Assessment of the safety and efficacy of sodium benzoate (Protural™) as a feed additive for weaned piglets and other growing *Suidae*

Reference number RP666

Regulated Products Risk Assessment Unit
Science, Evidence and Research Division, FSA

Risk Assessment Team
Science Division, FSS

Regulated Product Dossier Assessment
Assessment finalised: 04/12/2023

Contents

List of tables

Abbreviations

Acronym	Definition
ACAF	Advisory Committee on Animal Feedingstuffs
AFFAJEG	Animal Feed and Feed Additives Joint Expert Group
AME	Apparent metabolizable energy
CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
EURL	European Union Reference Laboratory
FSA	Food Standards Agency
FSS	Food Standards Scotland
HACCP	Hazard Analysis and Critical Control Points

Summary

An application was submitted to the Food Standards Agency in March 2021 from Taminco Finland Oy ("the applicant") for the renewal of authorisation and new use of an additive (sodium benzoate-Protural™), under the category of 'zootechnical additives" and functional group "Other zootechnical (increase of performance/weight gain parameters)". The additive is proposed to be used in piglets from weaning to 35 kg (renewal), as well as in other growing *Suidae* (new use), with a proposed level of inclusion in feed of 4 kg/ 1,000 kg or 0.4% of complete feedingstuffs with a moisture content of 12%.

To support the Food Standards Agency (FSA) and Food Standards Scotland (FSS) in evaluating the dossier, the Animal Feed and Feed Additives Joint Expert Group (AFFAJEG) and the Advisory Committee on Animal Feedingstuffs (ACAF) were asked to review the dossier and the supplementary information from the applicant.

Following clarification with the applicant, ACAF was able to conclude on a recommended dose of 4000 mg/kg of complete feed with a moisture content of 12%. The Committee had no other causes for concern in Section II of the application.

The initial EFSA evaluation in 2011[2] confirmed that the additive is safe for the target species, consumers and the environment at the proposed conditions of use. The applicant conducted a literature review covering the period January 2000 to February 2020 and found no reported negative effects in this time. Regarding user/worker safety, the additive is considered as potentially harmful by inhalation and an eye irritant. The additive is not a skin irritant.

Given that the efficacy data that were provided only assessed its efficacy in piglets, the ACAF could conclude on the efficacy of sodium benzoate in piglets (suckling), piglets (weaning) and piglets (suckling and weaned piglets). Members concluded that Protural™ at a proposed level of inclusion in feed of 4 kg/ 1,000 kg has the potential to improve performance in these groups of animals. Results can be extrapolated to other growing *Suidae* at the same developmental stage.

The views of AFFAJEG and ACAF have been taken into account in the safety assessment which represents the opinion of the FSA and FSS.

1. Introduction

The FSA and FSS have undertaken a risk assessment for a feed additive (sodium benzoate-Protural™, Taminco Finland Oy, Typpitie 1, 90620 Oulu, Finland) under regulation (EC) No 1831/2003[1] under the category of 'zootechnical additives" and functional group "Other zootechnical (increase of performance/weight gain parameters)". The additive is proposed to be used in piglets from weaning to 35 kg, as well as in other growing *Suidae*, with a proposed level of inclusion in feed of 4 kg/ 1,000 kg or 0.4% of complete feedingstuffs with a moisture content of 12%.

To support the safety assessment by FSA and FSS, the AFFAJEG and the ACAF provided advice to the FSA and FSS outlined in this document.

The dossier was evaluated on behalf of the FSA and FSS by the AFFAJEG and ACAF. In line with Article 8 of 1831/2003, the assessment has considered whether the feed additive complies with the conditions laid down in Article 5, including: safety considerations for human, animal and environmental health; efficacy of the additive for its intended effect; potential impairment of the distinctive features of animal products. This, and the guidance put in place by EFSA for the evaluation of feed additive applications, has formed the basis and structure for the assessment.

With thanks to the members of the AFFAJEG and ACAF during the course of the assessment, who were: Professor Nicholas Jonsson, Martin Briggs, Professor Katrina Campbell, Susan MacDonald, Professor Matthew Fisher, Christine McAlinden, Dr. Donald Morrison, Derek Renshaw, Dr. Michael Salter, Dr. Adam Smith, Dr. Helen Warren and Dr. Nick Wheelhouse.

