Eighty third Advisory Committee on Animal Feedingstuffs meeting

4th April 2023 – Online meeting

ACAF	FSA
Nicholas Jonsson (Chair)	Nathan Allen
Martin Briggs	Alexander Cooper
Katrina Campbell	Michael Dickinson
Christine McAlinden	Donal Griffin
Susan MacDonald	Emily Hudson
Donald Morrison	Michelle Hutchison
Derek Renshaw	Kaitlyn Jukes
Mike Salter	Francisco Matilla
Adam Smith	Barry Maycock
Helen Warren	Lucy Smythe
Nick Wheelhouse	Johann Trotter

1. Apologies

Matthew Fisher 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 nine applications are undergoing suitability checks and fifty-one are ready to commence the assessment process. Twenty-one applications are currently under assessment by the Committee. Lastly, twenty 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 Committee was also briefed on the agreed terminology for the two different outputs of their assessments. The Committee's assessment will be named "Committee's Advice". The FSA/FSS-owned document adopting the Committee's conclusions and any other pieces of evidence (such as the NRL's conclusions) will be named "Safety Assessment".

4. Policy Update

Members of the Feed Additives Policy Team sent their apologies for the meeting. Further updates would be provided at the following meeting.

5. Minutes from 82nd Meeting

The Committee reviewed the minutes from the 82nd ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP859 – Chlorophyllins

Susan MacDonald declared an indirect conflict of interest and was allowed to stay for the discussion.

An application was evaluated requesting a new authorisation of "chlorophyllins" as a feed additive for its use in poultry for fattening, under the category "zootechnical additives" and functional group "other zootechnicals". The additive is intended to act as a marker to detect faecal matter contamination in poultry carcasses.

The Committee noted that, although a qualitative description of the additive's components had been provided, these had not been expressed as a percentage of the final product**. It was requested that the applicant should be asked to provide a quantitative description of the additive's composition.** While the application presented data of impurities and the correspondent certificates of analyses, these were out-of-date and did not specify the method of analysis in the final product. Furthermore, the application did not present impurity testing on dioxins, pesticides and PCBs. **Members requested that the applicant should be asked to provide updated certificates of analysis for all relevant impurities, specifying the method of analysis for each impurity.**

The stability studies in feed were evaluated by members, who noted that a stock solution that was not fully characterised had been added to the test feed, instead of the final form of the additive. Furthermore, while the applicant proposed to administer the product through drinking water, no water stability studies were presented. After considering the application's rationale for its absence, **the Committee concluded that the applicant should be asked to provide a stability test in water using the final form of the product**, and **to indicate the expected shelf-life of the product after being mixed in water**.

Members evaluated an acute oral toxicity and a 90-day toxicity studies in rats, supporting safety for the target species, and concluded that there were no adverse effects. However, the studies could not be considered further due to the lack of quantitative composition description of the additive, which impedes identifying the test substance as the additive. **The Committee requested that the applicant should be asked to provide evidence that the additive tested in the studies is the same as the one proposed for authorisation**.

The Committee noted that the claim that the additive has low oral bioavailability was not supported by any ADME studies. A parallel study from the literature on a chemically related substance (chlorophyllide a) showed that intraperitoneal doses were rapidly excreted into faeces. However, members did not think these results could be extrapolated to show the pharmacokinetics of chlorophyllins, and

requested that the applicant should be asked to provide further evidence of ADME processes and oral bioavailability. Given the absence of data provided supporting safety for users and workers, and considering the product was shown to be very dusty, members **concluded that the additive would have to be considered potentially hazardous for the skin, eyes and respiratory routes of exposure**, unless further information was provided. The applicant explained that no environmental safety studies were required since chlorophyllins occur naturally, but the Committee questioned this argument given that, when concentrated, naturally occurring substances can pose a risk. **It was requested that the applicant should be asked to provide an environmental risk assessment following guidance recommendations.**

Members evaluated an efficacy proof-of-concept study, noting that the compound could be detected in poultry faecal matter. A discussion ensued in which it was concluded that the study design of three efficacy trials presented was not up to standard, and that evidence of efficacy was insufficient. Furthermore, the application was not clear in describing the practical incorporation of the additive into the slaughter line. **The Committee requested that the applicant should be asked to provide further evidence of efficacy following the principles listed in the efficacy guidelines.**

7. Dossier for assessment: RP1039-40 – VTR-Xylanase

Adam Smith declared an indirect conflict of interest and remained in the meeting for the discussion.

