# Ethoxyquin (EQ)
# Frequently Asked Questions (FAQs)

## Product Information (including safety)

### 1. What is EQ? / Why is EQ used as an additive in feed?

Ethoxyquin (EQ) is an antioxidant used as an additive in animal feed.

EQ is mostly used in feed raw materials that have a high fat content or are susceptible to oxidation. During storage of animal feed, lipid oxidation may occur. This process results in rancidity which reduces quality through effects on taste, scent, and colour and decreases the shelf life of the feed. Rancidity also leads to a reduction or loss of nutritionally important omega-3 fatty acids and vitamins. Antioxidants protect against lipid oxidation and generation of potentially toxic substances (*i.e.,* ketones and aldehydes) thereby preserving the quality and nutritional value of the product. EQ is one of the most effective antioxidants known, providing feed protection at lower concentrations.

Based on the meanwhile suspended authorisation in the European Union (EU), EQ has been used in feed materials and compound feed for incorporation in compound feed for all animal categories up to a maximum level of 150 ppm (150 mg/kg complete feed alone, or as the total value of all synthetic antioxidants).

For safety reasons, use of antioxidants during transportation of certain high-fat ingredients is required by international shipping regulations and insurance policies. EQ is important in fishmeal transportation to stabilise the product, to protect against self-heating and to manage the risk of combustion during shipping. The International Maritime Organisation (IMO[1]) requires that shipped fishmeal contains at least 100 mg/kg EQ or butylated hydroxytoluene (BHT[2]). The IMO codes require levels of antioxidant in fishmeal above a minimum, whereas EU animal feed legislation requires antioxidant concentrations below a maximum level in feed.

### 2. What can be said about the risk profile of EQ as regards human and animal health?

EFSA reviewed the scientific evidence on the risk associated with EQ to consumers, fed livestock and the environment submitted by the applicant between 2010 and 2015 and published a Scientific Opinion[3] on the safety of EQ in November 2015. In this first opinion, EFSA determined that EQ itself is safe at current dosages and conditions of use. It is neither genotoxic nor carcinogenic and therefore EQ *per se* does not represent a toxicological concern. However, due to a lack of data EFSA could not conclude on the safety of two substances in EQ, ethoxyquin quinone imine (an EQ transformation product) and commercial EQ containing *p*-phenetidine (an impurity in the product).



[1] http://www.imo.org/en/Pages/Default.aspx

[2] Based on trials performed by IFFO, the International Maritime Dangerous Goods Code was amended to reduce the minimum required level of EQ to 50 ppm and allowed the use of tocopherols as alternatives. The new parameters are applicable voluntarily from 01/01/2019, and mandatory in the IMDG Code from 01/01/2020, for transport of fishmeal in containers but further action is needed to have it applicable for bulk transport under the IMSBC Code.

[3] http://www.efsa.europa.eu/en/press/news/151118

Between 2017 and 2021, the applicant submitted additional data to allow EFSA to complete the assessment of the safety of EQ for animals, consumers of animal tissues and products, and the environment. Moreover, a new highly purified ethoxyquin was proposed by the applicant to address the issue of potential health risks of certain impurities such as *p*-phenetidine, which was reduced at the time from 15000 to <2.5 mg/kg.

After a thorough evaluation of the available scientific data related to EQ, EFSA published a second scientific opinion in March 2022[4]. In this new opinion EFSA acknowledges that many of the concerns and data gaps identified in the first opinion have been clarified through the information provided by the applicant since 2017. However, the presence of the impurity p-phenetidine at concentrations of < 2.5 mg/kg additive has led to an inconclusive outcome on the safety of additive at any level for long living and reproductive animals and on the safety for the consumer. In addition, data gaps are identified regarding the safety of the additive for the environment (terrestrial and aquatic compartments).

### 3. Can EQ be used outside the EU?

Third countries' regulatory agencies, for example the United States Food and Drug Administration (FDA)[5] and the Ministry of Agriculture (MOA) in China[6], have examined the safety of EQ and maintained its use as an antioxidant in animal feed under defined conditions of use that are comparable to those currently prevailing in Europe. US legislation also authorises certain food uses of EQ, such as its addition to food grade paprika powder for stabilisation.