The dossier was evaluated by the AFFAJEG at their July 2022 meeting and by ACAF at their October 2022 and February 2023 meetings. Further information was provided by the applicant in May 2021 and January 2022, responding to queries by the FSA. The conclusions by the AFFAJEG were reviewed and approved by the ACAF at their October 2022 meeting. Further information was provided by the applicant in September 2022 and January 2023.

This document outlines the discussion and conclusions of the AFFAJEG's and ACAF's assessment on the safety and efficacy of sodium benzoate as a feed additive.

2. Assessment

2.1. Section II: Identity, characterisation and conditions of use

Sodium benzoate is the active substance in Protural™, of which two preparations are available: a granular form and a powder formulation. The preparations contain a minimum of 99% (w/w) sodium benzoate, with up to 1% (w/w) moisture. Protural™ consists of sodium benzoate without carrier materials. The applicant provided data in several batches for the composition, impurities and physico-chemical properties as described in Table 1:

Table 1: Identity table

Composition	**w/w %**
Sodium benzoate	Minimum 99% (Average 99.6%)
Moisture	Up to 1%
Physico-chemical properties	
Dusting potential Granular form Powder form	 492-572 mg/m^3 787-919 mg/m^3
Particle size distribution Granular form Powder form	 5.13% < 50 µm / 1.19% < 1 µm 34% < 50 µm / 6.1% < 1 µm
Purity	
Coliform bacteria	Negative in 10 g
Staphylococcus aureus	Negative in 10 g
Salmonella spp.	Negative in 25 g
E. coli	Negative in 10 g
Fungal contamination	< 100 CFU/g
Mercury	< 0.05 mg/kg
Arsenic	< 0.10 mg/kg
Cadmium	< 0.05 mg/kg
Lead	< 0.05 mg/kg
Nitrite	< 5 mg/kg
Fluoride	< 5 mg/kg
Dioxins	< 0.45 ng/kg
Dioxin-like PCBs	< 0.061 ng/kg
Non-dioxin-like PCBs	< 0.51 µg/kg

The Committee evaluated the identity and characterisation section of the additive, for which no concerns were raised. The manufacturing process was noted to be FAMI QS certified, following a strict HACCP scheme. The physico-chemical and technological properties were evaluated by members, wherein the stability studies were deemed to be acceptable, including in feed and following pellet production. It was not clear if the studies were for the powder or the granular formulation, but members judged that the two formulations would be very similar in relation to stability.

In their first evaluation, members noted a disparity around the recommended dosage, as the dosage differed throughout the introduction, the label provided and the current EU authorisation. Upon a request for further information, the applicant confirmed that the recommended dose is 4000 mg/kg of complete feed with a moisture content of 12%. An arithmetic error was also detected with regards to level of inclusion in the feed, which the applicant was able to correct as 4 kg/ 1,000 kg or 0.4%.

The proposed conditions of use of the additive are described in Table 1.

Table 2: Proposed conditions of use of sodium benzoate

Proposed mode of use in animal nutrition			
Additive	Sodium benzoate		
CAS No	532-32-1		
Category of additive	Zootechnical		
Functional group of additive	Other technical (increase of performance/weight gain parameters)		
Trade name (if appropriate)	Protural™		
Conditions of use			
Target species	**Min. content**	**Max content**	**Other provisions**
	mg of active substance/kg of complete feedingstuffs with a moisture content of 12%		
Piglets from weaning to 35 kg	4000	4000	The additive is added to the feed during mixing with other feed ingredients, as such, or in a premixture. Proposed level of inclusion in feeds: 4kg/1,000 kg or 0.4%. For weaned piglets, the additive is administered from weaning up to 35 kg. No withdrawal period is proposed due to the nature of the substance.

2.1.1. Conclusions on Section II

The ACAF was satisfied with the confirmed recommended dose of 4000 mg/kg of complete feed with a moisture content of 12% and an inclusion level of 4 kg/1,000 kg or 0.4%.

No further concerns were raised for Section II of these dossiers.

2.2. Section III: Safety

The applicant conducted a literature review to cover the period Jan. 2000 – Feb. 2020. The initial EFSA evaluation in 2011[2] confirmed that Protural™ is safe for the target species, the consumers and environment at the proposed conditions of use (4,000 mg/kg feed), and providing the adequate protective measures are applied. Subsequent opinions concerning sodium benzoate (and sodium benzoate containing products) in weaned piglets and pigs all supported the safety of sodium benzoate[3-6]. The literature review found no reported negative effects. There have also been no recall or safety issues reported for the additive since its initial placing on the market.