An application was evaluated for the additive VTR Xylanase. The application seeks new authorisation under the category “zootechnical”, functional group “digestibility enhancer” for its use in all pig (RP1039) and avian species (RP1040).

The Committee highlighted that a comprehensive analysis of antimicrobial DNA sequences and viable cells in the final product had been performed. Assessment of impurities data showed an absence of aflatoxin B1 analysis. **The applicant would be asked to provide information on the presence / absence of aflatoxin B1 in line with guidance.** The dossier did not contain FAMI QS and HACCP documentation for the manufacturing process and several SDS documents provided contained errors (e.g., no exposure limits included in documentation). **The applicant would be asked to provide appropriate FAMI QS and HACCP documentation as well as corrected SDS documents.** Whilst evaluating the stability and homogeneity of the additive members noted that the pelleting process was only conducted at 70°C with no evidence of holding time provided. Furthermore, the homogeneity of the additive in its granular form was not well demonstrated with CVs of 39% powder in mash and 30% powder in pellets. **The applicant would be asked to provide further pelleting data ensuring scientific guidelines are followed. The applicant would also be asked to provide further information to demonstrate homogeneity of the additive in its granular form.**

As the enzyme was derived from a QPS organism, safety for the consumer, target species and the environment did not require evaluation. The Committee evaluated the safety of the additive determining that the absence of toxicological studies was acceptable owing to its QPS status. Although the dusting potential had been demonstrated to be low, the Committee discussed the potential respiratory nature of the additive as an enzyme. The Committee concluded the additive should be considered a respiratory sensitiser and therefore determined that appropriate PPE should be used when handling. The Committee considered the suitability of *in vitro* eye irritation studies in the investigation of enzymes, with members concluding the studies provided were acceptable for assessment. Discrepancies between the safety recommendations in the dossier and the MSDS provided were highlighted by the Committee. **The applicant would be asked to provide an updated version of the MSDS document to include the safety information described in the dossier as well as to correct the spelling mistakes throughout.**

Efficacy data presented within the dossier was assessed with the Committee noting it was unclear as to which form of the additive was used in each of the studies provided, with the length of the studies presented for laying hens noted to be below the minimum trial duration as defined in guidance. Further inconsistencies in the inclusion level of the additive in both pig and avian species were noted throughout the dossier. **The applicant would be asked to clarify the form of the additive used in each of the efficacy trials and the reason for the deviation from EFSA guidance in the length of the efficacy trials in laying hens. The applicant would also be asked to review the documentation provided and to clarify the minimum inclusion rate for both porcine and avian species ensuring all documents are corrected to ensure consistency throughout.**

8. Dossier for assessment: RP1047 – Magni-Phi

No conflicts of interest were declared for this item.

An application was evaluated for Magni- Phi®, a preparation of powdered dry *Quillaja saponaria* (85% w/w) and dry *Yucca schidigera* (15% w/w) with a minimum saponin content of 3.5% (w/w). The applicant is requesting a new authorisation under the category "zootechnical additives" for its use in all avian species (excluding laying and breeding birds).

There was uncertainty surrounding the identity of the product and the comparison to other substances referenced by the applicant through the literature. **The Committee requested that the applicant should be asked to provide a more detailed description and analytical characterisation of their product, explaining exactly how it relates to the other products they have described.** Members evaluated the manufacturing process, noting that only brief details were provided, namely around the blending and drying phases, and that no HACCP information was given, therefore members requested **that the applicant should be asked to provide a more detailed account of the manufacturing process, including HACCP information.** It was noted that there was no explanation given for why only 10g of

product were tested for *Salmonella* as opposed to 25g as per guidance recommendation. **Members requested that the applicant should be asked to explain why only 10g of product were used for these tests.** Members discussed the potential for issues with contaminants in the final product. The **applicant would be asked to provide further analytical data from different batches, and to describe how they manage any potential contaminant risk.** The coefficients of variation for homogeneity ranged from 9 to 15%, which is outside the recommended range of 10%. It was concluded **the applicant should be asked to explain this higher variation within their homogeneity results.** It was noted that the GMP+ certificates provided by the applicant are no longer valid, **therefore it was requested that the applicant should be asked to provide valid certificates.**

