Eighty Seventh Advisory Committee on Animal Feedingstuffs meeting

31st October 2023 – Meeting in York (Foss House)

ACAF	FSA
Nicholas Jonsson (Chair)	Nathan Allen
Martin Briggs	Aaron Bradshaw
Emily Burton	Alexander Cooper
Matthew Fisher	Michael Dickinson
Hannah Kane	Emily Hudson
Katrina Campbell	Michelle Hutchison
Oonagh Markey	Kaitlyn Jukes
Susan Macdonald	David Kovacic
Christine McAlinden	Francisco Matilla
Donald Morrison	Barry Maycock
Derek Renshaw	Chris Rundle
Mike Salter	Shila Sultana
Adam Smith	
Helen Warren	

1. Apologies

Nick Wheelhouse sent his 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 updated the Committee on the publication of 20 Safety Assessments covering 25 applications in September. Members were briefed on the proposed changes in the assessment process that would start taking place soon in order to speed up the process and reduce the dependence on the Committee. It was also mentioned that in future suitability checks, the Secretariat intends to push back unsuitable applications.

4. Policy Update

No Policy colleagues could attend the meeting. Instead, Fran Matilla-Garcia gave a brief explanation of the way some the conclusions from the Committee are considered in the risk management process.

5. Minutes from 86th Meeting

The Committee reviewed the minutes from the 86th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Ways of working

The Committee gave feedback on the updated proposed ways of working document the version that would be intended to be made public on the ACAF website.

7. Dossier for assessment: RP1282 – *L. brevis* DSMZ 21982

An indirect conflict of interest was declared by Helen Warren, who was allowed to stay in the discussion for the application.

An application was evaluated for *Levilactobacillus brevis* DSM 21982. The applicant requested a renewal of authorisation of the additive for its use in all animal species. The additive falls under the category and functional groups “technological additives – group K silage additives”.

Members discussed the testing for aflatoxin and whether testing for ochratoxin would be required. It was decided that additional testing for ochratoxin is not required as this is not in the regulation. It was also noted that the applicant would need to **provide analysis for *Bacillus cereus* for *bacilli*** as per the guidance.

The Committee commented that the genome sequencing was carried out to a high standard. Members **concluded that antimicrobial resistance was not a cause for concern for this additive**.

A set of questions were sent from the FSA as a Request for Information (RFI) prior to this meeting. Members discussed the RFI response from the applicant, they were satisfied with the responses relating to the identification and manufacturing process of the additive.

Members discussed whether the applicant will need to provide 5 batches in total to show the batch to batch variation of the active agent as the applicant only provided 3. It was stated that although the 3 batches showed good replication, **the applicant would be asked to provide the additional 2 batches as this will support the conclusion**.

The Committee clarified that additional testing for particle size distribution and density would not be required. It was stated that **the applicant would be asked to provide data on the dusting potential on their freeze-dried bacteria product** or accept the additive would be regarded as very dusty. It was also discussed that multilocus sequence typing had been used to test the genetic stability of the bacterial strain where no changes were observed, the testing is not as precise as pulsed field gel electrophoresis (PFGE) analysis, therefore, **the applicant would be asked to provide data using PFGE analysis**.

Members discussed the stability of the additive, the applicant mentioned the terms “ambient” for the stability in storage conditions and “room temperature” for the

stability in water conditions, **the applicant would be asked to clarify what these temperatures were. The applicant would also be asked to provide the annexes/certificates of analysis for the stability in storage and stability in water**.

Members discussed the RFI response regarding the sample label of the final product, they suggested that **the applicant should include in the label how long the additive is stable in water for and to clarify the conditions the additive was tested for**.

The applicant provided a list of ingredients, it was stated by members that **the applicant will need to provide an MSDS for each ingredient and these would need to be provided in English**. It was mentioned that the applicant has provided a description of the manufacturing process, however the Critical Control Points (CCPs) were not clear, **the applicant would be asked to provide a HACCP plan, including the CCPs, and also provide a FAMI-QS certificate to support the application**.

No new safety studies were provided for this application and no further concerns were made on the safety section. The Committee **concluded that the additive remains safe for the target species, consumer and the environment, and that it should be considered a respiratory and skin sensitiser, as well as a potential skin and eye irritant, applying the principle of precaution based on the absence of data.**

Efficacy was not evaluated for the additive as this is not required for this type of authorisation.