2.2.1. Safety for the user

On a precautionary basis, in the absence of any studies of inhalation toxicity, Protural™ is considered as potentially harmful by inhalation, but it is not a skin irritant. Measures should be taken to reduce exposure. Data related to eye irritation was provided in the initial application with a study conducted according to OECD 405. The additive is classified as a serious eye irritant, which is flagged in the MSDS and the label with the recommended use of safety glasses. Despite no problems having been reported during the prior use of the additive, members concluded that it should be considered an irritant to eyes.

2.2.2. Conclusions on safety

Members did not have concerns regarding the safety of the additive for consumers as it has already been authorised as a food additive. The ACAF concluded that the additive can be considered safe for the target species, the consumer and the environment. However, members have concluded that it should be considered as potentially harmful by inhalation and an irritant to eyes.

2.3. Section IV: Efficacy

The efficacy evidence presented in the application was largely based on previous EFSA opinions from 2011. Members requested the original efficacy studies to enable them to make an informed decision regarding the efficacy of this product and its potential extrapolation to all growing *Suidae*. Upon receiving these studies from the applicant, members discussed the possibility of extrapolating the efficacy data received to all "growing *Suidae*". The efficacy data provided only assessed efficacy in piglets, therefore, it was decided that the ACAF could only conclude on the efficacy of sodium benzoate in growing *Suidae* at the equivalent developmental stage of piglets (suckling), piglets (weaning) and piglets (suckling and weaned piglets).

3. Analytical methods evaluation

Conclusions on the analytical methods are presented here as an extract from the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of the Analysis for Sodium Benzoate (Protural™)[7]:

"For the determination of sodium benzoate in the feed additive a titrimetric method [Monograph 01/2008:0123] described in the European Pharmacopoeia is recommended for official controls.

For the determination of sodium benzoate in the premixtures and feedingstuffs the in-house validated HPLC-UV (high-performance liquid chromatography- ultraviolet) method developed by the AGES is recommended for official controls."

FSA/FSS accepts the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Conclusions

After the applicant had confirmed the proposed conditions of use, the additive Protural™ was fully characterised and no causes of concern were identified by the ACAF in the identity, production and characterisation sections.

Protural™ continues to be considered safe for the target species, the consumer and the environment. However, for user/worker safety it should be considered as potentially harmful by inhalation and an eye irritant.

The ACAF could conclude on the efficacy of sodium benzoate in piglets (suckling), piglets (weaning) and piglets (suckling and weaned piglets). Members concluded that Protural™ at a proposed level of inclusion in feed of 4 kg/ 1,000 kg has the potential to improve performance in these groups of animals. Results can be extrapolated to other growing *Suidae* at the same developmental stage.

FSA/FSS accepts the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

5. References

1. EC (European Commission), 2003. Regulation No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition.

2. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific opinion on the safety and efficacy of Protural (sodium benzoate) as feed additive for weaned piglets. EFSA Journal 2011;9(2):2005. https://doi.org/10.2903/j.efsa.2011.2005

3. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific opinion on the modification of the terms of authorisation of Protural (sodium benzoate) as a feed additive for weaned piglets. EFSA Journal 2011;9(12);2443. https://doi.org/10.2903/j.efsa.2011.2443

4. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific opinion on safety and efficacy of sodium benzoate, propionic acid and sodium propionate for pigs, poultry, bovines, sheep, goats, rabbits, horses. EFSA Journal 2012;10(5);2681. https://doi.org/10.2903/j.efsa.2012.2681

5. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific opinion on the safety and efficacy of sodium benzoate as a silage additive for pigs, poultry, bovines, ovines, goats, rabbits and horses. EFSA Journal 2012;10(7);2779. https://doi.org/10.2903/j.efsa.2012.2779

6. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP); Scientific opinion on safety and efficacy of sodium benzoate, propionic acid and sodium propionate for pigs, poultry, bovines, sheep, goats, rabbits, horses. EFSA Journal 2011;9(9);2357. https://doi.org/10.2903/j.efsa.2011.2357

7. EURL-FA (European Reference Laboratory for Feed Additives), 2017. Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003. Protural. Available at: FAD-2009-0005 (europa.eu)

For enquiries about this publication, contact the Food Standards Agency.

Follow us on Twitter: @foodgov

Find us on Facebook: facebook.com/FoodStandardsAgency