REGULATED PRODUCTS SAFETY ASSESSMENT

Safety Assessment on the Proposed Inclusion of Up to 75% Inert Copper in a PARNUT Bolus (RP2059)

Food Standards Agency[1], Food Standards Scotland[2]

[1] Regulated Products Risk Assessment, Food Standards Agency, UK, [2] Risk Assessment, Food Standards Scotland, UK

Keywords: Regulated products, Safety assessment, PARNUT

https://doi.org/10.46756/001c.124547

FSA Research and Evidence

An application was submitted to the Food Standards Agency in May 2023 to extend the scope of the conditions of use associated with an existing feedstuff for particular nutritional purposes (PARNUT).

Intraruminal boluses can be used to provide a long-term supply of trace elements and vitamins to grazing animals, specifically ruminants with functional rumen. Under this use, they are classified as a PARNUT. Up to 20% inert, non-bioavailable iron can be added to the bolus as a means to increase density and ensure that the bolus is retained in the reticulum of the animal. The applicant proposed the inclusion of up to 75% inert, non-bioavailable copper in a bolus as an alternative to iron.

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

The FSA/FSS concluded, based on the ACAF's advice, that copper in a bolus ballast is inert and that leaching of copper into the rumen is highly unlikely. The copper in a bolus ballast is not bioavailable to the animal, therefore the risk of toxicity to target animals and consumers is low. The use of up to 75% inert copper as an alternative to up to 20% inert iron in a PARNUT bolus poses no additional risk to the target animals, consumers, users or the environment.

The views of the 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 safety assessment of a proposal to extend the conditions associated with an existing feedstuff for particular nutritional purposes (PARNUT). Under current legislation (EC, 2020) in Great Britain, an intraruminal bolus can be used to provide grazing ruminants (specifically those with a functional rumen) with a long-term

supply of trace elements and/or vitamins. The bolus can contain up to 20% inert, non-bioavailable iron in order to increase the density and ensure that the bolus is retained in the reticulum of the animal.

The applicant claimed that the that the current provision does not allow sufficient density of the bolus when combined with the trace minerals. The applicant proposed the use of up to 75% inert, non-bioavailable copper as an alternative to iron.

To support the safety assessment by FSA and FSS, the ACAF provided advice to the FSA and FSS as outlined in this document. The safety assessment considered whether the proposed change was likely to have any adverse effects on animal health, human health, the environment or animal welfare.

The dossier was evaluated by ACAF at their October 2023 and June 2024 meetings.

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

2. Assessment

The applicant presented a proposal to allow the use of up to 75% inert, non-bioavailable copper in a PARNUT bolus as a means to increase density. The proposal was supported by a dossier of evidence, including a risk assessment considering safety for the target animal, safety for the consumer, safety for the user and safety for the environment. The applicant also provided three studies to support the proposal.

One of the studies submitted was a published *in vivo* study demonstrating that intraruminal boluses can be used to meet the trace mineral requirements of beef cattle, as an alternative to dietary supplementation (Lee et al., 2020). The applicant claimed that the boluses used in the study contained a copper ballast, and that the lack of safety concerns observed during the study was evidence of the safety of the proposal.

However, the Committee noted that the paper did not specify the densifying agent used in the bolus ballast and therefore did not accept the applicant's conclusion regarding the safety of the proposal based on this study. Furthermore, the ACAF noted several shortcomings of the study, including the fact that copper levels in the animals were measured in blood plasma rather than liver tissue. The strict homeostatic control of copper means that toxicity may not be detected if blood plasma measurements alone are relied on.

The Committee noted that the remaining two studies provided were unpublished, lacking in detail and failed to directly examine the effects of the copper. The ACAF questioned whether leaching of copper from the bolus ballast into the rumen may occur, with consequent adverse effects such as copper toxicity in the animal and/or effects on the ruminal microbiome. The Committee requested a more comprehensive risk assessment to quantify the extent of leaching from the device in the ruminal environment.

