Ninety-fifth Advisory Committee on Animal Feedingstuffs meeting
18th December 2024 – Online meeting

ACAF	**FSA**
Nick Jonsson (Chair)	Nathan Allen
Martin Briggs	Krystle Boss
Emily Burton	Emily Davies
Katrina Campbell	Edward Fuller
Hannah Kane	Rebecca Greenaway
Susan MacDonald	Beth Hall
Donald Morrison	Natasha Hawkins
Derek Renshaw	Emily Hudson
Mike Salter	Michelle Hutchinson
Adam Smith	David Kovacic
Christel Wake	Kaila Lee
Helen Warren	Francisco Matilla
Nick Wheelhouse	Barry Maycock
	James Metcalfe
	Shila Sultana
	Abigail Timothy
	Johann Trotter
	Alba Ureña Rusillo

1. Apologies

Matthew Fisher and Chris McAlinden 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Leader Francisco Matilla-Garcia provided an update, informing members that applications RP1055 and RP1582 have been withdrawn pending confirmation. An update was also given regarding the number of upcoming applications assigned to each of the three assessment routes – ACAF, Other Regulators Opinions (ORO) and the Abbreviated process (ABB), however these numbers are subject to change. There are several applications wherein confirmation is needed as to whether they require a risk assessment. Lastly, the Committee were thanked for their significant contributions in getting assessments published.

4. Policy update

Animal Feed Policy Advisor, Beth Hall, provided an update for policy, indicating that the next set of assessments are expected to be published for consultation by the end of January, one of which is a feed additive. With regards to reform, a paper on the removal of renewals went to the board in December and the legislation is moving forward to hopefully be introduced by the end of January, with the aim of coming into force from April onwards. A presentation was then given on market holder authorisations, highlighting the differences between holder and generic authorisations.

5. Minutes from 94th Meeting

The Committee reviewed the minutes from the 94th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP1904 Biomin C5

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

The Committee assessed an application for the additive Biomin C5, which falls under the category “zootechnical additives”, functional group “gut flora stabilisers”. The additive is a multi-species microbial feed additive consisting of five selected lactic acid producing bacterial strains – *Enterococcus faecium* (DSM 33761), *Pediococcus acidilactici* (DSM 33758), *Bifidobacterium animalis* (DSM 16284), *Limosilactobacillus reuteri* (DSM 33751) and *Ligilactobacillus salivarius* (DSM 16351).The applicant is seeking a new authorisation for use in chickens for fattening, chickens reared for laying, turkeys for fattening and reared for breeding and minor avian species other than laying species.

Members reviewed the four efficacy trials originally submitted for assessment, noting that one of the trials was poorly reported and that two of the studies could not be regarded as independent, and therefore could not be accepted for assessment. Based on the original data provided, the Committee were unable to conclude on the efficacy of the additive.

Owing to EFSA’s lack of conclusion on Efficacy, the Applicant provided supplementary data, containing a further three trials to demonstrate the efficacy of the additive. The Committee reviewed all seven trials submitted, noting that a positive effect was observed under the proposed conditions of use. However, Members noted that the trials were only performed using mash feed, and no trials representative of heat treatment were provided. **The Committee decided to further review the data provided offline prior to concluding on the efficacy of the additive**.

Addendum: The Committee further evaluated the efficacy data provided offline, concluding that the additive has the potential to be efficacious for chickens for

fattening under the proposed conditions of use. This conclusion can be extrapolated to chickens reared for laying, turkeys for fattening and reared for breeding and minor avian species other than laying species based on the data provided.

7. Dossier for assessment: RP2071 Enterosure conc

Emily Burton declared a direct conflict of interest and left the meeting for the discussion.

The Committee assessed an application for the additive Enterosure Conc, which falls under the category of “zootechnical additives”, functional group “gut flora stabilisers”. The additive contains viable spores of three microorganisms: *Bacillus velezensis* ATCC PTA-6737 (PB6), *B. velezensis* ATCC PTA-127114 (FxA) and *B. licheniformis* ATCC-127113 (G3). All three strains are suitable for the EFSA Qualified Presumption of Safety (QPS) approach. The applicant is seeking a new authorisation for use in all growing avian species.

The application referred to Enterosure Conc, but also to a less concentrated form in a calcium carbonate carrier, termed Enterosure. It was unclear whether the applicant was also seeking authorisation for Enterosure but the Committee agreed that for the purposes of the discussion, both forms would be considered.

