Guidance for trials using feed additives not authorised

Guidance summary for trials using feed additives not authorised

This guidance is intended to support individuals interested in conducting a field trial, including the application submission process.

Purpose of the guidance

This guidance is intended to support individuals interested in conducting a field trial, including the application submission process.

Only feed additives which are authorised may be placed on the market, processed or used. A definition of feed additives is available.

Feed additives which are not authorised may be used for a scientific trial only following the approval of an application made to either the Food Standards Agency (FSA) or Food Standards Scotland (FSS).

Prior to EU exit, the FSA was the competent authority carrying out animal feed trial authorisations on behalf of UK. Following EU exit, the decision to approve trials in GB transferred and now rests with respective Ministers. In accordance with Regulation (EC) 1831/2003) Article 3 (2) 'For experiments for scientific purposes, the appropriate authority (i.e. Ministers) may authorise the use, as additives, of substances which are not authorised, with the exception of antiobiotics, provided that the experiments are carried out in accordance with the principles and conditions laid down in Regulation 767/2009 or the guidance set out in in Article 7(4) of this Regulation and provided that there is adequate official supervision.

The animals concerned may be used for food production only if the authorities (i.e. FSA/FSS and Ministers) establish that this will have no adverse effect on animal health, human health or the environment'. Therefore, the final decision as to whether to authorise a trial and whether animals from the trial can enter the food chain lies with the Minister. The decision to approve trials in Northern Ireland (NI) is the FSA's responsibility.

These trials are specific to feed additives, and do not apply to other feedstuffs such as feed materials, which do not require authorisation before market use.

For coccidiostats and histomonostats, or any other substance that could be considered a veterinary medicine under the Veterinary Medicines Regulations (2013), as amended, please initially direct your query to the Veterinary Medicines Directorate (VMD: postmaster@vmd.gov.uk). To conduct a clinical field trial of a veterinary medicine in animals in GB and/or NI, i.e., under

normal conditions of animal husbandry or as part of routine veterinary practice, applicants must first be granted an Animal Test Certificate (ATC) by the VMD.

The applicant will need to consider whether a Home Office licence is required to undertake the feed trial, in addition to an agreement from the FSA; for example, if blood or rumen sampling is proposed during the trial. Please refer to the Home Office guidance on animal testing and research for more information about the licences required under the Animals (Scientific Procedures) Act (ASPA) 1986 to conduct ‘regulated’ scientific procedures in animals.

Legal status of the guidance

Regulatory Compliance: This Guidance is in compliance with all relevant assimilated EC regulations refrenced in the 'purpose' section of this page.

Who is this publication for?

- farmers and growers
- manufacturers and processors
- other (individuals or organisations intending to submit feed additive trial applications)

Which UK countries does this guidance apply to?

- England
- Wales
- Northern Ireland

Review date

We will review this guidance by April 2027.

Key words

- meat and livestock
- products (for example: eggs or milk from animals fed the additive)

Contact us

We welcome your feedback on this guidance.

Guidance for trials using feed additives not authorised

Only feed additives which are authorised may be placed on the market, processed or used. A definition of feed additives is available on the following link.

Application process

The process is set out in legislation (Article 3(2)) in assimilated Regulation (EC) 1831/2003 for trials in GB. Regulation (EC) 1831/2003 sets out the requirements for trials in NI. Both regulations allow for the use of non-authorised feed additives in trials.

Annexes II and III of assimilated Commission Regulation (EC) 429/2008 and for NI Regulation (EC) 429/2008 can be used as a guide as to what information might be submitted.

- For trials taking place in England, please submit your request and documentation to FeedAdditives@food.gov.uk
- For trials taking place in Wales, please submit your request and documentation to regulated.products.wales@food.gov.uk
- For trials taking place in Northern Ireland please submit your request and documentation to nioperationalpolicy@food.gov.uk
- For trials taking place in Scotland please submit your request and documentation to feedadditivetrials@fss.scot

FSA/FSS requests that feed additive trial applications are submitted at the earliest opportunity. If information required for the safety evaluation of the trial is not provided in the original submission, supplementary information will be requested and the application will be paused until supplementary information is received.

The FSA/FSS application process is expected to take 12 weeks, although timescales may vary depending on whether additional information is required.

The application process consists of an FSA/FSS review of the safety of the feed additive itself, and an appraisal of the trial design undertaken by an expert third party organisation in confidence.

All information shared by applicants will only be shared with those involved in the authorisation process as required. FSA/FSS complies to UK Privacy Laws, including the UK GDPR and Data Protection Act 2018.

Information required

England, Northern Ireland and Wales

WORD
View Animal feed trials application form as Word(Open in a new window) (97.45 KB)

Applicants must complete the trial application form and return to the FSA/FSS.

The trial (experimental) protocol- applicants must supply the full trial protocol when submitting an application.

