Eighty Sixth Advisory Committee on Animal Feedingstuffs meeting

15th September 2023 – Online meeting

ACAF	FSA
Nicholas Jonsson (Chair)	Nathan Allen
Martin Briggs	Amanda Blackler
Emily Burton	Aaron Bradshaw
Matthew Fisher	Alexander Cooper
Hannah Kane	Michael Dickinson
Susan MacDonald	Michelle Hutchison
Oonagh Markey	Edward Fuller
Christine McAlinden	Kaitlyn Jukes
Donald Morrison	David Kovacic
Derek Renshaw	Francisco Matilla
Adam Smith	Barry Maycock
Helen Warren	Hannah Reid
Nick Wheelhouse	Lucy Smythe
	Shila Sultana
	Johann Trotter

1. Apologies

Mike Salter, Olivia Champion and Katrina Campbell sent their apologies.

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 Fran Matilla-Garcia gave an update on the status of feed additive applications currently being processed by the Regulated Products Risk Assessment Team. Currently one application has been published, and a further 20 documents covering 25 applications are expected to be published by the end of the month. Two applications are undergoing suitability checks and fifty-four are ready to commence the assessment process. Twenty-eight applications are currently under assessment by the Committee. Lastly, fourteen applications have been completed or are going through safety assessment completion.

The Secretariat will be carrying out a recruitment campaign to replace both senior assessor roles that are now vacant. The Committee was briefed on future plans for adapting ways of working to reduce member's workload and increase output levels. This would also include future training meetings for further development of the Secretariat's assessment capacity.

4. Policy Update

Feed Additives Policy Advisor, Amanda Blackler, briefed the group on the number of feed additives currently in the system. A ministerial decision is still pending for the Tranche 2 batch of 13 applications. It is expected that the authorisation will be in force by the end of 2023.

5. Minutes from 85th Meeting

The Committee reviewed the minutes from the 85th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Ways of working

The Committee received an updated presentation on proposed ways of working and agreed on producing a reference document that will be published in the ACAF website.

7. Dossier for assessment: RP1137 – CanBiocin K-9

No conflicts of interest were declared for this item.

An application was evaluated requesting authorisation of 'CanBiocin K-9 Heritage Probiotic Blend' as a feed additive for dogs, under the category 'zootechnical additive' and functional group of 'gut flora stabiliser'. The additive is composed of lactic acid bacterial strains; *Lacticaseibacillus casei* strain K9-1, *Limosilactobacillus fermentum* strain K9-2, *Levilactobacillus brevis* strain WF-1B and *Enterococcus faecium* strain WF-3 with maltodextrin added to achieve the desired concentration.

The Committee agreed with previous EFSA conclusions that raised concern over the presence of *E. faecium* WF-3 as part of the additive, as it contains an antimicrobial resistance gene. The Chair noted that removal of *E. faecium* WF-3 from the proposed active ingredients was requested by the applicant, however, this request was rejected at this stage due to application already having entered the assessment process.

The Committee discussed the additive composition and noted the increased CFU of *L. casei* relative to the other bacterial strains. Members concluded that the applicant's explanation required further clarity but agreed that the upper limit for a QPS microorganism posed no greater risk. **The Committee requested that the applicant should be asked to provide further clarification of the increased CFU observed for *L. casei*.**

It was noted that no assessment had been undertaken to ensure that culture medium was fully removed from the final product as per EFSA guidance. As such, **the Committee requested that the applicant should be asked to provide documentation to demonstrate no incubation medium be found within the final product.** Microbial detection was discussed, and the lack of testing for *Bacillus cereus* was highlighted. The dossier did provide *B. cereus* checks on the initial media however **the Committee request this be performed on the final product**

as per EFSA guidance. Furthermore, the applicant provided documentation relating to *Salmonella* testing per 10 g of sample. As per the guidance, **the applicant would be asked to perform *Salmonella* testing in 25g.**

The Committee discussed the antimicrobial properties demonstrated by the microorganisms within the additive. **Members were satisfied with the antimicrobial properties of the microorganisms and concluded that the additives were selected for their antimicrobial peptides.**

With regards to the antimicrobial resistance, members commented on the lack of analysis submitted by the applicant. A significant discussion was held over the lack of transposable elements identified within *E. faecium* WF-3. **The Committee concluded that the applicant should be asked to provide further analysis and information relating to the whole genome sequencing to prove the claims of non-mobile elements. The applicant would also be asked to undertake further analysis to ensure that each strain found within the additive is correctly identified.**

The stability of the additive was evaluated by the members. It was noted that the conditions of the studies were satisfactory, however, further evidence of replicates should be provided to allow comprehensive assessment. **Members noted that stability studies were still ongoing at the time of application and requested the remaining studies to be submitted.**

Members reviewed the safety for the user/worker noting that the additive is dusty and poses a potential risk to unprotected operators through inhalation during product handling. As the additive was microorganism-based, the Committee concluded that the additive should be classified as a potential respiratory sensitiser. Members also noted that no studies of skin sensitisation or eye irritation had been conducted and **concluded that in the absence of data the additive should be classified as a potential eye and skin irritant and a dermal sensitiser**.