## Legislation

### 1. What is the present legal situation of EQ as feed additive in the EU?

Further to the publication of the inconclusive EFSA Opinion in November 2015, the EC and national authorities agreed to suspend the use of EQ in feed. Short transition periods were set for non-essential uses and longer transition periods for specific uses requiring time to find, test and validate alternative ingredients. For example, feed materials of aquatic origin[7] were allowed to continue to incorporate EQ until the 31st of December 2019. The regulation providing for this suspension (so called "Suspension Regulation") was published on 8th June 2017 and entered into force on 28th June 2017[8].

Successive packages of supplementary data have been submitted to EFSA and to the EC (i.e. March 2016, December 2017, March 2018, July 2018, February 2019, December 2020, June 2021) for which data generation entailed delays in the process, in particular to demonstrate the safety of EQ for the environment. Reasons for those delays included the need for additional studies in order to comply with data requirements set out in Commission Regulation (EC) No 429/2008 and the related detailed guidance of EFSA, as well as difficulties in finding appropriate laboratories or testing facilities to conduct certain studies.

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[4] https://www.efsa.europa.eu/en/efsajournal/pub/7166

[5] https://www.fda.gov/animal-veterinary/ingredients-additives/labeling-and-use-ethoxyquin-animal-feed

[6] Analysis of ethoxyquin and its oxidation products in swine tissues by gas chromatography-tandem mass spectrometry for evaluating the feed-to-animal tissue transfer of ethoxyquin and its metabolites

[7] Entry 7.1.2 and Chapter 10 of the EU Catalogue of Feed Materials (Regulation (EU) 2017/1017 amending Regulation (EU) 68/2013)

[8] Commission Implementing Regulation (EU) 2017/962 of 7 June 2017 suspending the authorisation of ethoxyquin as a feed additive for all animal species and categories

In view of the above, in 2021 the European Commission (EC) amended the "Suspension Regulation", which shall be reviewed by 31st December 2022 at the latest and in any event after the adoption by EFSA of a non-favourable opinion on the safety and efficacy of the additive ethoxyquin[9].

The conclusions reached by EFSA in its scientific opinion from 3 March 2022 will be discussed between the EC and the Member States (MS) at the Standing Committee on Plants, Animals, Food and Feed (SCoPAFF) to decide what follow up risk management measures should be implemented.

## 2. What are the consequences for the feed sector and for your members if EQ is banned or its use level decreased?

In follow up to the second EFSA Scientific Opinion, the EC shall adopt risk management decisions in the coming months on the use of EQ in the EU. In case a permanent ban is established in the EU, the impact of such a decision could be severe as there are only few, if any, antioxidants that provide stabilisation in fishmeal at the same level as EQ. The Marine Ingredients Organisation (IFFO) is working with antioxidant manufacturers to identify alternative substances for efficacious fishmeal stabilisation. Some of these substances are not authorised under the EU feed additives legislation and it could take quite some time before market entry and commercial use would be possible in the EU.

Access to fishmeal and fish oil from third countries may also be hindered if the EU is the only region where EQ is not authorised. Although European operators have reduced the proportion of fishmeal and fish oil in fish feed, they still need access to the global market to meet the European demand for seafood. While this demand is high, it might not be high enough for third country suppliers to consider switching to another antioxidant. One consequence could be constraints put on European aquaculture and therefore the aquafeed sector, while imports from third countries of farmed fish, shrimps and prawns fed with feed containing EQ might remain possible.

## 3. Why has been EQ in the re-authorisation process since 2010?

In the EU, any feed additive to be placed on the market requires pre-market authorisation. Part of the authorisation process is a thorough scientific risk assessment carried out by the European Food Safety Authority (EFSA). This is then followed by a decision of EU Member States upon proposal of the EC.

Regulation (EC) No 1831/2003 sets the current EU legal framework applicable to all feed additives. Those feed additives authorised in the EU prior to publication of Regulation (EC) No 1831/2003 required re-authorisation to stay on the market. This re-authorisation process is therefore not specific to EQ but applies in general to all feed additives. Application dossiers were requested to be submitted to the EU authorities by November 2010, and were processed progressively, including the one for EQ. EFSA has published two Opinions on EQ: (i) in November 2015[10] and (ii) in March 2022[11].