Risk assessment of the animal feed trial

A risk assessment should be undertaken by the applicant and should include consideration of safety for humans, animals and the environment.. Supporting data may be required, for example characterisation information of the additive. Justification should be provided if any of these are not submitted. If further information is required, the applicant will be contacted by the FSA/FSS.

Any changes in trial will require an updated FSA/FSS trial protocol, to be sent to FSA/FSS. Once a trial is authorised, the experimental protocol cannot be amended.

Post trial animals entering the food chain

If applicants wish to place any trial animals into the food chain (control animals only or all animals) or products (e.g. eggs or milk from animals fed the additive) then this should be made clear in the trial protocol and the trial application form. Further information should be provided on the onward destination of the animals including; details of the registered onward farm, the growing on period before slaughter, the location of slaughter, and the withdrawal period from the unauthorised feed additive (pre-slaughter).

If animals are not to enter the food chain, following approval this decision cannot be changed.

Contact Details

- England: FeedAdditives@food.gov.uk
- Wales: regulated.products.wales@food.gov.uk
- Northern Ireland: nioperationalpolicy@food.gov.uk
- Scotland: feedadditivetrials@fss.scot

Relevant websites

- Animal feed additives
- Feed additives authorisation guidance
- GB Register of Feed Additives
- EU Feed Additives Register
- Gov.uk for home office licenses
- FSS webpage on feed trials in Scotland
- Veterinary Medicines Directorate (VMD) (for non-authorised coccidiostats and histomonostats or veterinary medicinal substances).
- For EU applications and rules on pre-notification please refer to: Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC (Text with EEA relevance)

Annex A: List of relevant legislation

- Regulation (EC) 1831/2003) Article 3 (2)
- Regulation 767/2009
- Regulation (EC) 429/2008
- Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC (Text with EEA relevance)

Advice to applicants on performing a risk assessment to submit in support of a UK

feed trial application for a non-approved feed additive

Applicants should submit a risk assessment relating to the intended feed trial.

Applicants should submit a risk assessment relating to the intended trial, using any evidence already held in relation to:

- Safety for the consumer
- Safety for the target species
- Safety for the environment
- Safety for the worker

It is understood that feed additives to be trialled will be at different stages of the R&D pipeline, and that a trial application will not contain all the final safety data required for a complete feed additive dossier. However, enough safety data should be provided, along with a relevant risk assessment, to address any concerns relating to safety for the target species, consumers, environment and workers, relevant for this trial application.

Safety for the consumer

Safety for the consumer applies if it is the intention to have subsequent animal products going into the food chain from trial animals exposed to the test item during the trial. In short, the applicant's risk assessment should consider the fate of the additive in the animal system, the toxicity of the additive and any relevant metabolites, the exposure of food consumers to these from consumption of the animal products, and the characterisation of the risk.

In cases where the active compound is present in a fermentation product, the whole fermentation formulation should be assessed, which should be identical to the product intended for the market.

If an additive has several active compounds, the safety of each should be assessed, and a discussion provided on potential combined effects. Residue studies should be undertaken on the final form of the product, including the combination of active compounds, to account for any metabolic interactions. For mixtures where potential active compounds cannot be each characterised, the combined mixture should be evaluated.

The risk assessment should evaluate consumer exposure following EFSA's guidance on the safety of feed additives for the consumers (Section 4). This should include establishment of a toxicological health-based guidance value (HBGV), such as an acceptable daily intake (ADI), an exposure assessment based on residue data in the edible animal products, and comparison of exposure to the HBG.

In certain cases, safety, ADME and residue studies are not required as outlined in Section 3 of EFSA's guidance on the safety of feed additives for the consumers.

In summary, studies that could be provided as evidence alongside the applicant's risk assessment include:

- An ADME study following Organisation for Economic C-operation and Development (OECD) Test Guideline (TG) No. 417. To show the metabolism of the test item(s) in laboratory animals and the intended target species as a basis for its toxicological evaluation. This study(s) should also establish the metabolism kinetics of the test item, e.g. major metabolites as potential marker residues.

- A baseline set of data to evaluate genotoxicity from a reverse mutation (OECD TG 471) and a micronucleus assay (OECD TG 487). These should then be complemented if appropriate by further studies to evaluate if the observed genotoxic result occurs in vivo. For example, a mammalian erythrocyte micronucleus test (OECD TG 474), a transgenic rodent somatic and germ cell gene mutation assay (OECD TG 488) and/or an in vivo Comet assay (OECD TG 489), as appropriate.
- (In order to reduce the number of test animals, a single study combining the analysis of different endpoints (e.g. micronucleus and comet assay) should be considered).
- A sub-chronic oral toxicity study (OECD TG 408).
- An in-vivo chronic oral toxicity study (OECD TG 452), if considered required based on the results of the sub-chronic toxicity study.
- A carcinogenicity study (OECD TG 451) or combined with a chronic toxicity study as per OECD TG 453), if there are indications for any potential carcinogenic effect.
- In-vivo reproductive and prenatal developmental toxicity studies if there are any indications for a potential effect on reproduction and/or development (OECD TG 416, a two-generation reproduction study or OECD TG 443, an extended one-generation reproductive toxicity study, and OECD TG 414, a test guideline for prenatal developmental toxicity studies.
- Other toxicology studies if there are potential adverse effects not adequately addressed by the above studies.
- Residue studies providing data for the relevant animal products to enter the food chain, using the highest inclusion concentration intended for the feed trial. A total and/or marker residue study should be undertaken following EFSA's guidance on the safety of feed additives for the consumer (Section 2.1.2). If relevant the marker residue should be derived from the ADME data and the established ratio of marker to total residues should be provided for the appropriate animal products.
- A literature review covering past published safety evaluations of the additive to complement the studies above or provide evidence that a new study is not required. Reviews should be undertaken and reported following the EFSA guidance by Glanville et al. (2014) .

