Ninety-first Advisory Committee on Animal Feedingstuffs meeting
11th June 2024 – Meeting in London (Clive House)

ACAF	**FSA**
Nick Jonsson (Chair)	Nathan Allen
Martin Briggs	Mark Bond
Emily Burton	Aaron Bradshaw
Katrina Campbell	Emily Davies
Matthew Fisher	Edward Fuller
Hannah Kane	Beth Hall
Oonagh Markey	Lindsay Holden
Susan MacDonald	Emily Hudson
Chris McAlinden	Michelle Hutchinson
Donald Morrison	David Kovacic
Derek Renshaw	Kaila Lee
Mike Salter	Francisco Matilla
Adam Smith	Barry Maycock
Christel Wake	James Metcalfe
Helen Warren	Lucy Smythe
Nick Wheelhouse	Johann Trotter
	Alba Ureña Rusillo

1. Apologies

No apologies were received.

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 updated the Committee, stating that no further Safety Assessments have been published since the last meeting. There are nine Safety Assessments set to be published in July, including six which ACAF provided advice on. 74 renewal applications that were in different stages of the authorisation process have now been temporarily paused, pending decisions on potential changes to the legislative framework regarding renewal applications. Members were informed that the Register of Regulated Products Applications is now live and available to the public. Members were also notified of a tracker that covers each application that has gone to the Committee and includes information such as rapporteurs and in which meetings each application

was assessed. Lastly, the Committee were reminded to submit their claims within 90 days of each meeting.

4. Policy Update

Feed Additives Senior Policy Advisor, Mark Bond, briefed the Committee on the number of new applications received since the last meeting. It was highlighted that as we are currently in a pre-election period, there is a restriction in terms of engagement and messages that can be conveyed, particularly with regards to discussing future policy developments. Members were also notified that mechanisms are currently being put in place for post-market monitoring.

5. Microbiology presentation

Members of the Committee and the Secretariat received a presentation on bioinformatics, particularly whole genome sequencing. This presentation was prepared and delivered by three members of the ACAF.

6. Minutes from 90th Meeting

The Committee reviewed the minutes from the 90th ACAF meeting and provided feedback to be reviewed by the Secretariat.

7. Dossier for assessment: RP1366 ECONASE® XT

Emily Burton, Adam Smith and Michael Salter declared indirect interests, but these were deemed not to pose a conflict and they were allowed to remain for the discussion.

The Committee assessed an application for the zootechnical additive ECONASE® XT. The applicant had requested authorisation for a new use in laying hens, minor poultry species and fattening pigs. Members were informed that the renewal authorisation for this application missed the deadline, therefore it was to be assessed as a renewal in terms of guidance requirements but considered a new authorisation from a legal perspective. The additive falls under the category “zootechnical”, functional group “digestibility enhancers”.

The Committee discussed the whole genome sequencing analysis of the production strain that was provided by the applicant. The characterisation of the production organism has been assessed in previous opinions, and the Committee concluded that no further information was required from the applicant. The applicant had been requested by the Secretariat to provide evidence of testing for Enterobacteriaceae in the final product. The applicant had provided analysis for *Escherichia coli* and coliforms which Members were satisfied with. **The applicant would be asked to provide testing for dioxins and polychlorinated biphenyls (PCBs).** Members reviewed the manufacturing process and noted that many of the Safety Data Sheets

(SDSs) provided by the applicant were quite old. **The applicant would be asked to provide more recent MSDSs for all chemicals used in the manufacturing process.** Members noted that one form of the additive (Econase XT 25) had a high proportion of small particles and that it was not possible to exclude the possibility that the other solid forms of the additive (Econase XT P and Econase XT 5 P) also had a high proportion of small particles that could deposit in the respiratory system if inhaled. However, this was not considered a concern for user safety due to the very low dusting potential of all three solid forms of the additive.

Members reviewed the stability data and observed that the additive appears to be stable under the recommended storage conditions, although it was noted that there was a lower recovery for the liquid version of the additive when added to piglet feed. The applicant had provided pelleting stability data at temperatures of up to 95 °C but had not provided a retention time. **The applicant would be asked to provide the retention time and temperature for pelleting and state this on the product label.** Members also evaluated the homogeneity data and concluded that homogeneity was acceptable.

The Committee reviewed the safety data and concluded that the additive is safe for the target species, consumers and the environment. The applicant provided an updated literature review to demonstrate safety in the target species. Members indicated that, as an enzyme, a Maximum Residue Limit (MRL) and withdrawal period were not required. Members concluded that the additive is not an eye or skin irritant. It is not a skin sensitiser but should be considered a respiratory sensitiser. No further information would be required from the applicant.

Members reviewed several short and long-term efficacy studies provided by the applicant and concluded that the additive is efficacious in laying hens, minor poultry species and fattening pigs.

