation/maintenance of stable emulsions of otherwise immiscible or poorly miscible feed ingredients.**

Efficacy of feed additives

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End-points for all categories/functional groups

- Additive which require *in vivo* studies
  - Additives which exert their effect once ingested

Target mycotoxin(s)	Most relevant end-points
Aflatoxin B_1	Aflatoxin M_1 in milk/egg yolk
Deoxynivalenol	DON/metabolites in blood serum
Zearalenone	Zearalenone + α- and β-zearalenol in plasma Excretion of zearalenone/metabolites
Ochratoxin A	Ochratoxin in kidney (or blood serum)
Fumonisins B1+B2	Sphinganine/sphingosine ratio in blood, plasma or tissues

Efficacy of feed additives

End-points for all categories/functional groups

- Additive which require *in vivo* studies

- **Bioavailability/bioequivalence studies**
  - Specific endpoints
- **Digestion/balance studies**
  - digestibility (e.g., apparent or true, faecal or ileal) and/or retention of a specific nutrient/energy
- **Palatability studies**
  - Feed consumption/choice

Efficacy of feed additives

End-points for all categories/functional groups

- Additive which require *in vivo* studies

Performance: Feed intake, initial and final body weight, body weight gain, feed to gain ratio, *water intake*. Clinical observations including general health status, morbidity and mortality (including culling).

Hygiene quality of food products: e.g. numbers of spoilage organisms, potential human or animal enteropathogens

Environmental effects: reduction on methane, ammonia, carbon dioxide emissions, reduction odour or odorous compounds

Efficacy of feed additives

Study design

- **Animals, housing and husbandry**

- **Animals:** species (for aquatic species intended for human consumption: identification should be made by their colloquial name followed in parenthesis by the Latin binomial), breed, age (and size/length for aquatic species), initial body weight, sex, identification procedure, physiological stage and general health.

- **Husbandry conditions:** feeding and rearing conditions (pen/tank size, stocking density, temperature, lighting); for aquatic species water quality including water flow rate, water temperature and salinity, where relevant;

- **Diets:** description of manufacture and quantitative composition of the diet(s) in terms of ingredients used, relevant nutrients (calculated and analysed values) and energy (digestible, metabolisable or net). In addition for studies with enzymes, the diets should be analysed for the enzyme-specific substrate.

Efficacy of feed additives

Study design

1) Study location, dates and responsible individuals.
2) Study duration.
3) The type of design of the study (e.g. factorial, stratified, cross-over).
4) Experimental groups: number of treatment and control groups, numbers of replicates (experimental unit) per group and number of animals per replicate.
5) The experimental unit (e.g., individual animal, pen) should be indicated.
6) The basis for the different measurements (e.g., individual animal, pen) should be indicated for each parameter measured.
7) Rationale for the selection of the number of animals/replicates used.
8) Steps taken to minimise bias including randomisation and blinding Test item: intended concentration of the active substance(s) or agent(s) in the feedingstuffs.
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Efficacy of feed additives

Study design

Efficacy

- **Minimum recommended use level**
- **Facultative: other use levels (higher or lower)**

4) Experimental groups: number of treatment and control groups, numbers of replicates (experimental unit) per group and number of animals per replicate.

Control group

- **Negative control group**
- **Facultative: positive control**

e indicated for

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Efficacy of feed additives

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Number of animals/replicates

- Sample size calculation
- Difference testing vs non-inferiority

tem: intended

ngstuffs.

Efficacy of feed additives

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What's new

- One document
- Harmonised requirements
- Reduction animal testing
- Clear instruction
- Transparent assessment

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Thank you!