Members noted that the applicant had provided Certificates of Analysis (CoAs) for five batches of Enterosure Conc to demonstrate the total number of viable cells. Although results had been reported for five batches of Enterosure, CoAs had not been provided for all the batches. **The applicant would be asked to provide CoAs for the remaining two batches for Enterosure.** In addition, the number of viable cells had not been determined separately for each strain and it was not clear from the dossier whether the three strains were in equal proportions in the final product. The Committee acknowledged that the quantification method submitted by the applicant was unable to differentiate between the three strains and discussed the potential for use of alternative methods to provide this information, such as quantitative PCR (qPCR). However, Members were satisfied that all three microorganisms were likely to have a similar stability profile in the additive and therefore a clear demonstration that cell counts were equal when mixed during manufacturing process would suffice. **The applicant would be asked to confirm whether the proportions of each strain in the additive are equal and provide evidence that this is the case during the standardisation step of the manufacturing process.**

Members noted that the dusting potential of Enterosure Conc and Enterosure was high and there was a high proportion of particles of diameter 50µm or less. Furthermore, Enterosure contained a high proportion of particles smaller than 1 µm, likely due to the calcium carbonate carrier. **The applicant would be asked to further characterise the fraction of small particles, using a method such as electron microscopy.**

Members considered the whole genome sequencing (WGS) analysis and phenotypic data provided to assess safety with regards to antimicrobial resistance (AMR). Members agreed that B. *velezensis* PB6 has been extensively characterised in previous applications and is not an AMR safety concern.

Members discussed the manufacturing process. It was noted that there were some discrepancies between the raw materials listed in the manufacturing process and the Safety Data Sheets (SDSs) provided. **The applicant would be asked to clarify exactly which raw materials were used in the manufacturing process and provide the appropriate SDSs for these.**

Members considered the compatibility of the additive with coccidiostats. Although *B. velezensis* PB6 had been demonstrated as compatible *in vivo* with a number of coccidiostats, *B. velezensis* FxA and *B. licheniformis* G3 both showed MICs below the cut-off in *in vitro* tests, and therefore **the applicant would be asked to provide data to demonstrate that *B. velezensis* FxA and *B. licheniformis* G3 are compatible *in vivo* with coccidiostats, and be advised that in the absence of data, the ACAF would be unable to conclude on compatibility of the additive with coccidiostats.**

Although all three organisms are suitable for the EFSA QPS approach, the applicant had provided a tolerance study in broilers. The Committee were unable to conclude on safety for the target species with the data provided, and **the applicant would be asked to provide further analysis and explanation of the findings.**

Members assessed the user safety studies provided and concluded that Enterosure Conc was not a skin or eye irritant but should be considered a respiratory sensitiser based on its proteinaceous nature. In the absence of data, it was assumed to be a skin sensitiser. Although studies had not been provided for Enterosure, the Committee were satisfied that the data supplied for Enterosure Conc could be extrapolated to Enterosure. Based on the potential for skin and respiratory sensitisation, the Committee recommended measures to protect users from respiratory and dermal exposure.

Members reviewed three long-term efficacy studies in chickens for fattening. One of the study reports referred to an additional two treatment groups for which the results were not provided. Members disagreed with the applicant's claim that the additional treatment groups were outside the scope of the study, and **the applicant would be asked to provide data for the two additional treatment groups.** Although two of the trials demonstrated evidence of efficacy, Members were unable to accept the third trial. In the absence of a third study, members were unable to conclude on the efficacy of the additive in chickens for fattening, and consequently, were unable to extrapolate and conclude on efficacy in all growing avian species.

8. Dossier for assessment: RP2107 Availa CR

Helen Warren declared an indirect conflict of interest and remained in the meeting for this item.

An application was evaluated for Availa Cr wherein the applicant requests a new use of the additive for salmonids. The additive falls under the category "zootechnical additives", functional group "other zootechnical additives". An application containing the same additive for use in dairy cows (RP16) was previously submitted to FSA, and partially assessed by the Committee.

The Committee supported the conclusion of the previous assessment for the identity of the additive, no causes for concern were identified. Availa Cr is a product that could form a dust on handling and inhalation by workers could result in the deposition of a large number of particles in the respiratory tract. It was noted by members that the active substance, Chromium chelate of DL-methionine, was well characterised. Members were satisfied with the flowchart detailing the manufacture of the active substance, the HACCP plan during the production process and the updated MSDSs of the raw materials.

