Eighty second Advisory Committee on Animal Feedingstuffs meeting

15th February 2022 – Online meeting

ACAF	FSA
Nicholas Jonsson (Chair)	Nathan Allen
Martin Briggs	Amanda Blackler
Katrina Campbell	Aaron Bradshaw
Matthew Fisher	Michael Dickinson
Christine McAlinden	Donal Griffin
Susan MacDonald	Emily Hudson
Donald Morrison	Kaitlyn Jukes
Derek Renshaw	Francisco Matilla
Adam Smith	Barry Maycock
Helen Warren	Olivia Osborne
Nick Wheelhouse	Shila Sultana
	Katie Schulz

1. Apologies

Mike Salter extended his apologies for the meeting.

2. Welcome

The Chair welcomed members of the Committee, Secretariat and observers from the Devolved Administrations.

3. Risk Assessment update

The Regulated Products Team Leader Donal Griffin gave an update on the status of feed additive applications currently being processed by the Regulated Products Risk Assessment Team. Currently fourteen applications are undergoing suitability checks and fifty-two are ready to commence the assessment process. Nineteen applications are currently under assessment by the Committee. Lastly, nineteen applications have been completed or are going through opinion completion.

Members were briefed on the ongoing recruitment campaigns for new Committee and Secretariat members to increase work capacity. The Secretariat will try out changes to the cover paper at the April meeting looking to reduce member's workload. It was also mentioned that a new trial is currently ongoing for associate members, who are not full committee members, allowed to participate in specific areas of discussion but without having voting rights. Members will be updated with any changes as they occur.

4. Policy Update

Feed Additives Policy Advisor, Amanda Blackler, briefed the group on the status of applications. It was said that preparations were being made for the release of the third batch of authorisations, where responses to the consultation process are expected for the end of 2023. Currently, eleven applications are going through consultation as part of the second tranche.

5. Minutes from 81st Meeting

The Committee reviewed the minutes from the 81st ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP812 – Intellibond C

Helen Warren declared an indirect conflict of interest and was allowed to stay for the discussion.

An application was evaluated requesting a renewal of authorisation of the additive "dicopper chloride trihydroxide". The additive is currently authorised as a feed additive for use in all animal species and falls under the category "nutritional additives" and functional group "compound of trace minerals".

Overall members found this is to be a well-prepared submission, providing an appropriate level of information and thereby minimising the number of times the annexes were consulted. The applicant wishes to update the additive name to include the term "granulated", which was deemed to be a reasonable request by the Committee. The identity and characterisation sections were well described, with the applicant noting that a substantial amount of product was not meeting the previous specification, which was for less than 1% of the particles to be below 50 µm in diameter. Particle size was found to vary with production site; therefore, the applicant proposes a modification in the specification for less than 5% of the particles to be below 50 µm. Members had no issue with this change in specification. The manufacturing process is well-described and there were no other concerns with identity and characterisation section.

Regarding safety, a well-documented literature review was provided comprising ninety-four relevant papers. All target species were covered, and the review demonstrated similar or better efficacy of dicopper chloride trihydroxide when compared to copper sulphate, with no safety concerns. The Committee was able to conclude that, in light of current knowledge, the additive remains safe for consumers under the recommended conditions of use. Members discussed dusting potential and whether particle size is as significant when the dusting potential is low. It was suggested that a register of decisions regarding regulation and guidance interpretation could be kept by the Secretariat for the Committee's future reference. Members were happy with the skin sensitisation conclusion, however, could not conclude on eye irritation as they do not have access to the original studies. The substance is REACH registered, but **members requested that the applicant**

should be asked to provide the original eye irritation studies and documentation for evaluation.