8. <u>Dossier for assessment: RP1298 – Ronozyme HiPhos</u>

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

An application was evaluated requesting a renewal and modification of Ronozyme HiPhos (6-Phytase) as a feed additive for its use in poultry, weaned piglets, pigs for fattening and sows, under the category ‘Zootechnical additive’ and functional group ‘Digestibility enhancer’. The modification requested is a change in production organism to an optimised strain from the same line with higher yield. The applicant states the enzyme, the activity, the formulation, the production process, target species and conditions of use remain unchanged.

It was noted by the Committee that the presence of two microorganisms (*Salmonella* and *Enterobacteriaceae*) were tested but that total yeast, filamentous fungi, and *Bacillus cereus* were still required. **The Committee requested the applicant should be asked to test the additive for total yeast, filamentous fungi, and *Bacillus cereus*.** Members evaluated a temporary dataset provided by the applicant at the time of submission, noting that, given the time elapsed since submission of the application and its evaluation, the full experimental dataset should now be available and as such shared with the Committee before providing a conclusion. **The applicant would be asked to provide data from the completed stability trials.**

Members discussed the methodology of production of the additive and noted that identical raw materials were used to that of the original authorisation.

The Committee found the literature review to be carried out to an acceptable standard.

Members of the Committee noted that two of the new safety studies were conducted with a different strain than that intended for authorisation. The application is for authorisation of the additive produced by DSMZ 33699. An Ames test and 90-day toxicity study were conducted with DSMZ 33737. An in vitro micronucleus test was conducted with DSMZ 33699. Hence, the Committee discussed whether there were any significant differences between the strain used to produce the test article evaluated in two of the toxicological studies (Ames test and 90-day oral toxicity study) and the new production strain proposed that could result in differences in conclusions for these two toxicology studies**. The Committee concluded that further review would be required offline by microbiology specialists.**

It was noted that, depending on the conclusions of this offline review, the applicant may need to provide evidence that the two strains were similar enough and that there were no differences expected in the results of the toxicology reports. Regardless of the outcome of that offline discussion, **the Committee requested that the applicant should be asked to provide further justification or evidence to demonstrate that the two strains have a similar toxicological profile.** The applicant would have to demonstrate toxicological similarity between the strains. Otherwise, a bacterial reverse mutation test and a 90-day toxicity study of the correct production strain would have to be provided.

No concerns were raised by the Committee over the data provided for safety for the user/worker, and **concluded that the additive is not a skin or eye irritant, but is a respiratory sensitiser, and, in the absence of skin sensitisation tests, a potential skin sensitiser.**

The Committee were unable to conclude on the studies provided for efficacy owing to the potential differences regarding the original and new proposed production strain. It was noted that, if the strains were significantly similar, then the efficacy studies would be acceptable and demonstrate the efficacy of the product.

9. PARNUT for assessment: RP2059 – Copper bolus

No conflicts of interest were declared for this item.

An application was evaluated requesting a modification of an existing PARNUT, entry no. 59, for the long term supply of grazing animals with trace elements and/or vitamins, contains the condition, under “other provisions” that: “application in the form of bolus is allowed. A bolus may contain up to 20% iron in an inert, non-bioavailable form, in order to increase its density.” The applicant has proposed the modification of this provision to additionally include up to 75% copper.

The Committee found the risk assessment to be relatively weak as inadequate evidence was provided to support their assertion that there is no possibility of copper leaching into the rumen fluid from the copper bolus. Out of the three studies provided, only one had been through a peer review process. The other two studies did not specifically address the effects of the copper and lacked information regarding quality assurance, such as good laboratory practice (GLP). These two studies also had no information relating to when and by whom the work was carried out, and they were undated.

The Committee decided that the effect of microbial action within the rumen on the availability of copper was not addressed fully. The argument that the bolus device would only be used in copper-deficient animals is misleading, as the studies provided show that the bolus might be used to address selenium, cobalt, or potentially other deficiency states. Furthermore, members questioned the basis for the selection of 75% as the highest level of copper in the device. If the copper is truly inert in the rumen, a maximum level would not be needed.