The Committee evaluated the tolerance studies provided, commenting that they were not carried out to GLP, but methods were well described, and the study conducted and monitored by persons with appropriate experience. However, members requested that **the applicant should be asked to provide details on how blood samples were collected, stored and analysed, as well as certificates for assurance of quality to be provided for this study.** Members concluded that the explanation given for the lack of toxicological data was not sufficient. The EFSA opinion provided was for a *Quillaja* extract product only, as opposed to the blend used for this feed additive. As no inhalation toxicity data were provided**, the additive must be regarded as potentially harmful by inhalation. The additive should also be regarded as a potential skin sensitiser for the same reason**. Members commented that the results of the in vitro test for eye irritation were strongly positive, indicating the potential to cause serious eye damage. **Members requested that the applicant should be asked to revise the SDS with regards to both the potential for eye damage and the need for respiratory protection.**

Members assessed the four *in vivo* efficacy studies provided by the applicant, noting inconsistent performance results, but acceptable digestibility results. The Committee queried if trials in broilers can be used to extend to all avian species excluding layers and breeders, noting the animal categories listed by the applicant for authorisation were not clear. **Members requested that the applicant should be asked to clarify if their intended extrapolation is for other poultry for fattening and ornamental birds**. Members agreed that no further studies on the quality of animal products would be required.

9. Dossier for assessment: RP1087 – Guanidinoacetic acid

No conflicts of interest were declared for this item.

An application was evaluated for Guanidinoacetic acid (GAA) currently authorised for its use in chickens for fattening, weaned piglets and pigs for fattening. The applicant requested an extension of use to all animal species. The additive falls under the category “Nutritional Additives” and the functional group “Amino acids, their salts and analogues”.

It was noted that the microbial impurities were described in the application, however no certificate of analysis was provided. **The Committee requested that the applicant should be asked to provide the certificate of analysis for tests carried out on the final formulation of the product**. Within the manufacturing process section, it was mentioned that the HACCP details were not provided. **The Committee requested that the applicant should be asked to provide the HACCP protocol**. Members discussed whether the high dusting potential shown in the application dossier was due to the formulation or the production process. **The Committee requested that the applicant should be asked to identify the source of the dust**.

It was mentioned that the stability of the product in premixes, water and feed is acceptable, however two samples within the poultry mash homogeneity trial were discarded, but the reason for discarding them was not given. **The Committee requested that the applicant should be asked to clarify this uncertainty**. It was also noted the applicant provided data for stability of pelleting at temperatures of 86^{o}C and above for up to 30 seconds. Members stated that, for breeding poultry, feed is commonly processed at 86^{o}C for up to 6 minutes and **requested that the applicant should be asked to provide data of stability under these conditions**. The Committee discussed a table showing the content of GAA at two inclusion levels in the pelleted, starter, and grower feeds over a period of 48 months. Some readings showed an inaccuracy of up to 5% of higher content of GAA than initially included. **It was concluded that the applicant should be asked to clarify the reason for this 5% GAA content increase.**

The Committee concluded that the literature search carried out for safety for the target species appeared to be detailed and comprehensive. It was noted there were no concerns from the literature review on tolerance studies, including no adverse effects on toxicological testing. Members evaluated a reference to a previous EFSA conclusion that the mutagenicity and genotoxicity studies provided evidenced absence of concerning effects, however, the original data could not be accessed**. The Committee requested that the applicant should be asked to provide the evidence that additive is non-mutagenic and non-genotoxic.** It was noted that overall, the studies provided showed that GAA had no adverse toxicological effects.