Regarding safety for the environment, the applicant concluded that dicopper chloride trihydroxide will dissociate into its component ions, all of which are naturally present in the environment. Committee members discussed the potential for the copper to reach locally toxic levels, as the REACH registration states it is very toxic to aquatic life with long-lasting effects. Conversely, the product is essential for healthy livestock production and there are limits that must be adhered to. In addition, there are similar products on the market with similar conditions of use. **The Committee concluded that an independent expert from the Register of Specialists should be contacted to provide their expertise in this instance.**

The additive presented in the renewal application appears to be more soluble than that of the original application, however the applicant deems this difference in solubility as insignificant. From the data provided, members noted that the difference appears to be quite substantial. **The Committee requested that the applicant should be asked to provide a full justification for why they do not think this change in solubility will have any effect physiologically.**

7. <u>Dossier for assessment: RP814 – Intellibond Zinc</u>

Helen Warren declared an indirect conflict of interest and was allowed to stay for the discussion.

An application was evaluated for the additive Intellibond Zinc (Zinc chloride hydroxide monohydrate). The application seeks renewal of authorisation under the category “nutritional additive”, functional group “Compounds of trace elements” for its use in all animal species.

The Committee evaluated the identity and characterisation of the additive highlighting the proposed name change from tetra-basic zinc chloride to granulated zinc chloride monohydrate. Members concluded analysis by powder x-ray diffraction demonstrated the product to be within the specifications detailed by the applicant. The changes made to the manufacturing process since the previous authorisation were assessed. Members noted that, although the product included a higher number of smaller particles, the low dusting potential and the new formulation would prevent new safety risks to user and worker safety.

The Committee evaluated the safety for the target animal, safety for the consumer and safety for the user/worker. A literature review detailing a range of efficacy studies in which zinc chloride hydroxide was fed to target species was reviewed. Whilst none of the studies were designed as tolerance studies, the Committee concluded that the information provided was adequate for the assessment of safety of the additive. Discrepancies were noted in the conditions of use of the additive with the label suggesting a need for respiratory, hand, skin, and eye protection and the proposed safety data sheet (SDS) stating ‘none required’. As the *in vitro* eye irritation study provided could not draw a conclusion on the potential irritation or corrosive

nature of Intellibond zinc, the Committee agreed that precautionary labelling as an eye irritant would be required. In the absence of primary skin sensitisation studies for the additive the Committee concluded that precautionary labelling for skin sensitisation would also be recommended. **The applicant would be given the choice to accept this conclusion or carry out the additional studies required to determine user safety.**

The Committee discussed safety to the environment raising concerns over the potential of antimicrobial resistance from accumulation of zinc in the environment with prolonged use of the additive. Further concerns were raised over the potential dissociation of zinc in water prior to consumption on pasture and when used in fish feed and whether this could lead to toxic levels in water courses. Members noted that higher concentrations than proposed are regularly used in animal feed, however, in this case were unsure if there should be a requirement for the applicant to provide environmental studies for the additive. **The Committee concluded that an independent expert from the Register of Specialists should be contacted to provide their expertise in this instance.**

Efficacy was not evaluated for the additive, as it is a renewal of authorisation.

8. Dossier for assessment: RP1015 – *Lactococcus lactis*

No conflicts of interest were declared for this item.

An application was evaluated for Lactococcus lactis NCIMB 30117. The applicant seeks a renewal of authorisation under the category “Technological Feed Additive” and functional group “Silage Additive” for its use on all animal species.

The Committee evaluated the identity and characterisation section of the dossier. It was concluded the microbial strain had been adequately characterised through rDNA sequence analysis, DNA fingerprint and whole genome sequencing (WGS), confirming it is a qualified presumption of safety (QPS) organism. The manufacturing process was evaluated by the Committee, who noted that the process had been unchanged since the first authorisation. The Committee noted that testing had not been carried out for *Salmonella* on three batches of the final product. The application lists *Salmonell*a testing as part of the HACCP plan, but this was not provided. **The applicant would be asked to provide the HACCP plan and test results for *Salmonella* in the final product.** The Committee noted the SDS was out of date and requested the applicant to provide an updated version of the document, including a complete list of ingredients used in the manufacturing process.