## 4. Why was EQ still used as feed additive when it was no longer permitted as pesticide in the EU?

Ethoxyquin had been widely applied to inhibit superficial scald (formation of brown spots) due to oxidative damage in pears and apples at storage. That is why this use was regulated under the scope of pesticide substances. In the EU, regulation of the use of pesticides and feed additives falls under different legislation and a separate risk assessment process applies to each. EQ was evaluated for safe use as a pesticide but there was a lack of data available at that time leading to it not being fully

[9] Commission Implementing Regulation (EU) 2021/412 of 8 March 2021 amending Implementing Regulation (EU) 2017/962 as regards the review of the suspension of the authorisation of ethoxyquin as a feed additive

[10] http://www.efsa.europa.eu/en/press/news/151118

[11] https://www.efsa.europa.eu/en/efsajournal/pub/7166

assessed for risk to the environment and non-target organisms.[12] Consequently EQ was not included in the EU-list of approved pesticides. EFSA subsequently published a Reasoned Opinion[13] in 2013 on the review of the existing Maximum Residue Levels (MRLs) for EQ under the pesticide legislation.

# MRLs

## 1. What does Maximum Residue Level (MRL) mean?

According to Regulation (EC) No 396/2005, maximum residue levels (MRLs) are the upper levels of pesticide residues that are legally permissible in or on food or animal feed, based on good agricultural practice (GAP) and the lowest exposure necessary to protect vulnerable consumers. They are derived after a comprehensive assessment of the properties of the active substance and the intended uses of the pesticide. These legal limits also apply to imported food, set as "import tolerances" to meet the needs of international trade. They are established for control purposes and enables authorities to protect the health of consumers.

MRLs may be established for feed additives, pesticides, veterinary medicinal substances, or biocides following a risk assessment considering the potential exposure of consumers to the substance.

Under the feed additive law MRLs may be set for certain feed additives that could be present as residues in animal products due to transfer from feed to food. Based on the outcome of the recent assessment by EFSA, the EC might choose to set an MRL for EQ in farmed fish.

For pesticides, Regulation (EC) No 396/2005 foresees that MRLs are set when needed for substances, authorised or not as pesticides in the EU, and for different commodities such as cereals, oilseeds, fruits, vegetables, meat, fish and feed. For pesticides non-authorised in the EU, the MRL for plants destined as food and for certain animal products has been set at the level of detection (LOD), the lowest measurable level of a residue (*i.e.*, ethoxyquin) by standard methods of analysis, which is between 0.01 and 0.1 ppm depending on the method of analysis.

## 2. Are there MRLs for EQ in food products?

EQ was authorised for use as a feed additive in the EU under Directive 70/524/EU. The Directive did not require setting an MRL for EQ in animal products when used as a feed additive.

Under the EU pesticides legislation, an MRL has been set for EQ in products of vegetable origin and in animal products, except those from aquatic animals. This MRL was set up for default commodity entries in Annex V of Regulation (EC) No 396/2005[14] in order to address residues in animals being fed with feed of vegetable origin that was treated with the pesticide or that contained residues of EQ from carry-over in the environment. Since the use of EQ as a pesticide is not authorised in the EU, the MRL has been reduced to the limit of quantification. However, an MRL for EQ in this regulation was set only for *"products of animal origin- terrestrial animals"* not for aquatic animals, including fish. A respective note indicates that "*no MRLs are applicable until individual products have been identified and listed within this category."*

At a global level, there is an MRL for EQ established as recommendation by the Codex Alimentarius of the FAO/WHO. It refers to a pesticide use for pears (3 mg/kg), a use which has been revoked in the EU.

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[12] COMMISSION DECISION of 3 March 2011 concerning the non-inclusion of ethoxyquin in Annex I to Council Directive 91/414/EEC and amending Commission Decision 2008/941/EC

[13] Reasoned opinion on the review of the existing maximum residue levels (MRLs) for ethoxyquin according to Article 12 of Regulation (EC) No 396/2005.