In response, the applicant provided a brief statement appealing to the principles of chemistry, asserting that because metallic copper is less reactive than metallic iron, it is assumed that a copper ballast should be inert, and possibly even less reactive than an iron ballast.

Following consultation with the Veterinary Medicines Directorate, the evidence supporting the assertion that copper was inert in the rumen was deemed insufficient. The applicant was requested to provide a comprehensive and detailed explanation of the principles of why leaching would not be a concern. Furthermore, the applicant was asked to supply all experimental data from the unpublished trials alongside validation data, in addition to a risk assessment for user safety.

In response, the applicant provided a systematic evaluation of the potential for copper leaching from the ballast, prepared by a consultant chemist. The copper in the ballast is in a powdered, metallic form that is unavailable to the animal, as opposed to copper salts which have a higher bioavailability for absorption. Although copper can react with acids, resulting in formation of slightly water-soluble copper salts, the rumen is only mildly acidic. Furthermore, the rumen is anaerobic, lacking the oxygen that must be present for the weak acids to react with the copper. It is a highly reducing environment, meaning any exposed copper ions would be reduced back to the metal state and rendered inert. The Committee agreed with the applicant's argument that the risk of copper leaching from the ballast is very low. It was concluded that the unpublished studies and the published *in vivo* study (Lee et al., 2020) provided in the initial dossier were of little value in supporting the applicant's proposal.

The ACAF concluded that the copper in the bolus ballast is inert and that leaching of copper into the rumen is highly unlikely. The copper in the bolus ballast is not available to the animal, therefore the risk of toxicity or other adverse effects in the animal or consumers is low.

The applicant provided a user safety risk assessment, and the Committee were satisfied that the layer of beeswax around the bolus prevents contact between the user and the copper matrix, thus limiting dermal exposure.

Oral and inhalation routes of exposure were deemed improbable because of the solid form of the bolus. The ACAF concluded that the proposed modification does not pose a risk to users.

The applicant claimed that the bolus remains intact and is removed at slaughter where it can be appropriately disposed of. The ACAF accepted the applicant's assertion that the copper would not enter the environment and concluded that the proposed modification does not pose a risk to the environment.

3. Conclusions

The ACAF concluded that the proposed inclusion of up to 75% inert copper in a PARNUT bolus intended for use in grazing ruminants with a functional rumen poses no additional risk to the target animals, consumers, users or the environment. The FSA/FSS agree with the conclusions reached by the ACAF.

Abbreviations

Acronym	Definition
ACAF	Advisory Committee on Animal Feedingstuffs
FSA	Food Standards Agency
FSS	Food Standards Scotland
PARNUT	Feedstuff for Particular Nutritional Purposes

Acknowledgements

With thanks to the members of the ACAF during the course of the assessment, who were: Professor Nicholas Jonsson, Martin Briggs, Professor Emily Burton, Professor Katrina Campbell, Professor Matthew Fisher, Hannah Kane, Susan MacDonald, Dr. Oonagh Markey, Christine McAlinden, Dr. Donald Morrison, Derek Renshaw, Dr. Michael Salter, Dr. Adam Smith, Christel Wake, Dr. Helen Warren and Dr. Nick Wheelhouse. With thanks also to the Veterinary Medicines Directorate.

Published: October 31, 2024 GMT.

References

EC (European Commission). (2020). *Regulation No 354/2020 on establishing a list of intended uses of feed intended for particular nutritional purposes and repealing Directive 2008/38/EC*.

Lee, C., Copelin, J. E., Dieter, P. A., & Berry, E. A. (2020). Effects of trace mineral supply from rumen boluses on performance, carcass characteristics, and fecal bacterial profile in beef cattle. *Animal Feed Science and Technology*, *269*, 114626. https://doi.org/10.1016/j.anifeedsci.2020.114626