8. <u>Dossier for assessment: RP1400 L-lysine</u>

No conflicts of interest were declared for this item.

The Committee reviewed the identity information provided by the applicant, concluding that the additive was correctly identified. Members noted the extensive detail provided for characterisation, stating a thorough approach had been applied by the applicant with no further information required for assessment. Members noted that although the bioinformatic analysis of AMR genes in the production strain was only conducted against one database, the strain is historically well characterised and demonstrated negative MICs in the current application. Therefore, Members considered the AMR analysis of the strain to be satisfactory and unlikely to pose a risk with respect to AMR.

Members highlighted the absence of HACCP documentation for the manufacturing process. **The applicant would be asked to provide HACCP documentation for the manufacturing process.** The Committee concluded that stability had been adequately demonstrated for the additive and in premixtures, however, pelleting

stability and stability in water required further review before a conclusion could be drawn. **Members would review the information provided offline before a request for information is communicated to the applicant.** It was also noted that a proposed label had not been provided for assessment, **the applicant would be asked to provide the proposed text for the label for the additive.** Members discussed the absence of a proposed inclusion rate for the additive and noted that this is considered standard practice for amino acids which are added in line with dietary requirements.

Members reviewed the data provided for safety of the additive, noting that tolerance testing is not required for lysine as an amino acid as per the EFSA guidance on the assessment of the safety of feed additives for the target species (2017). The Committee noted that safety for the target species was supported via extrapolation from a repeat-dose 90-day oral toxicity study in rats with the least pure form of the additive. This was considered appropriate for assessment of all forms of the additive. The Committee concluded that the additive is not genotoxic and does not cause oral toxicity and does not pose a toxicological risk for the target species or consumers. Members noted that the skin and eye irritation studies provided for assessment were not performed on the final product, and owing to its low pH, concentrated liquid lysine could be corrosive to the skin and eyes. **The applicant would be asked to provide skin and eye irritation tests on the final product and in the absence of data from the final product the additive would be classified as a potential eye and skin irritant.** The additive is dusty and therefore measures should be taken to avoid inhalation. The additive is not a skin sensitiser in any of its forms. Members concluded that the additive does not pose issues for environmental safety.

9. Dossier for assessment: RP1460 Miya-Gold (*Clostridium butyricum* FERM BP-2789)

No conflicts of interest were declared for this item.

A risk assessment was undertaken primarily focusing on the efficacy section of the dossier for Miya Gold (*Clostridium butyricum* FERM BP-2789). The applicant had requested a new use and modification of the existing authorisation in chickens for fattening to allow for use in chickens reared for laying and minor avian species (excluding laying birds). The modification involves lowering the dose for use in chickens reared for laying and minor avian species (excluding laying birds). The additive falls under the category ‘zootechnical’, functional group ‘gut flora stabiliser’.

In relation to the *in-vivo* studies, the Committee noted that both Spanish studies and the Hungarian trials 3.2 and 3.3 were carried out at the same time and therefore could not be considered independent. It was also noted that the use of new litter over old litter failed to comply with welfare regulation EC 2007/43 and as such the study within Annex 3.4 cannot be accepted. The Committee also commented on the use of only male birds in all provided studies, which is poor practice. Therefore, due to an insufficient number of appropriate studies, the Committee were unable to conclude on efficacy. It was also noted that all studies were conducted on mash feeds, which is not representative of chickens for fattening where pelleted feed prevails. **The applicant would be asked to provide further efficacy studies in support of the**

application.

10. Response to RFI: RP1026/1027 VTR-phytase

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

Members were satisfied with the response from the applicant regarding the production process of the additive, MSDSs and labelling. New studies were provided for skin sensitisation and eye irritation, which confirmed that the additive is a powerful skin sensitiser but not an eye irritant.

The applicant was asked to repeat the stability and homogeneity tests; however, these were not undertaken within a reasonable time since the request was made, therefore, the available information was presented to the Committee instead. It was discussed that, while it is normal practice to use overage when using enzymes, currently no conclusion can be drawn on the stability during pelleting and storage or the homogeneity of the additive.

At this stage, the application will move onto the Safety Assessment drafting step.

11. Response to RFI: RP1070 Avatec (Game birds)

No conflicts of interest were declared for this item.