The Committee noted the efficacy section was very confusing and failed to define efficacy based on the parameters chosen. The three *in vivo* trials and one *in vivo* study presented lacked an appropriate study design, failing to clearly state what the outcome variables were, and not measuring the effect of the treatment on the gastrointestinal microbiome of the target species. **Members noted that based on the data provided, the efficacy of the additive was not demonstrated.** These conclusions aligned with those of EFSA in their previous evaluation of the additive.

8. <u>Dossier for assessment: RP1243 – L-methionine</u>

An application was evaluated for the additive L-methionine. The application sought new authorisation under the category “nutritional additives”, functional group “amino acids, their salts and analogues” for its use in all animal species.

Members reviewed the impurities data provided, noting that testing for *Bacillus cereus* had not been provided. **The applicant would be asked to provide the appropriate testing for *Bacillus cereus***. It was also noted that testing for residual

solvents was absent from the dossier. **The applicant would be asked to provide testing for residual solvents**. Members highlighted the absence of MSDS documents for the raw materials used during the manufacturing process. Furthermore, the flow diagram provided did not provide adequate detail for assessment, with HACCP documentation and quality assurance documentation both for the applicant and the manufacturer also not provided. **The applicant would be asked to provide MSDS documents for the raw materials, as well as an updated flow diagram of the process. HACCP and quality assurance documentation for both the applicant and the manufacturer would also be requested. In the absence of HACCP documentation, the applicant would be asked to provide detail of how they are compliant with hygiene regulations and the risk management measures they have in place.**

Stability has only been demonstrated in two forms of feed, owing to the remit of the authorisation for all animal species, the Committee concluded **further stability trials in other forms of feed would be required form the applicant.** The heat treatment described by the applicant does not clarify if a pelleting process has taken place. **The applicant would be asked to clarify if a pelleting process has taken place, and if so the parameters for this process. In the absence of pelleting data, the applicant is asked to provide pelleting stability data for each form of the additive.** Whilst a label has been provided by the applicant for each of the forms, the text is unreadable due to its size. **The applicant would be asked to provide the label in a readable format**.

Safety to the user/worker was reviewed by the Committee who noted that only one of the SDSs presented described the need to use PPE. **The applicant would be asked to provide a justification for this discrepancy or to provide amended documentation ensuring PPE requirements are included in both.**

9. <u>Dossier for assessment: RP1258 – Enviva PRO 202 GT</u>

No conflicts of interest were declared for this application.

An application was evaluated for Enviva® PRO 202 GT. The applicant requested a new authorisation under Regulation (EC) No 1831/2003 for turkeys (for fattening). The additive falls under the category “zootechnical additives” and functional groups “gut flora stabiliser”.

The Secretariat pointed out some questions prior to the meeting for members to discuss. The Committee clarified that further testing for particle size distribution would not be required as the product is not very dusty. The Committee noted that there appears to be no time limit for testing in the scientific guidelines.

Members noted that the data for the Whole Genome Sequence (WGS) of the additive was not provided in the application, and discussed the rationale presented by the applicant indicating that the need to provide further data to support the WGS analysis is only a guideline. The Secretariat would take the discussion offline with expert analysts in the Committee. Members discussed the genetic stability of the

additive by pulsed field gel electrophoresis (PFGE), they stated that the batches of the organisms were out of date. **The applicant would be asked to provide up to date genetic stability analysis of the additive**.

It was noted by members that the FAMI-QS certificate was expired so **the applicant would be asked to provide an up to date certificate**. Members stated that the HACCP plan provided by the applicant is sufficient which included four Critical Control Points, however no ingredients MSDSs were provided. **The applicant would be asked to provide up to date MSDSs for all ingredients from their current suppliers**. There was also reference to other ingredients present in the finished additive, including mineral oil, calcium carbonate and sodium aluminosilicate, **the applicant would be asked for the MSDS for these ingredients and evidence of the purity (and food grade) of the mineral oil**.