It was noted that the applicant had provided data to show that the additive is stable in its original state for storage for up to 2 years at 25^{o}C, and it was recommended that the additive is used on the day of dilution unless kept refrigerated. Members pointed out the additive’s high dusting potential of 5.12 g/m^{3} as well as a high percentage (21.5%) of particles of less than 10 µm diameter, which is in the inhalable range. The applicant recommended the use of protective equipment to reduce exposure. The Committee discussed the data presented for stability in water,

and concluded it was only demonstrated when refrigerated. No information on the proposed label text about the stability of the product once diluted was provided. **The Committee requested that the applicant should be asked to provide information referring to the stability or storage of the additive once mixed with water**.

Members stated that, as this is a QPS application, no safety studies were required for the target species, consumer or the environment. When evaluating the safety of the user/worker, the additive was deemed to be quite dusty with a high percentage of small particles. Applying the principle of precaution, the additive would be considered as a respiratory sensitiser. Given this would imply the need to use protective equipment to avoid inhalation, the Committee concluded that no acute inhalation test would need to be carried out.

A question was raised on the potential risk to workers from silicosis, however, members concluded this would not be the case given the formulation of the additive. Furthermore, members pointed out that the applicant would be asked to treat the additive as a respiratory sensitiser, so the precautions taken to reduce the dust exposure would also minimise the risk for developing silicosis.

The Committee stated that, since the applicant did not carry out any studies on the effect on eyes and skin, it would have to be considered a potential skin irritant, eye irritant and skin sensitiser. These conclusions were requested to be clear on the SDS and the label. Members emphasised how, according to the UK Health and Safety Law, the employer is expected to assess the risk to his employees who may handle materials, and for this, it is very important to have the information provided on an SDS clearly reflecting the potential hazards. **The applicant would be asked to provide an updated SDS reflecting the conclusions of the risk assessment on safety for the user**.

Efficacy was not evaluated for the additive, as it is a renewal of authorisation.

9. <u>Dossier for assessment: RP1026/27 – VTR-phytase</u>

Adam Smith declared an indirect conflict of interest and was allowed to stay for the discussion.

An application was evaluated requesting a new authorisation of the additive “VTR-Phytase” (6-phytase) under the category “zootechnical-digestibility enhancers” for its use in all avian species (RP1026) and all pigs (RP1027).

The Secretariat clarified that the applicant was not required to provide a unique identifier for the parent strain as no genetically modified material remained in the final product. The WGS analysis confirmed that manufacture strain used was the QPS microorganism *Komagataella phaffii.* The manufacturing process did not refer to a HACCP plan nor did it list all the ingredients used. Several errors were also detected in the SDS document. **The Committee requested that the applicant should be asked to provide an updated production process including HACCP**

plan details, full list of ingredients and SDS reflecting the different formulations of the product.

When evaluating the stability and homogeneity of the additive in feed, members noted that the studies presented were carried out at a concentration of 1000 u/kg of feed, as opposed to the 500 u/kg dose proposed in the conditions of use of the additive. Furthermore, the stability tests lasted three months, but the applicant claimed stability in feed for six months. **The Committee requested that the applicant should be asked to repeat the stability testing in feed and homogeneity testing, using a dose and duration representative of the conditions of use**. The liquid formulation of the product was proposed to be kept under refrigeration conditions of ≤ 5ºC and 60% of relative humidity to ensure stability in storage. Members noted that these were difficult conditions to meet in practice at a feed mill and **requested that the applicant should be asked to update the label to reflect the requirement to be kept refrigerated.**

Members evaluated the safety data presented by the applicant, including a subchronic toxicity study and two genotoxicity studies, at the proposed safe doses of 89 mg/kg of feed for chickens for fattening, 133 mg/kg for laying hens, 160 mg/kg for piglets, 192 mg/kg for pigs for fattening and 233 mg/kg for sows. The additive was considered to be safe for the target species at the proposed dose. No further evaluation of safety for the consumer was required, as the additive is an enzyme produced by a QPS organism.

When evaluating the safety of the user/worker, the additive was deemed to be quite dusty. Applying the principle of precaution, the additive would have to be considered a respiratory sensitiser. Given that this would imply the need to use protective equipment to avoid inhalation, the Committee concluded that no acute inhalation test would need to be carried out. The skin irritation test presented was evaluated and concluded to be negative. No further tests for eye irritancy or skin sensitisation were provided, so **the Committee concluded that the additive would be considered a potential skin sensitiser and eye irritant unless further testing were carried out by the applicant.** No evaluation of safety for the environment was required, as the additive is an enzyme produced by a QPS organism.

