Focus on European feed additives:
Complexity, change and challenges ahead

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Abstract
Feed additives have been legislated in the EU since 1970, originally under Directive 70/524. The first feed additive list was a copy-paste of food additives, many with technical functions such as feed conservation, anti-oxidant actions, or gelling effects, plus antimicrobial growth promotors and coccidiostats. There were many amendments over the following decades, but major changes arrived in the early 1990s, with the advent of feed enzymes and feed probiotics, revolutionary products that enabled radical changes in feed formulations as well as non-antibiotic approaches to gut health and animal performance. The food chain crises of the 1990s, especially mad cow disease (BSE – bovine spongiform encephalopathy), salmonella and dioxins also heralded a radical review of all food chain legislation, with major changes applied first to animal feed additives, then to food ingredients, enzymes and food additives.

A new feed additive regulation, Regulation 1831/2003, was one of the first legislative acts to emerge from Regulation 178/2002, the "General Food Law" regulation, followed by legislation on genetically modified organisms (GMOs), a feed hygiene regulation and a new feed regulation. All feed additives were subject to notification and re-evaluation by the European Food Safety Authority (EFSA), dossier deadlines in November 2010. In addition, Regulation 1831/2003 completed the EU prohibition of antimicrobial growth promoters. Amino acids, silage inoculants, and urea were reclassified as feed additives. There were around 11,000 notifications, condensed to around 500 dossiers for re-evaluation, a task that EFSA is still completing.

Today, the feed additive regulation covers technological, sensory, nutritional, zootechnical and coccidiostat categories of feed additives. EFSA is completing a detailed update of key guidance documents and the EU Commission is re-assessing the feed additive regulation after 15 years in force. The current changes and complexity of the authorisation procedures offer opportunities and challenges to applicants.

What is a feed additive?

In the EU a feed additive is defined as any substance, micro-organism, enzyme, or preparation, excluding feed materials and premixtures, which is intentionally added to feed or water in order to perform, in particular, one or more of the following functions:

- Favourably affect the characteristics of feed
- Favourably affect the characteristics of animal products
- Favourably affect the colour of ornamental fish and birds
- Satisfy the nutritional needs of animals
- Favourably affect the environmental consequences of animal production
- Favourably affect animal production, performance or welfare, particularly by affecting the gastro-intestinal flora or digestibility of feedingstuffs
- Exert a coccidiostatic or histomonostatic effect.

With the exception of coccidiostats and histomonostats, feed additives must not prevent, treat or cure diseases, and therefore are understood to target animals in good health.

Over the years, the categories of feed additives have grown and changed. For example, antimicrobial growth promoters were prohibited from 31 December 2005 and removed from the feed additive register. At the same time, amino acids, silage additives and urea were reclassified as feed additives. Since 2006 several additional categories of feed additives have been added or are pending to add, and indeed an applicant can propose a new category of feed additive at the time of submission (see Table 1).

Dossier applications and evaluations

Feed additive dossiers are submitted via the "one-door – one key" approach. The application is sent to the EU Commission, but the full technical dossier is submitted to EFSA for evaluation. The only fees paid are to the European Union Reference Laboratory (EURL), typically €6,000, and accompanied by reference samples of the feed additive. The EURL is responsible for evaluation of the analytical methods proposed by the applicant, for the feed additive, and for the feed additive in premixtures and feeds.

EFSA evaluates "quality", "safety" and "efficacy" of the feed additive, and in theory there is a six-month evaluation period. This is rarely achieved, due to EFSA "clock-stops" and EFSA work overload. The timescale from dossier submission to EU approval also depends on the quality of the dossier submitted and the nature of the feed additive. Pioneer dossiers may take longer, due to the additional challenges of being novel. EFSA "clock-stops" must be addressed within a set timeframe, though applicants can request extensions to generate the additional data requested. Applicants can assume three to five years from dossier submission to product launch.

The main EFSA evaluation is conducted in working groups (WGs), coordinated by the EFSA Scientific Secretariat, FEEDAP. A draft EFSA opinion is produced by the WG, then endorsed for publication by the EFSA FEEDAP Plenary Meeting. It is not uncommon for additional questions for applicants to arise at EFSA plenary meetings. The

Table 1: Categories of feed additives.*				
Technological	**Sensory**	**Nutritional**	**Zootechnical**	**Coccidiostats & histomonostats**
Preservatives	*Colourants*:	Vitamins	Digestibility enhancers[1]	Coccidiostats
Antioxidants	⇢ of feeds	Trace elements	Gut flora stabilisers[2]	Histomonostats
Emulsifiers	⇢ of animal food products	Amino acids	Environmental enhancers[3]	
Stabilisers	⇢ of pet fish & birds	Urea	"Other"[4]	
Thickeners	*Flavours:*		↑ Animal welfare[5]	
Gelling agents	↑ feed smell			
Binders	↑ feed palatability			
Radionucleotide controllers				
Anticaking agents				
Acidity regulators				
Silage additives				
Denaturants				
Mycotoxin binders				
Hygiene condition enhancers				

[1]Typically enzymes; [2]Typically probiotics; [3]So far unused; [4]Miscellaneous, eg, immune enhancement or improved faecal quality; [5]New category, pending to add.