The physical-chemical and technological properties were discussed, and members noted that although the stability of the additive in premixtures, mash and pelleted feed look satisfactory, this has only been tested in one batch instead of three, as stated in the guidance. **The applicant would be asked to provide stability testing results in three different feeds**. Members discussed the conditions of use table, Table II.29, which stated that conditioning and pelleting temperatures should not exceed 95ºC, however a retention time was not provided. **The applicant would be asked to provide the retention time in the conditions of use table and on the proposed label, Figure.3. The applicant would also be asked to update the proposed label text to include appropriate PPE including respiratory protection** as the text, “Do not breathe dust” is not sufficient to describe the necessary respiratory protection.

Members stated that as the product has not been tested for inhalation toxicity, the additive would be regarded as potentially harmful if inhaled. However, it was noted that workers would be exposed to minimal amounts of inhalation whilst handling the additive. Members were satisfied with the studies carried out on the effects on the respiratory tract and on the effects on eyes and skin, and **concluded the additive should be considered a potential irritant to eyes, but not to skin, and not a skin sensitiser**.

The Committee raised a query on the validity of extrapolation of results from older efficacy studies, based on the original study design and potential changes in current feed conversion ratios. **Members concluded that the similarities between species would outweigh these concerns, and therefore there is sufficient evidence to support the extrapolation to turkeys for fattening**.

10. Dossier for assessment: RP1275 – Quantum Blue

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

An application was evaluated for the additive Quantum Blue, a 6-phytase enzyme preparation. The application sought authorisation for fin fish, under the category ‘zootechnical additives, functional group ‘digestibility enhancers’.

The Committee noted that the applicant had not tested their additive for *Bacillus cereus* as outlined in the guidance and so **the applicant would be asked to provide results for *Bacillus cereus* or justify their exclusion.** A number of the qualitative and quantitative compositions for the products were based on studies from 2011-2013. Some of the reports provided were not in English, but a summary table of results had been provided instead. To be in line with the guidance, **the applicant would be asked to provide more recent impurity testing and the original results obtained must be provided as opposed to a reproduction or summary of the results**. Similarly, the following sections relied on data from more than five years ago: absence of antibiotic activity, absence of production strain, absence of mycotoxins and absence of DNA from production strain. **The applicant would be asked to provide more recent test results for each of these sections to support their application.** A number of the material data safety sheets were out of date; therefore, **the applicant would be asked to provide a full set of more recent MSDS for the starting components.**

The Committee had noted that in the response to the previous request for information from October 2022, it was stated that one of the annexes provided contained additional stability data to support the shelf-life claim. However, members could not locate this file and so **the applicant would be asked to provide this additional stability data**. Concerns were raised regarding the stability data provided, with the Committee concluding that the 40P formulation cannot be considered stable at 12 months due to a loss in 40% of its activity after only 6 months and a further decline to 62% of its target after 11 months. The data provided does not provide support for this shelf-life claim, therefore **the applicant would be asked if they accept this conclusion or if they would like to provide further data to support their claim**. Additionally, low recoveries were observed when determining the additive's stability in animal feed. At 3 months, a loss in activity of 24-48% was determined for seabream and turbot feed, with even lower values of 57-68% observed in trout feed. The Committee could not conclude positively on the additive's stability in feed at 3 months. **The applicant would be asked to provide an explanation or reasoning for these significant losses in activity.** It was noted that the liquid form of the additive is water soluble and is to be sprayed onto the outside of fish feed pellets. Concerns were raised that the additive may potentially be washed off when the pellets are placed into the water to feed the fish. **The applicant would be asked to comment on the potential for loss of additive when placed in water.** Dusting potential was measured for only one batch of the additive; therefore, **the applicant would be asked to provide dusting potential for three batches.**

The Committee had requested to ask for more information on the diet used in the tolerance study for trout, as there is a lack of information on the diet and its formulation. **The applicant would be asked to provide more information on how often the diet was formulated and how the stability and homogeneity of the diet was maintained throughout the trial.** Concerns were raised that the *in vivo* micronucleus test failed to prove that there was exposure of the target tissue to the additive. **The applicant would be asked to provide results for an *in vitro***

micronucleus test to allow for a conclusion on the potential genotoxicity of the additive. The active ingredient of the additive is an enzyme, so, despite its low protein content, **the Committee applied the principle of precaution and concluded the additive would be assumed to be a respiratory sensitiser.** The applicant provided no discussion regarding the potential for inhalation toxicity, therefore **the applicant would be asked to provide a discussion, and relevant studies if required, to evaluate inhalation toxicity of the additive.** The applicant stated that there is no expected risk to the environment. Although phytases are generally considered low risk to the environment if used correctly, a risk assessment must still be performed. Therefore, **the applicant would be asked to provide evidence of a phase I environmental risk assessment for the additive.**

The Committee assessed the efficacy data provided and were able to conclude on the efficacy of the additive in trout when used at a level of 500 FTU/kg. **Efficacy is potentially limited for other species of fin fish, with the additive only being potentially efficacious at levels of 2,500 FTU/kg.**

11. Response to RFI: RP709 – ProAct 360

Adam Smith declared a direct conflict of interest and left the meeting for the discussion.