Twelve efficacy studies, (three each for laying hens, broilers, piglets and sows) were evaluated by the Committee. The studies were found to be carried out to a good quality standard and to be representative of the conditions of used proposed. Members noted that the effect is notably better in piglets and pigs for fattening than in sows and all bird categories. Lactating sows also showed larger improvements than dry sows. Members concluded that the studies evidenced that the additive is efficacious as a digestibility enhancer for the target species, but that the strength of the effects differs with the species and stage of development.

10. Response to RFI: RP634 – Chromium propionate

No conflicts of interest were declared for this item.

The Committee re-evaluated several queries answered by the applicant. A discussion was held around the new data provided for the in vitro mammalian cells micronucleus test, and members concluded that the results supported the interpretation of the study. The applicant's justification for the absence of prenatal developmental studies (PNDT) was questioned by the Committee, which concluded that **a rat PNDT study would have to be provided**. Members could not conclude on the validity of the efficacy trials presented and **decided that the input of a poultry nutrition specialist would be required**.

11. Response to RFI: RP1071 – Avatec (Turkeys)

No conflicts of interest were declared for this item.

Members discussed the evidence presented in support of safety for the target species and concluded that the additive could be considered safe for turkeys for fattening. The efficacy data was reviewed, and it was concluded that the additive has the potential to be efficacious for turkeys for fattening. The applicant presented an exposure model for consumers to support the reduction of the withdrawal period from five to three days. Members detected an inconsistency in the data that questioned the validity of the conclusions. **The applicant would have to clarify the origin of the data point before being able to draw a conclusion.**

12. Response to RFI: RP665 – Dimethylglycine sodium salt

No conflicts of interest were declared for this item.

The Committee reviewed both responses provided by the applicant, which were deemed unsatisfactory, as the dusting potential was not expressed in mg/m^3 and no data was provided for a specific impurity. **The applicant would be asked to revisit the Committee's queries on dusting potential and impurities.**

Addendum: The application was later withdrawn by the applicant.

13. Response to RFI: RP666 - Protural

No conflicts of interest were declared for this item.

The Committee evaluated the label provided, which had been updated with the correct inclusion level and conditions of use. The label was considered to be correct, and members had no further concerns. At the December meeting, the Committee had concluded on the efficacy of Protural in piglets (suckling), piglets (weaned) and piglets (suckling and weaned piglets). However, they could not conclude on the efficacy of Protural in pigs for fattening. The applicant accepted these conclusions. The application would move to the opinion formulation stage.

14. Response to RFI: RP694 – *Saccharomyces cerevisiae* CNCM I-1079

Helen Warren declared an indirect conflict of interest and was allowed to stay for discussion.

The applicant had provided more information on undesirable substances in the final product. Members were satisfied with this data and the accompanying information on the manufacturing process and removal of residues. A material safety data sheet was also provided, which the Committee accepted with no concerns. Members evaluated the further information provided regarding quality assurance of the efficacy studies, as well as full protocols for the studies. The appropriate information has now been shared and there were no outstanding concerns. The application would move to the opinion formulation stage.

15. Draft opinions

Members were presented with draft opinions for applications RP226 and RP686. Feedback was provided to be reviewed by the Secretariat.

The Committee was also presented with the final version of opinions for applications RP597/600. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

16. Nanoparticles

The ACAF received an informative presentation by the Secretariat on nanoparticles, the ongoing research at FSA on the subject and the relevance for the Committee's future work.

17. FSA ongoing research update

The ACAF received a verbal update on the ongoing research projects carried out by the FSA secretariat.

18. Any Other Business

- Members agreed to add one more meeting to the calendar year. *Addendum: After the meeting, the previous dates for October 5th and December 7th were substituted with September 15th, October 31st and December 14th.*

Next ACAF meeting: Tuesday 4th April 2023 on Microsoft Teams.