**GMOs, GMMs, zootechnical, coccidiostats & histomonstats are holder-specific approvals.*

applicant may proof-read the draft opinion, but not make changes. Once the EFSA opinion is published and the full opinion is in the public domain, it is subject to SCOPAFF comitology debate and qualified majority vote (QMV). If the applicant has delayed publication of the full EFSA opinion while confidentiality issues are clarified, then this will also delay member state debate and voting. The outcome of comitology is usually a regulation authorising the feed additive. In cases where the EFSA opinion is inconclusive or negative, the European Commission (EC) offers the applicant the opportunity to submit additional data, or to withdraw the application. In rare cases, where EFSA has raised serious safety concerns, the EC and member states will vote to prohibit authorisation.

EFSA came into being in 2002, and since then has published more than 20 guidance documents for applicants, some of which have been updated several times. During 2017 and 2018 FEEDAP is focussing on renewing guidance documents over five key areas:

- Guidance on the assessment of the safety of feed additives for the consumer
- Guidance on the identity, characterisation and conditions of use of feed additives
- Guidance on the assessment of the safety of feed additives for the target species
- Public consultation on the FEEDAP panel's guidance on the assessment of the efficacy of feed additives
- Public consultation on the FEEDAP panel's guidance on the characterisation of microorganisms used as feed additives or as production organisms.

The first three guidance documents above will enter into force in May 2018, whereas the last two are closed consultations, subject to EFSA final review and publication, and likely to enter into force by the end of 2018.

Improving EFSA engagement with stakeholders

EFSA has been criticised in the past for failure to enter into dialogue with applicants and the feed/food additive industries, and so has made strenuous efforts recently to improve stakeholder engagement, also looking to the European Medicines Agency (EMA) for models and benchmarks of good practice. This has no doubt benefited the process of updating EFSA guidance, with widespread and in-depth consultation of industry and stakeholder experts.

The key pending issue is efficacy, especially the number and duration of studies required. Under current EFSA zootechnical guidance, at least three *in vivo* efficacy studies are required per target animal category, or a meta-analysis of four or more studies. Table 2 illustrates that such a requirement is a high burden for any applicant wishing to register a zootechnical feed additive for all animal species.

Applicants argue that, whereas industry accepts the need to demonstrate the potential for efficacy, there is no feed additive that will be 100% effective, 100% of the time. Hence a reduced data package should be acceptable, especially as EFSA also recognises that no feed additive will work under all conditions. Hence, for example, a single *in vivo* study in each category could be a more appropriate minimum, and would greatly reduce the burden on applicants. In addition, there is a case for more flexibility on the duration of efficacy studies, since feed additives may be given for short time periods under commercial conditions, for example creep/prestarter feeds are typically fed for two to three weeks over the weaning period.

Industry would also like EFSA to offer enhanced extrapolation of

Table 2: Number and duration of efficacy studies required for zootechnical feed additives.

Target animal category	Minimum duration	Minimum number of studies
Broiler & pullets	35 days	3
Laying hens	168 days	3
Turkeys	84 days	3
Breeding turkeys	168 days	3
Suckling piglets	14 days	3
Weaned piglets	42 days	3
Fattening pigs	70 days	3
Breeding sows	2 cycles	3
Sows/piglets	42 days, pre-partum-weaning	3
Rearing calves	56 days	3
Veal calves	84 days	3
Fattening cattle	168 days	3
Dairy cows	84 days	3
Breeding cows	2 cycles	3
Rearing lambs	56 days	3
Fattening lambs	56 days	3
Dairy sheep	84 days	3
Breeding ewes	2 cycles	3
Rearing kids	56 days	3
Fattening kids	56 days	3
Dairy goats	84 days	3
Breeding goats	2 cycles	3
Salmon/trout	90 days	3
Suckling/weaned rabbits	56 days	3
Fattening rabbits	42 days	3
Breeding does	2 cycles	3
Does/kits	42 days, pre-partum-weaning	3
Horses	56 days	3
Dogs	28 days	3
Cats	28 days	3
Other non-food animals	28 days	3
Minimum number of studies for approval in all animal categories		93

efficacy data across related species, for example among poultry, pig and ruminant categories, and to address innovation in animal nutrition. *In ovo* and peri-hatch feeding are novel approaches to improving early nutritional status in poultry. Key nutrients can be delivered *in ovo* at 18 days incubation, including amino acids, trace elements, vitamins, probiotics and enzymes. Spray-gels are a novel way to supply newly-hatched chicks with essential hydration and nutrients. Such approaches improved chick viability and performance, especially in early life. Industry would appreciate EFSA's guidance on acceptable safety and efficacy parameters for these new uses of feed additives.

While EFSA is busy finalising the 2018 FEEDAP guidance documents, the EC is undergoing a regulatory fitness and performance (REFIT) programme for all food chain legislation, aimed at making EU laws simpler and less costly. Other objectives are to ensure that EU legislation delivers results for citizens and businesses effectively, efficiently and at minimum cost, and to remove unnecessary burdens, adapting existing legislation without compromising on policy objectives.

Industry applauds EFSA and EC initiatives, but would prefer that EFSA adjust guidance documents post-REFIT, to align with EU legislation. One longstanding complaint of industry is that EFSA does not respect existing flexibility in the legislation, eg, that applicants may propose shorter application periods of a feed additive – hence should not be obliged to run efficacy studies for longer than the proposed use recommendation.

With respect to REFIT, industry has a key proposal – protect innovation. Key industry players have highlighted that the feed regulation allows nutritional and physiological claims on feed products, with no requirement to submit a pre-market dossier for EU/EFSA evaluation and approval. Feed additive manufacturers are willing and able to develop new, non-antibiotic feed additives to enhance animal nutrition, health, welfare and performance, but they need the EU to protect their investment and innovation with holder-specific authorisations.

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