REGULATED PRODUCTS SAFETY ASSESSMENT

# Safety Assessment on the Safety and Efficacy of an Additive of Zinc Chloride Hydroxide Monohydrate (IntelliBond® Z) as a Feed Additive for All Animal Species (RP814)

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An application was submitted to the Food Standards Agency in March 2021 from Trouw Nutrition GB ('the applicant') for the renewal and modification of authorisation of an additive (IntelliBond® Z) containing zinc chloride hydroxide monohydrate, under the category of 'nutritional additives' and functional group 'compounds of trace elements'. The additive is proposed to be used at a maximum inclusion rate of:

- 200 mg/kg in dogs and cats
- 180 mg/kg in salmonids and milk replacers for calves
- 150 mg/kg in piglets, sows, rabbits and all fish species other than salmonids
- 120 mg/kg in all other species and categories

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 the additive was correctly identified and characterised and that the changes made to the manufacturing process did not pose an unacceptable risk to safety.

The additive is safe for consumers and the target animal species. The additive is not a skin irritant or dermal sensitiser and is unlikely to form harmful amounts of respirable dust. The additive should be considered a potential eye irritant. The additive poses an acceptable risk to the environment under the proposed conditions for terrestrial species and land-based aquaculture systems. The Committee were unable to conclude on the safety of the additive for marine sediment when used in sea cages.

The ACAF concluded that the proposed minor modifications to the specifications and other provisions would not affect efficacy and therefore efficacy could be extrapolated from the original authorisation to this renewal.

The views of 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 for a feed additive (IntelliBond® Z, Trouw Nutrition GB, Blenheim House, Blenheim Road, Ashbourne, Derbyshire, DE6 1HA, United Kingdom) containing zinc chloride hydroxide monohydrate under Assimilated Regulation (EC) No 1831/2003 (EC, 2003), under the category of 'nutritional additives' and functional group 'compounds of trace elements', for its use in all animal species.

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

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.

The dossier was evaluated by the ACAF at their February 2023 meeting, after which an environmental specialist was consulted and a request for further information communicated to the applicant. The applicant's response to this request was evaluated at the December 2023 ACAF meeting.

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

Table 1. Table showing products included in this assessment

| Title | Product type | Intended use/s | Intended species or categories of animals |
|---|---|---|---|
| Zinc chloride hydroxide monohydrate | Feed additive | Nutritional additive | All animal species |

# 2. Assessment

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

The additive is a preparation containing zinc chloride hydroxide monohydrate (min. 84% purity, min. 54% zinc), combined with a small amount of starch or other food grade binding agent (ca. 5%). The applicant provided data from five batches supporting the composition values for the active ingredient, outlined below (Table 2):

Table 2. Identity table of the additive zinc chloride hydroxide monohydrate

| | |
|---|---|
| **Composition** | |
| **Mineral Composition** | |
| Simonkolleite; $Zn_5(OH)_8Cl_2.(H_2O)$ | 92.5 – 94.2% |
| Zincite; ZnO | 5.8 – 7.5% |
| Sum of mineral species | 100% |
| **Additive composition** | |
| Zinc | 57.0 – 57.6 % |
| Moisture | 0.2-0.5 % |
| Purity | 93 – 94 % |
| Binding agent | ~ 5 % |
| **Appearance** | Off-white/tan crystalline powder |
| **Chemical-physical specifications** | |
| Bulk density | 780 – 877 kg/$m^3$ |
| Particle size | 158 – 203 µm |
| Dusting potential | 0.14 – 0.18 g/$m^3$ |
| **Impurities** | |
| Arsenic | < 1 mg/kg |
| Lead | 7.21 – 13.7 mg/kg |
| Cadmium | 0.43 – 2.42 mg/kg |
| Mercury | < 0.01 mg/kg |
| Dioxins | 0.091 – 0.21 ng/kg |
| Sum of dioxins and dioxin-like PCBs | 0.12 – 0.24 WHO-TEQ (ng/kg) |
| Non-dioxin-like PCBs | 0.42 – 0.44 WHO-TEQ (µg/kg) |

The Committee reviewed the changes made to the manufacturing process since the original authorisation, noting an increase in the permitted number of fine particles (maximum number of particles of diameter 50 µm or less raised from 1% to 5% w/w) that could impact on respiratory safety if breathed in. Owing to the inclusion of a binding agent and a low dusting potential, the Committee concluded that the increase in fine

particles does not pose a concern to user and worker safety. The additive was demonstrated to be homogeneous in premixtures and complete feedingstuffs.