Members were satisfied with the analysis for *Bacillus cereus* that had been provided for three batches of the additive. The applicant was previously asked to demonstrate the stability of the production strain using an appropriate technique. Although the applicant had provided analysis of the morphological and physiological characteristics of the strain, members considered that insufficient information had been provided to demonstrate genetic stability. **The applicant would be asked to provide molecular characterisation of the production strain and demonstrate genetic stability using an appropriate technique.**

The Committee noted that the literature review provided by the applicant had identified possible interactions between florenfenicol and nicarbazin. **The Committee recommend that this information is added to the product label.**

12. Response to RFI: RP1317 25-hydroxycholecalciferol

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

The applicant had been asked to clarify whether the *Saccharomyces cerevisiae* strain SC0639 was the same for application RP1317 and RP1350, which the applicant confirmed. Testing of the additive for *Salmonella*, Enterobacteria, total yeast, filamentous fungi, and *B. cereus* had been requested. In their response, they stated that the product placed on the market is spray-dried, meaning that it is subjected to very high temperatures. The Committee noted that while the nozzle

temperature was sufficient for sterilisation, there was no evidence provided that the product would attain that temperature and so microbial testing was required to meet the appropriate guidance. **The applicant was asked to provide microbial testing of the additive.**

The Committee were satisfied with the quantification of the culture media in the final product, as well as the stability data provided. The HACCP documentation provided by the applicant was deemed satisfactory by the Committee. An updated manufacturing process alongside an updated composition list was provided, as well as SDS for fermentation aids. As requested, the applicant provided the dusting potential using the appropriate units and the Committee were able to conclude that the additive is a 'dusty product'.

Studies for skin and eye irritancy were provided, however members noted that the results table was absent from the eye irritancy report. Therefore, **the applicant would be asked to provide this results table.** The Committee requested criteria for inclusion rates used for the additive in ruminants and were satisfied with the response provided.

13. Response to RFI: RP1298 Ronozyme HiPhos

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

Upon request by ACAF, the applicant provided information regarding the testing methods used for the testing of *B. cereus*, yeast, and filamentous fungi. The applicant also provided certification for ISO9001 **however the Committee again requested documentation to show that the laboratories used are compliant with internationally recognised standards**. Members were satisfied with the phylogenetic analysis provided for DSMZ 22594 and DMSZ 33699, as well as the overage data provided from previous batches and predictions for future batches with the new production strain.

14. Response to RFI: RP1512 PB6 (*Bacillus velezensis* ATCC PTA-6737)

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

The applicant provided results for *Bacillus cereus* testing as requested, however members stated that the methodology used to test for *B. cereus* is not clear. **The applicant would be asked to provide further information on the testing method used, including evidence supporting that this is an accredited test used for testing for this microbiological contamination.** The applicant had provided certification relating to FAMI-QS for GeneFerm biotechnology, as well as certification for ISO 9001. However, the question posed by the Committee requested evidence of compliance with international standards for testing and calibration laboratories, such as accreditation to ISO 17025 or an equivalent recognised standard. Regulation 429/2008 requires that methods used are validated, reliable and accurate, therefore **the applicant is asked to provide evidence of compliance with these standards,**

such as accreditation to ISO 17025. As requested, a flowchart of the manufacturing chart, indicating critical control points has been provided, as well as HACCP. The applicant has also provided the requested MSDS and an updated label taking conditioning time into consideration.

15. Response to RFI: RP2059 TraceSure

No conflicts of interest were declared for this item.

As requested, the applicant provided raw data files for the study used to demonstrate the effect of the copper ballast bolus on blood copper concentration in lambs. The study was carried out at AFBI, Northern Ireland, which is claimed to have ISO 17025 accreditation. Members have requested that **the applicant would be asked to provide evidence of ISO 17025 accreditation**. A detailed report prepared by an external chemical sciences consultant has been provided to explain why the leaching of copper from the ballast is not a concern. A user risk assessment was also included in this report. The Committee were satisfied with this report and concluded that copper toxicity is not an issue, therefore the PARNUT can be considered safe for use.

16. Post-market monitoring RP140-141-142-284 Coxidin

It was discussed that, for coccidiostats and histomonostats, there is a legal requirement to carry out a post-market monitoring plan to evaluate the antimicrobial resistance of the substance. Results from the post-market monitoring plan for a previously evaluated application of Coxidin® (monensin sodium) were presented to the Committee for assessment. Three anticoccidial sensitivity tests were provided, with variable endpoint results. The Committee concluded that, on their own, these reports did not show evidence of resistance to monensin sodium as a coccidiostat, and that based on the efficacy testing carried out as part of the application, the additive appears to remain efficacious for the control of *Eimeria spp*. The Committee recommended that the applicant should develop and implement their next post-market monitoring plan if the additive were to be authorised.

17. Draft safety assessments: RP812, RP814, RP1039/1040, RP1111 and RP1579.

Members were presented with draft Committee's Advice documents for application RP1579.

The Committee was also presented with the final drafts of the Committee's Advice documents for applications RP812, RP814, RP1039/1040 and RP1111. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

18. Any other business

An update on upcoming applications was provided.

Next ACAF meeting: 17th July on Microsoft Teams.