The Committee reviewed the responses to the request for information noting that the HACCP documentation provided and study reports were suitable for assessment. **The safety data provided allowed conclusion that the additive is not a skin irritant and has the potential to be an eye irritant. In the absence of data, the Committee were unable to conclude on the additive's potential to be a skin sensitiser**. The applicant provided no reports of studies to investigate effects on the respiratory system and did not challenge the Committee's earlier conclusion **that the additive will need to be regarded as a respiratory sensitiser.**

12. Response to RFI: RP746 – Agal-Pro BL

No conflicts of interest were declared for this application.

The third Request for Information (RFI) was evaluated for Alpha-Galactosidase and Endo-1,4-betaglucanase. The applicant seeks authorisation under the category "zootechnical additives", functional group "digestibility enhancers", which was previously authorised by the EU.

The Secretariat asked the applicant in the previous RFI to provide an MSDS for all ingredients, members were not satisfied with the applicant's response. **The applicant would be asked to provide up to date MSDSs for all ingredients from their current suppliers**.

Members noted that the HACCP plan provided by the applicant in their response lacked detail and unclear Critical Control Points (CCP). **The applicant would be asked to provide a HACCP document showing clearly what the CCPs are**.

Members were satisfied with the missing documents that were provided in the response.

13. Response to RFI: RP812-814 Intellibond

Hannah Kane and Helen Warren declared indirect conflicts and remained in the meeting for the discussion.

The Committee assessed the specialist's responses to the questions regarding environmental safety. It was agreed that there is insufficient information provided to determine the risk of this product to the environment when used to treat terrestrial animals. Therefore, **the applicant would be asked to justify the environmental safety of the product through performing a Phase I assessment as described in the guidance. The applicant would be issued an RFI including the queries raised during the February 2023 ACAF meeting.**

14. Response to RFI: RP1047 Magni-Phi

No conflicts of interested were declared for this item.

The Committee had requested a more detailed description and analytical characterisation of the product, with an explanation for how it relates to the other products described. The Committee were satisfied with the additional information provided by the applicant. The applicant also provided a more detailed account of the manufacturing process and HAACP information, as requested. The Committee had asked for clarification on the testing methods used for *Escherichia coli* and *Salmonella* spp. The applicant confirmed that as per the guidelines, 10 g of product was tested for *E. coli* and 25 g for *Salmonella*.

Additional information relating to quality control and how potential risks are managed were provided, as well as an explanation for the high variation within the homogeneity results. A valid GMP+ certificate had now been provided and the applicant provided a detailed method on blood sample collection and storage for the tolerance studies, as well as a link to the quality certifications of the lab that performed the analysis. The applicant had provided a revised MSDS, however the Committee were not satisfied with a number of the changes. The information relating to safety is not consistent throughout the MSDS and sections were considered to be misleading. **The applicant would be asked to rephrase these sections, taking into consideration that the additive has not been tested and to make this clear. They also need to amend the inconsistencies found throughout the MSDS.**

The applicant had been asked to clarify the avian species that they wished to extrapolate the efficacy data to, confirming that they wished to extrapolate to other poultry for fattening (e.g., turkeys, ducks, geese, pheasants, quail, guinea fowl, ostrich) and ornamental birds. **The Committee concluded that this extrapolation request was acceptable.**

15. Response to RFI: RP1087 Creamino

No conflicts of interest were declared for this application.

The Request for Information (RFI) response from the applicant was evaluated for guanidinoacetic acid (Creamino®).

Members noted that the additive is clearly very stable when exposed to a range of temperatures, pressures and moisture contents for different durations. However, as only two of the four trials used short term conditioning and temperatures at or below 86ºC for 6 mins, **members were not able to conclude that the additive will be stable in breeder feed processed at 86ºC for 6 mins.**

The Committee were satisfied with the remaining responses provided by the applicant.

16. Draft safety assessments: RP309, RP593, RP1307

Members were presented with draft Committee's Advice documents for applications RP309 and RP593. Feedback was provided to be reviewed by the Secretariat.

The Committee was also presented with the final draft of Committee's Advice documents for application RP1307. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

17. Efficacy guidance and decision log

Due to lack of time, it was agreed that members will be updated on the process of logging previous decisions at the following meeting.

18. Any other business

No other business was discussed.

Next ACAF meeting: Tuesday 31st of October 2023 in York and online