Studies involving animals should respect the rules on animal welfare laid down by EU legislation (see Directive 63/2010/EU). Studies should not be repeated if data are already available.

Safety for the target species

All applications should address the safety implications for the target species within the risk assessment, following EFSA's guidance on the assessment of the safety of feed additives for the target species.

This should cover the intended inclusion concentration(s) for the trial and use data from toxicity data from repeated dose studies in laboratory animals and/or relevant tolerance studies if available. This should include studies from the published literature in the first instance. Reviews should be undertaken and reported following the EFSA guidance by Glanville et al. (2014).

Interspecies extrapolation of data can be used within the applicant's risk assessment if this extrapolation is between physiologically similar species (see Table 3 in EFSA's guidance on the assessment of the safety of feed additives for the target species4) and the margin of safety (the ratio of tolerated to maximum proposed use level) is established as ? 10 for the species used for the extrapolation. This extrapolation margin of safety criteria may be lower for certain additives such as e.g. organic acids, certain coccidiostats.

Any known interactions of the test item with other relevant feed ingredients, other additives or veterinary products should be described within the application.

In certain cases, safety studies are not required as outlined in Section 2 of EFSA's guidance on the assessment of the safety of feed additives for the target species.

If the application does not fully address the above guidance the applicant should indicate what monitoring and controls are in place to quickly identify and manage any adverse effects that occur during the trial.

Safety for the environment

All applications should consider and discuss risks to the environment regarding the trial. Please see EFSA guidance on safety for the environment. The FSA may use an external contractor to support the evaluation of this assessment.

Safety for the worker

All applications should consider and discuss risks to the worker regarding the trial. Please see EFSA guidance on safety for the users. The FSA may use an external contractor to support the evaluation of this assessment.

Other considerations for the risk assessment

The efficacy trial should be designed following recommendations laid out in FSA/FSS Guidance on the assessment of the efficacy of feed additives. The risk assessment should indicate whether the trial design complies with the relevant animal welfare regulations (e.g., (England) Reg 2007/2078, (Wales) Reg 2007/3070, (Scotland) 2010/388, (Northern Ireland) 2011/16 and 2012/156, EC Dir 2010/63, EC Dir 98/58, EC Dir 1999/74, EC Dir 2007/43, EC Dir 2008/119 and EC Dir 2008/120). A trial that is not shown to comply with these requirements will not be accepted as part of the application dossier.

Where an application contains an additive produced from a production microorganism the applicant should provide as much information as possible on the production processes. Furthermore, safety data should be provided relating to this process where relevant. For example, data to show absence of the host production organism and/or fermentation products in the final product. If the host production organism has previously shown to be safe, for example on the EFSA list of QPS recommended biological agents, but is genetically modified, then it should be shown in supporting evidence that the molecular characterisation of the genetic modification does not give rise to concern.

Where an application relates to a microorganism, for example a probiotic strain, or uses a production microorganism, molecular characterisation and phenotypic testing for antimicrobial resistance (AMR) should be provided. The molecular characterisation should include taxonomic identification, genotypic screening for AMR genes, and an assessment of antimicrobial production, toxigenicity and pathogenicity. Results should be interpreted in-line with EFSA guidance.

All supporting studies provided as evidence within the feed trial application should be undertaken and documented according to appropriate quality standards and should respect the rules on animal welfare laid down by retained EU legislation, particularly those listed in retained EU Directive 63/2010/EU. Studies should be compliant with the criteria established by a recognised, externally audited, quality assurance scheme (e.g. good laboratory practice (GLP) in accordance with retained EU Directive 2004/10/EC).

Where a trial uses a different or modified form of a test item cited in the referenced studies, equivalence of the trial test item to the test item in the studies cited should be demonstrated and the specific differences described.

We encourage the continuing development of new approach methodologies (NAMs) and Integrated Approaches to Testing and Assessment (IATA) including high throughput screening, omics and in silico computer modelling strategies (e.g. Artificial Intelligence (AI) and machine learning) for the evaluation of hazard and exposure towards safety to complement required toxicological data. This also advocates the Replacement, Reduction and Refinement (3Rs) of animals.

All information provided to the FSA/FSS in relation to an application will remain confidential.

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