Eighty Eighth Advisory Committee on Animal Feedingstuffs meeting
14th December 2023 – Online meeting

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

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, noting that 12 Safety Assessments that had progressed through the Committee were due to be published the following day. An update was also provided on another form of assessment being used by the team, Other Reviewers Opinions (OROs), wherein other reviewers' opinions, mainly EFSA, are used to assess applications. The first panel meeting was held for OROs, with another 5 applications expected to be put through this process in February and a further 5 in March. Recent interviews for Committee members were also mentioned, as well as the current incorporation of three new members of staff into the Secretariat.

4. Policy Update

Feed Additives Senior Policy Advisor, Mark Bond, briefed the Committee on the number of feed additives currently in the system. It was also stated that Tranche 2 feed additives are due to come into force in Great Britain legislation next week. This Tranche includes 13 feed additives, one of which is 3-NOP. The Committee was thanked for their hard work on these assessments.

5. Minutes from 87th Meeting

The Committee reviewed the minutes from the 87th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP1341 Avizyme 1505

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

Members reviewed the complementary information provided by the applicant to address the areas of concern identified in the EFSA 2020 opinion.

Members discussed the information provided to demonstrate absence of viable production strain in the final product, noting that whilst the data demonstrated absence of the production strain the techniques used were not suitable for detection of spore formation. **The applicant would be asked to provide clarification of the methods utilised or to provide further data generated from a technique that allows germination.** The rationale behind the choice of primers was unclear from the data provided and the cycle time and limit of detection were not included within the dossier. **The applicant would be asked to clarify primer selection and to provide detail of cycle time and limit of detection.** The applicant states that there are no bands present on the gels provided, however, members noted that faint bands were visible on the gels. **The applicant would be asked to clarify the presence of these bands and to clarify the limit of detection for the studies.**

Members discussed the information provided on the production strain's ability to produce mycotoxins. Members concluded that the metabolic profile provided was not adequate for assessment as it was performed on an intermediate strain and not the final production strain. **The applicant would be asked to provide an updated metabolic profile performed on the final production strain to allow comprehensive analysis of secondary metabolites.** Members noted that the genetic modification documentation provided did not contain sufficient detail for assessment. **The applicant would be asked to provide further detail of the modifications.** Members noted that not all annex documentation was provided, **the applicant would be asked to provide the missing annex documentation.**

Members were unable to conclude on antimicrobial susceptibility from the data provided. **The applicant would be asked to provide further studies to allow comprehensive assessment of antimicrobial susceptibility**. Members assessed the genotoxicity studies provided, noting that the form of the additive used in each of

the studies had not been stated. **The applicant would be asked to clarify the form of the additive used in each of the mutagenicity studies.**

7. Dossier for assessment: RP1280 Formaldehyde

Martin Briggs declared a direct conflict of interest and so participation was limited to discussions regarding experience working with formaldehyde.

An application was evaluated requesting the authorisation of the additive formaldehyde under the category “technological additives” and the functional group “hygiene condition enhancer”. The applicant requested authorisation of the additive as a hygiene condition enhancer to be used in chickens for fattening, laying hens, weaned piglets and pigs for fattening.

The Committee evaluated the identity and characterisation section, noting that although the applicant had provided analytical data to support the composition of formalin, they had not provided any documentation outlining the necessary accreditation for the laboratory used. Therefore, **the applicant would be asked to provide the laboratory accreditation for the testing of formalin batches**.

With regards to homogeneity, the applicant did not deem homogeneity to be relevant as the active substance is fully soluble. However, the Committee decided that demonstration that the additive can be applied homogeneously to batches of feeding stuff is critical, therefore **the applicant would be asked to provide evidence of homogeneity**. In a previous request for further information, the applicant had been asked to explain how the high temperatures used during the pelleting process could affect the additive. The Committee discussed the explanation provided stating that since formaldehyde in feed is not in the gas form, polymerisation is not considered to be a concern under pelleting conditions. The Committee could not conclude on this explanation, also mentioning that if the feed additive is to be added to poultry breeder it could be exposed to 86°C for 6 minutes. **The applicant therefore would be asked to provide data to demonstrate stability during the pelleting process, demonstrating that the higher temperatures do not affect the additive.**

Members commented that the label provided did not include any details on application or storage and had no indication of dosing per species. The label also describes the additive as a preservative. **The applicant would be asked to provide an updated label taking these points into consideration and that would be in-line with the current application.** The proposed conditions of use were discussed by the Committee and they decided that they needed more clarity on these conditions, such as further elaboration on the statement that “the additive shall only be used in feed where contamination by Salmonella has been identified”. **The applicant would be asked to provide further detail on the proposed conditions of use, including the steps taken to determine when, or if, the application of the additive is needed.**

The safety section of the application was assessed by the Committee and members decided to reassess safety for target animals at the next available ACAF meeting using summaries of previous tolerance studies prepared by the Secretariat.