Stability of the additive in feed was based on one batch of additive in extruded fish feed; the guidance typically suggests providing stability data in at least one batch of the additive in three feeds. Members concluded they were satisfied with the use of one type of feed. Stability in feed was tested using fish feed at a maximum temperature of 128°C, members highlighted the applicant should provide details of a minimum, maximum and/or average temperature and a retention time, and the updated details should also reflect on the conditions of use label as stating, “the temperature must not exceed 130°C during extrusion/pelleting of the feed”, is not sufficient. **The applicant would be asked to provide an updated conditions of use label including processing conditions and more detailed information on the storage conditions.**

Members evaluated the study provided to demonstrate the safety of use in rainbow trout, noting that it was well conducted. It was highlighted that 11 of the 192 fish showed macroscopic abnormalities. Members were not satisfied with the applicant’s response in the RFI regarding the 10 times maximum recommended dose which led to a significant reduction in growth performance relative to the control, they deemed the response did not clarify the findings. The Committee could not conclude on the safety for target species due to the adverse effects seen at the maximum dose in the tolerance study.

The toxicological studies for chromium methionine were evaluated, the bacterial reverse mutation assay and the mouse lymphoma assay gave clearly negative results, while the *in vitro* micronucleus assay was positive at the top dose in the absence of S9 with 24-hour treatment. The results of the *in vivo* micronucleus test showed no evidence of mutagenicity, although there was no evidence that the target tissue (bone marrow) had been exposed. Members interpreted the results of the mutagenicity studies as indicating that chromium methionine showed a mutagenic potential *in vitro* and the possibility of the additive being mutagenic *in vivo* could not be discounted. The ACAF concluded that, in principle and in the absence of evidence to the contrary, chromium methionine should be regarded as mutagenic at the site of exposure. Given the lack of new evidence provided to ACAF to show the lack of genotoxic potential of the additive *in vivo*, **the applicant would be asked to provide further evidence that the additive is not genotoxic *in vivo*.**

The Committee discussed the results of a literature search regarding ADME and toxicology of chromium (III) and chromium methionine for the safety for the consumer. No additional information has been provided in relation to absorption, distribution, metabolism and excretion in fish, therefore **the applicant is asked to provide further literature that includes aqua species.**

The toxicological studies of chromium methionine that have been provided are not very relevant to the assessment of the consumer safety of use of Availa Cr in salmonids, but the data are relevant to target species safety and user safety. The applicant provided mutagenicity studies and a 90-day oral toxicity study of chromium methionine to demonstrate consumer safety. Members did not find these studies useful for assessing the consumer safety of this additive as chromium methionine is unlikely to be present as residues in foods derived from treated animals. Instead, the applicant would be asked to consider whether the use of the recommended amounts of chromium methionine in feed would cause chromium to be deposited in edible tissues at acceptable concentrations and whether consumers could be exposed to harmful intakes of chromium. Any additional literature information that may be available would also be useful as supporting information.

The Committee highlighted that the normal handling of Availa Cr is likely to generate a dust and as chromium methionine is considered mutagenic, measures should be taken to minimise exposure of users to dust. Members agreed that the additive is non-irritant to skin and eyes and is not a skin sensitiser. The Committee noted that the applicant stated that the additive does not pose a risk to the environment as it is a naturally occurring element and the FEEDAP Panel concluded that the contribution of Cr-Met in excretions of terrestrial animals to the natural levels of Cr in soil and the aquatic environment would not pose a risk to the environment, however, this conclusion is for terrestrial animals and not fish where feed is added directly into the water. **The applicant is asked to carry out a Phase I assessment for the safety for the environment and if needed a Phase II assessment.**

The Committee evaluated the three efficacy studies provided in this application, stating they were all well-conducted and show efficacy of the additive in relation to growth performance. There was a consistent effect on efficacy at 0.4mg/kg across all and either a significant effect (for two studies) or trend at 0.2mg/kg (for one study). Members highlighted the negative findings in the salmon trial at 0.6mg/kg and in trout at 6mg/kg, also including a significant reduction in final body weight at 4mg/kg. **The applicant would be asked to provide further evidence of efficacy above 0.4mg/kg to conclude on the applicant's proposal of an upper limit of 0.6mg/kg.** Without that extra evidence, the Committee may only be able to conclude on a maximum dose of 0.4mg/kg. It was also discussed that the trial with the drop in efficacy at 0.6mg/kg is in Atlantic salmon whereas the other two trials where higher doses are still beneficial are in rainbow trout. As there are physiological differences between these two species of fish (for example trout are glucose intolerant) and thus may be more beneficially impacted by the Cr than trout given its effect on insulin sensitivity. **If the applicant is to provide a further study, they may wish to specify that this is in Salmon to be sure both species follow the same trend.**

9. Response to RFI: RP1275 Quantum Blue

Adam Smith declared an indirect conflict of interest and remained in the meeting for this item. Emily Burton declared a direct conflict of interest and left the meeting for this item.