The Committee concluded that, based on the information provided, the additive should be considered not irritant to skin or eyes, and to not be a dermal sensitiser. Acute toxic effects of GAA (5.13 mg/L) after single exposure via inhalation was conducted on 10 healthy rats according to GLP. All animals survived exposure, exhibited irregular respiration for the first day and appeared active and healthy for the following 14-day observation periods with no abnormalities being reported. It was noted the application described respiratory protection not being required under normal use. However, members concluded that, given the dusting potential of the additive, use of respiratory protection would be advisable to reduce inhalation exposure.

The efficacy section was considered to be supported by a well conducted literature review. It was concluded that the efficacy in growing pigs and poultry was clearly

shown, as well as other avian species such as quail, ducks and turkeys. There was a discussion on whether the extension of authorisation to all animal species had been covered in this application, as the publications presented did not include the species listed in the technical guidance: laying hens, sows, calves, cows, salmonids and three other different fish species. **The Committee requested that the applicant should be asked to provide evidence of efficacy for the missing animal categories before being able to conclude on the efficacy of the additive for all animal species.**

10. Response to RFI: RP1307 – Colic sachet

No conflicts of interest were declared for this item.

The Committee re-evaluated the query sent to the applicant regarding the lack of safety and efficacy evidence shown. A change in the composition of the PARNUT was proposed by the applicant, and new references were provided. **The Committee concluded that the PARNUT application had now shown evidence of safety and efficacy and could move ahead in the assessment process.**

11. Response to RFI: RP593 – Hostazym C

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

Members discussed the evidence presented for various queries sent to the applicant. The response was concluded to be adequate for the updated conditions of use, homogeneity data and confirmation of absence of the production strain in the final product. Members noted the pelleting stability was not tested for extended retention times. **It was requested that the applicant should be asked to accept the Committee's conclusion of stability at high temperatures for a shorter time, or re-do the test with longer retention times.**

12. Response to RFI: RP791 – *L. buchneri*, etc.

No conflicts of interest were reported for this item.

The Committee evaluated the detailed explanation given for the absence of vancomycin resistance gene hits and the additional information. Members were satisfied with this explanation. The Committee had previously requested evidence demonstrating that the additives remain the same as in the original authorisation. Although there was discussion about issues regarding the testing used, members were convinced that the various samples of bacteria tested remained relatively stable. The applicant had provided documentation to support their stance that because the OECD in vitro methods are not validated for microorganisms, they do not need to perform them to support safety for the user/worker. The Committee discussed this and concluded that other factors needed to be taken into

consideration regarding the final product and not just the microorganism. Therefore, members still stated that they can only conclude on the one organism tested and the others must be regarded as potential skin sensitisers and irritants, as well as eye irritants. After providing the requested individual animal data from the eye irritancy test, the Committee concluded that *Pediococcus acidlactici* MA 18/5M is not an eye irritant. The application would move to the Safety Assessment formulation stage.

13. Response to RFI: RP416 – Axtra XB

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

The applicant provided a literature review as evidence that the production strain does not have the capacity to produce hazardous products. Members commented that a WGS analysis would have been preferred, but requesting it from the applicant would not add any additional information to what had already been provided, and concluded that the strain can be considered safe. The Committee also concluded that the applicant had demonstrated that the product under renewal is the same as that of the original application.

14. Response to RFI: RP420 – Axtra Phy Gold

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

Members evaluated the stability data presented by the applicant and concluded that stability at high temperatures during several minutes had been proven. The applicant had also been asked to carry out a new *in vitro* micronucleus test following OECD TG 487. Members concluded that absence of genotoxic potential had been demonstrated. The application would move to the Safety Assessment formulation stage.

15. Draft opinions

Members were presented with draft opinions for applications RP666, RP694 and RP748. Feedback was provided to be reviewed by the Secretariat.

The Committee was also presented with the final version of opinions for applications RP226 and RP686. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

16. Feedback on Committee Papers

The Secretariat prepared two cover papers in a new style, after carrying out a thorough search of the dossier to identify any potential risks and causes for concern

and point these out to members. The Committee provided very positive feedback on the new paper style, which will be adopted by the Secretariat for future meetings.

18. Any Other Business

The new dates for Committee meetings from September to December 2023 were confirmed to be September 15th, October 31st and December 14th.

Next ACAF meeting: Thursday 8th June 2023 in Clive House, London.