The proposed conditions of use of the additive are described in Table 3:

Table 3. Proposed conditions of use of zinc chloride hydroxide monohydrate

| Proposed mode of use in animal nutrition | | | | |
|---|---|---|---|---|
| **Additive** | | Zinc chloride hydroxide monohydrate | | |
| **Registration number/ EC No/No** | | -- | | |
| **Category(-ies) of additive** | | 3. Nutritional additives | | |
| **Functional group(s) of additive** | | b. Compounds of trace elements | | |
| Description | | | | |
| **Description** | **Chemical formula** | **Purity criteria** | | **Method of analysis** |
| Preparation of zinc chloride hydroxide monohydrate | $Zn_5(OH)_8Cl_2.(H_2O)$ | Min. 84%<br>Min. Zn content 54% | | EN ISO 15510:2007 |
| **Trade name (if appropriate)** | | IntelliBond® Z | | |
| **Name of the holder of authorisation (if appropriate)** | | -- | | |
| Conditions of use | | | | |
| **Species or category of animal** | **Min-max Age** | **Min. content** | **Max. content** | **Withdrawal period** |
| | | Maximum content of zinc in complete feedingstuffs containing 12% moisture | | |
| Dogs and cats | -- | -- | 200 mg/kg | -- |
| Salmonids and milk replacers for calves | -- | -- | 180 mg/kg | -- |
| Piglets, sows, rabbits and all fish species other that salmonids | -- | -- | 150 mg/kg | -- |
| All other species and categories | -- | -- | 120 mg/kg | -- |

## 2.1.1. Conclusions on Section II

The ACAF concluded that the additive was correctly identified and characterised and that the updated manufacturing process does not pose concerns to user safety. The additive was demonstrated to be homogeneous in premixtures and complete feed.

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

# 2.2. Section III: Safety

## 2.2.1. Safety for the target species

The Committee evaluated the literature review provided by the applicant and concluded that there are no additional concerns for safety for the target species since the original authorisation.

## 2.2.2. Safety for the consumer

The Committee evaluated the literature review provided by the applicant and concluded that there are no additional concerns for safety to the consumer since the original authorisation.

## 2.2.3. Safety for the user

The applicant presented the following tests to evaluate safety of the additive for the user/worker:

- In vitro human three-dimensional model (EPISKIN-SM; OECD TG 439)
- In vitro reconstituted human model (EpiOcular; OECD TG 492)
- Local lymph node assay (OECD TG 429)

Based on the data presented, the ACAF concluded that the additive is not a skin irritant or dermal sensitiser. The additive should be regarded as a potential eye irritant. The data presented on dusting potential indicated that the additive was unlikely to form an unacceptably high amount of respirable dust when handled normally by operators.

## 2.2.4. Safety for the environment

Safety for the environment was assessed by the Committee who raised concerns over the potential development of antimicrobial resistance with continued use of the additive, and whether the information provided by the applicant was sufficient in determining the concentration of zinc that will enter the environment under the proposed conditions of use. The Committee requested the input of environmental specialist, Dr. Chris Sinclair, who provided a detailed report, suggesting that the applicant should provide a Phase I environmental safety assessment prior to requesting further environmental studies. The Committee communicated this request to the applicant who provided additional information in response. The Committee assessed the applicant's response, determining that the information provided was suitable for assessment with no further environmental studies required. The Committee concluded that the additive poses an acceptable risk to the environment when used under the proposed conditions of use for terrestrial species and in land-based

aquaculture systems. The Committee were unable to conclude on the safety of the additive for marine sediment compartment when used in sea cages.