The Committee evaluated the statement provided by the applicant regarding the reference used to determine their acceptance limits for yeasts and moulds. Members decided to further discuss the information provided offline, in addition to locating the method used to determine yeasts and moulds. Members were satisfied that the formulation used was adequate to demonstrate the absence of the production strain. The additional MSDS that the Committee requested were provided.

Additional data to support the stability of the additive in animal feed was provided. Members discussed the stability data, highlighting the presence of mould on some of the samples. The Committee concluded that the additive remained stable in its liquid forms (Quantum Blue 5 L and Quantum Blue 10 L) for 2 months. Additional data demonstrating phytase activity of the additive after 1 and 2 minutes of soaking in water was also provided. Members were satisfied that the loss of phytase activity in these time periods was acceptable due to the feeding behaviour of the fish.

Addendum: The Committee further discussed the acceptance limits for yeast and moulds offline, concluding that these limits were acceptable, however **the applicant would be asked to provide the method they used to measure yeast and moulds.** Upon receipt of this method, members were satisfied regarding impurities in the additive.

10. Response to RFI: RP1696 *Bacillus velezensis* ATCC PTA-6737

No conflicts of interests were declared for this item.

Members discussed the applicant's response, noting they were satisfied with the queries relating to the assurance certificate provided for the manufacturer, clarification of the ingredients list and MSDSs and agreed that the additive is considered a potential respiratory sensitiser, not an irritant.

The Committee discussed the clarification of the efficacy study reports provided, agreeing that the reports provided were not acceptable as there are discrepancies in the formatting and the unedited original reports have not been provided. Therefore, members will not be able to conclude on the efficacy.

11. Response to RFI: RP1888 Lactiferm

Martin Briggs declared an interest, but this was not deemed to pose a conflict, and he was allowed to remain in the meeting.

The Committee reviewed the response to a request for further information, in which the applicant was asked to provide additional efficacy data or accept that the Committee would be unable to conclude on efficacy. The applicant had provided two scientific papers as supporting evidence, but Members agreed that these did not provide sufficient evidence for efficacy. Furthermore, the applicant had pooled data from two of the original efficacy trials in which efficacy could not be demonstrated. Members agreed that the pooled data provided weak evidence of efficacy. When considering the pooled data alongside all the data that has been provided as part of the dossier, Members agreed that there was still insufficient evidence to demonstrate a positive effect of the additive on zootechnical performance. **Members were therefore unable to conclude on efficacy in chickens for fattening, and**

consequently were unable to conclude on efficacy in all growing poultry and ornamental birds.

12. Internal Safety Assessment: RP1499 Balancius muramidase

The Committee provided feedback on an internal safety assessment prepared for an additive containing muramidase produced by *Trichoderma reesei* DSM 32338.

13. Draft safety assessments: RP1070/RP1071/RP1072, RP1243, RP1258, RP1317, RP1366, RP1393, RP1400 and RP1512

The Committee was presented with the final drafts of the Committee's Advice document for applications RP1070/RP1071/RP1072, RP1243, RP1258, RP1317, RP1366, RP1393, RP1400 and RP1512. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

14. Qualified Presumption of Safety (QPS) Committee Paper

The Secretariat presented a paper to the Committee to review the Qualified Presumption of Safety (QPS) approach as part of the Guidance framework and its validity for the assessment of feed additives in GB. The Committee concluded that, overall, the QPS system is a robust and thorough approach to assessing microorganisms as additives or for the production of additives, and agreed the continuation of its use remained scientifically sound and relevant to the UK. Members flagged the importance of understanding the limitations of the QPS system and to be able to question applicants on areas beyond the QPS framework when these are relevant to the safety of the microbe. The Committee stressed the critical importance of identifying the strain adequately in the application and recommended establishing some form of monitoring to track applications that were concluded to be safe under the QPS framework. It was recommended that the FSA should consider the QPS system at a wider level beyond the feed additive authorisation framework.

15. Any other business

The Committee commented on the recent public concern surrounding 3-Nitrooxypropanol and noted that this application was submitted with a detailed dossier of data and scientific evidence. The Committee reinforced the robustness of the assessment carried out on the extensive evidence and the conclusions reached on the safety of the additive for the target species, consumers, users and the environment.

An update on upcoming applications was provided.

Next ACAF meeting: 12th February 2025 on Microsoft Teams.