The applicant would be asked to provide a more comprehensive risk assessment, supported by quality assured studies, to quantify the extent of leaching from the device into a ruminal environment.

10. <u>Dossier for assessment: RP1341 – Avizyme 1505</u>

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

The Committee reviewed the identity and characterisation of the additive concluding that the batch-to-batch variation and purity data were acceptable for assessment. It was noted that the manufacturing process was in inadequate detail for assessment, with the HACCP documentation inaccurate for the product under discussion. Several SDS documents for components used in the manufacturing process were not included in the dossier. **The applicant would be asked to provide an updated version of the manufacturing process, the corrected HACCP documentation and SDS documentation for all components described in the manufacturing process.** Members noted that studies demonstrating the absence of the production strain were performed using an intermediate strain, rather than the final strain. **The applicant would be asked to justify the use of an intermediate strain for this study.** Pelleting stability was tested at 90^{o}C for 30 seconds, conditions concluded to be not suitable for poultry breeder feeds, for which a minimum exposure of 82^{o}C for 2 minutes would be expected. **The applicant would be asked to clarify the conditions of use and if used in poultry breeder the applicant would be asked to provide updated studies ensuring they cover the proposed conditions of use.**

Members were unable to conclude on the metabolic profile studies provided as the strain utilised was not clear from the documentation provided. **Members would assess this offline and conclude if further information were required from the applicant.** The Committee reviewed the user safety section of the dossier and

concluded that the additive is a respiratory sensitiser and appropriate PPE would be required by users/workers when handling the product. **The additive is also a mild skin and eye irritant**. A conclusion could not be drawn on dermal sensitisation owing to the absence of studies. **The applicant would be asked to provide studies for dermal sensitisation, and reminded in the absence of data the additive will be labelled a potential skin sensitiser.**

No concerns were raised by members regarding safety for the consumer or safety for the environment from the information provided in the main dossier. However, the applicant supplied complimentary data following the publication of an EFSA opinion in 2020. **Members would review the complimentary information offline, and this would be discussed further at the December 2023 meeting.** Efficacy was reviewed by members, highlighting that the original studies from laying hens were not provided for this assessment. Efficacy was reviewed by members but decision would be postponed until after consideration of supplementary information. **No further information would be required from the applicant at this stage.**

Addendum: *Following the November 2023 meeting, members provided further comment on the complimentary information provided by the applicant in response to the publication of the 2020 EFSA opinion. This information will be incorporated into the assessment template and presented at the December 2023 meeting and incorporated into the minutes before an RFI is issued to the applicant. Members also reviewed the metabolic profile studies and concluded that the same strain was used in the study as described in the dossier, no further information would be required from the applicant.*

11. Response to RFI: RP634 – Chromium propionate

No conflicts of interest were declared for this item.

The applicant had been asked to provide further evidence to account for the absence of prenatal developmental toxicity (PNDT) studies. The applicant provided an extensive justification, including reference to multiple other studies. The Committee concluded there was a data gap that was not addressed by the studies presented, and expressed concern due to the potential embryotoxicity showed by similar chromium substances in the literature and *in vitro* data. **The applicant would be asked to carry out the relevant PNDT study or accept the Committee's conclusion that the potential for prenatal developmental toxicity could not be excluded.**

16. Draft safety assessments: RP709, RP309, RP593

Members were presented with draft Committee's Advice documents for application RP709. Feedback was provided to be reviewed by the Secretariat.

The Committee was also presented with the final draft of the Committee's Advice documents for applications RP309 and RP593. The Committee provided feedback

on final corrections and approved the opinions to be finalised and sent to Risk Managers.

17. Safety for the user/worker consideration and Secretariat proposal

The Secretariat presented a proposal to reduce the burden of assessment on the Committee for those areas of dossiers that have a more audit-like nature, such as number of batches tested, MSDS and HACCP protocols and labelling. The Secretariat would evaluate these areas and draw a conclusion or request further information as appropriate, presenting this outcome to the Committee for reference.

It was confirmed that Members would continue to have full access to all the relevant data and would still be able to comment and raise concerns.

The Committee was receptive to the idea and recognised it could have a positive impact in the overall time management of the assessment process but did request for any changes to take place progressively.

18. Any other business

No other business was discussed.

Next ACAF meeting: Thursday 14th of December 2023 online