[14] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC

### 3. Will there be an MRL for ethoxyquin in fish and when?

The outcome of the EFSA assessment from March 2022 of the safety of the use of EQ as feed additive b will provide the basis to determine whether there is a need to establish MRLs for EQ for its use as feed additive.

### 4. Does the absence of an MRL mean that fish products may contain ethoxyquin at levels that can endanger public health?

No, the Scientific Opinions of EFSA did not identify any concerns that observed residue levels endanger public health.

## General (Market)

### 1. How many tonnes of EQ are produced yearly?

The worldwide use of EQ is estimated at about 20,000 tonnes per year. It is quite difficult to provide precise figures about the use of EQ in the EU since it is used globally, as well as due to the global trade of EQ treated feeds.

### 2. Who produces EQ worldwide?

The vast majority of EQ used worldwide is produced in China and the EU.

### 3. Which is the main sector EQ is produced for in the EU?

To our knowledge, in the EU EQ has only been used in the feed sector, especially for the preservation of fishmeal and final compound feed.

### 4. Within the feed sector, how many tons of EQ are used for each animal group?

As EQ is used worldwide to stabilise raw materials as well as other feed ingredients, it is not possible to provide reliable figures on the share between animal groups. In the EU, use of EQ has been permitted in feed for all animal species and categories, including most food producing animals.

### 5. Are there alternatives to EQ?

There are alternative antioxidants to EQ (synthetic as well as natural), but so far none have shown the same level of efficacy in mitigating quality and safety concerns. A few natural antioxidants are effective at preserving feed, but in many cases such protection alone is not sufficient. Synthetic antioxidants are used to ensure the process is effective. EQ is by far the most efficacious antioxidant for this application, and it can be used at lower concentrations than any other authorised antioxidants.

## Associations

### 1. What or who is FEFANA?

FEFANA is the EU association of Specialty Feed Ingredients and their Mixtures. It represents the EU operators producing, trading and pre-mixing a wide range of specialty feed ingredients that are important in animal nutrition. The nature and purpose of products is very diverse. It includes nutritional additives (*e.g.*, vitamins), zootechnical additives (*e.g.*, probiotics that have a beneficial effect on gut flora), and technological additives that are necessary for the manufacturing of feed (*e.g.*, preservatives or antioxidants).

## 2. What or who is FEFAC?

FEFAC is the European Compound Feed Manufacturers' Federation and represents compound feed and premix manufacturers via its national Associations in EU Member States as well as neighbouring countries. The EU compound feed industry employs over 100,000 persons app 3,500 production sites often in rural areas, which offer few employment opportunities. Farm animals in the EU-28 consume an estimated 480 million tonnes of feed a year, of which about 30% are produced by compound feed manufacturers. Turnover of the European compound feed industry is estimated at € 50 billion.

## 3. What or who is IFFO?

IFFO, the Marine Ingredients Organisation (www.iffo.net) is the international non-profit organisation representing and promoting the fishmeal-, fish oil- and wider marine ingredients industry worldwide. It is globally respected and regularly represents the industry at international fora, as well as holding observer status at the UN Food and Agriculture Organisation (FAO) and the EC and Parliament.

## 4. What or who is ANTOXIAC?

FEFANA helps operators to coordinate their efforts for the submission of re-authorisation dossiers through the creation of consortia. ANTOXIAC is one of these consortia. Each consortium takes care of several dossiers for a certain category of products that operators wish to sustain. ANTOXIAC is supporting the applications of certain antioxidants used as feed additives.

It is worth noting that operators' participation in a given application dossier is voluntary; not all EQ producers are part of the ANTOXIAC consortium.

## 5. Why was the consortium formed?

The ANTOXIAC consortium was formed to help companies coordinate their efforts to produce application dossiers for certain antioxidants that meets the requirements defined by EU legislation. Preparation of dossiers that meet the high level of scientific evidence required by EFSA is very demanding. Contrary to other legislative areas, there is no automatic obligation for each operator to participate in this effort. So, participation is based on the willingness of companies.