### 2.2.5. Conclusions on safety

The ACAF concluded that the additive can be considered safe for the target animal species and the consumer. The additive is not a skin irritant or dermal sensitiser and is unlikely to form harmful amounts of respirable dust. The additive should be considered a potential irritant to the eyes. The additive poses an acceptable risk to the environment under the proposed conditions for terrestrial species and land-based aquaculture systems. The Committee were unable to conclude on the safety of the additive when used in sea cages.

## 2.3. Section IV: Efficacy

As an application with only minor modifications to the specification, the Committee concluded that efficacy cold be extrapolated from the original authorisation and that the additive continues to be considered efficacious under the proposed conditions of use for all animal species.

# 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 zinc chloride hydroxide monohydrate (EURL-FA, 2011):

> "For the determination of total zinc in the feed additive, premixtures and feedingstuffs the Applicant submitted the internationally recognised ring trial validated method EN 15510, based on inductively coupled plasma atomic emission spectroscopy (ICP-AES). The following performance characteristics were reported: - a relative standard deviation of repeatability (RSDr) ranging from 1.7 to 8.8 %; - a relative standard deviation for reproducibility (RSDR) ranging from 5.0 to 19 %; and - a limit of quantification of 3 mg/kg. The EURL identified an alternative CEN ring-trial validated method (CEN/ TS 15621) based on ICP-AES after pressure digestion, for the determination of total zinc in the feed additive, premixtures and feedingstuffs. The total zinc concentration is determined using external calibration or standard addition technique. The following performance characteristics were reported for a feed for pigs, and for sheep, a rock phosphate, a mineral premix and a mineral mix, where the total zinc content ranged from 26.6 to 3618 mg/kg: - RSDr ranging from 1.5 to

> 5.4 %; - RSDR ranging from 2.7 to 22 %; and - LOQ = 1 mg/kg feedingstuffs. Furthermore, a Community method is available for the determination of total zinc in feedingstuffs, but limited performance characteristics for the method were provided. The UK Food Standards Agency recently reported results of a ring-trial based on the above mentioned Community method, and reported precisions (RSDr and RSDR) for feedingstuffs ranging from 1.0 to 9.5 %. Based on these acceptable method performance characteristics the EURL recommends for official control the CEN methods EN 15510 or CEN/TS 15621 to determine total zinc content by ICP-AES in the feed additive and premixtures. As for the determination of total zinc content in feedingstuffs, the EURL recommends for official control the Community method based on AAS and the above mentioned CEN methods (EN 15510 or CEN/TS 15621). Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005) is not considered necessary.".

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

The ACAF concluded that the additive was correctly characterised and no major cause for concern were identified.

The additive can be considered safe for the consumer and target animal. The additive is not an irritant to the skin and is not a dermal sensitiser. The additive has the potential to be an irritant to the eyes. Owing to the low dusting potential, it is unlikely the additive will form harmful amounts of respirable dust.

The additive poses an acceptable risk to the environment under the proposed conditions of use.

The FSA/FSS agree with the conclusions reached by the ACAF. FSA/FSS accepts the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

# Abbreviations

| Acronym | Definition |
|---|---|
| ACAF | Advisory Committee on Animal Feedingstuffs |
| EC | European Commission |
| EU | European Union |
| EFSA | European Food Safety Authority |
| EURL | European Union Reference Laboratory |
| EURL-FA | European Reference Laboratory for Feed Additives |
| FSA | Food Standards Agency |
| FSS | Food Standards Scotland |
| GB | Great Britain |
| ICP-AES | Inductively coupled plasma atomic emission spectroscopy |
| LOQ | Limit of quantification |
| OECD | Organisation for Economic Co-operation and Development |
| RSDr | Relative standard deviation of repeatability |
| RSDR | Relative standard deviation for reproducibility |

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# References

EC (European Commission). (2003). *Regulation No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition*. https://www.legislation.gov.uk/eur/2003/1831/contents

EURL-FA (European Reference Laboratory for Feed Additives). (2011). *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. Tetra-basic zinc chloride (TBZC)*. https://joint-research-centre.ec.europa.eu/reports-and-technical-documentation/fad-2011-0007_en