Members determined that they were unable to conclude on safety for target species based upon the information provided by the Applicant and, furthermore, that the updated literature review did not provide sufficient argumentation to change this decision. Members also determined that they could not conclude on the safety for turkeys and that for both turkeys and pigs, specific safety studies for those species would be required as set out in the guidance. Members could not conclude on the safety of the additive for the user/worker using the information currently provided. With respect to user safety, the Committee determined that they needed more information on the likely levels and routes of exposure and how they relate to the levels that are considered to be safe. **The applicant would be asked to provide additional literature, placing it in context with the additive in question, to further illustrate user/worker safety.**

The Committee discussed the efficacy of the additive, concluding that no further information was required from the applicant, as efficacy was demonstrated under the proposed conditions of use.

Addendum: *Following the meeting, a further issue was raised by the Committee, namely the potential for formaldehyde coming off the feed upon its arrival at the farm and its potential for posing a risk to the farmer who has to handle the formaldehyde-treated feed. Therefore, a request for* ***the applicant to describe how they manage the safety of farmers who will have to use formaldehyde-treated feed on their farms was added to the request for information letter.***

8. <u>Dossier for assessment: RP1317-RP1350 Vitamin D</u>

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

Applications were evaluated for the additive 25-hydroxycholecalciferol (25-OH-D3). The applications were for the renewal of authorisation in pigs and poultry (RP1350) and modification to extended to ruminants (RP1317), under the category “nutritional additive”, functional group “vitamins, pro vitamins and chemically well-defined substances having a similar effect”.

The Committee evaluated the identity and characterisation of the additive, noting that clarification is required to ascertain whether the *Saccharomyces cerevisiae* strain SC0639 from application RP1317 and RP1350 are the same. To ensure that information can be shared between dossiers, the **applicant would be asked to provide clarification as to whether different strains were used in each application.**

Members identified that purity information was absent from the dossiers for the additive in relation to microbiological contamination. As such, **the Committee would request that the applicant provide *Salmonella, Enterobacteria*, total yeast, filamentous fungi and *B. cereus* testing of the additive.** Furthermore, it was also noted that the extent to which the growth medium was incorporated into the final product was not determined. **The applicant would be asked to provide data to quantify the growth media within the final additive.**

The Committee evaluated the stability data and noted that pelleting stability was undertaken at 90°C with no retention time given. It was raised that poultry feed stability should be performed at 86˚C for 6 minutes. **The Committee requested that data for stability data for 86˚C for 6 minutes be provided.**

Within the manufacturing section of the dossier, members noted no HACCP was provided and only a single control point was provided. It was also noted that no assurance certification was submitted. **The applicant would be requested to provide a HACCP and relevant assurance certification**. Upon examining the chemical composition of the additive, it was observed that compounds were listed however their role within the manufacturing process was not explained. Furthermore, MSDS documents relating to the fermentation aids listed within the response document were noted as absent. **The Committee requested an updated manufacturing process that include the items listed within the composition list. Also, MSDS documentation relating to fermentation aids should be submitted.**

The particle size distribution and dusting potential was discussed where it was noted that the results had been given in inappropriate units. As such, the **Committee requested that the applicant provide dusting potential in the units g/m^3.** It was also identified by the Committee that within Annex II other formulations were referred to and as such further clarification was required. **Members requested that further clarification be given to the other formulations referred to.**

The safety section of the dossier was examined by the Committee, whereby members were satisfied with the target species literature review undertaken and agreed with the applicant's conclusions. Members agreed that the dietary exposure assessment was appropriate and upper intake levels were in line with EFSAs previous evaluations. For user/worker safety, members commented that study data was absent and therefore they were unable to determine the risk on eyes and skin as an irritant. As such, **the Committee requested reports relating to skin and eye irritancy studies.**

The efficacy section of the dossier was reviewed by the Committee. It was noted by the Committee that the efficacy results for RP1317 were in the form of published research papers. It was raised by members that no evidence of a proposed inclusion rate was provided and therefore over supplementation was a potential risk. As such, **the applicant would be asked to provide the inclusion rate for ruminants and to disclose the criteria for the inclusion.**

9. <u>Dossier for assessment: RP1393 Ronozyme® WX</u>

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

An application was evaluated requesting renewal authorisation of the additive RONOZYME® WX. The additive falls under the category "zootechnical additive" and the functional group "digestibility enhancer". The applicant also sought modification

of an existing authorization, wherein the new use concerns the use of an improved production strain and an extension of use of the additive for all poultry species and all pigs (Suidae).

Members reviewed the impurities data provided, noting that testing for total yeasts, filamentous fungi, and *Bacillus cereus* had not been provided. **The applicant would be asked to provide the appropriate testing for total yeasts, filamentous fungi, and *Bacillus cereus***. It was also noted that the extent to which spent growth medium is incorporated into the final product was not clearly indicated. **The applicant would be asked to provide quantification of how much medium is incorporated into the final product.** The applicant stated that batches of enzyme concentrates below specified activity or with slightly increased microbial counts are not necessarily discarded but are carefully evaluated on a case-by-case basis. It was unclear what was meant by slightly increased microbial counts. **Therefore, the applicant would be asked to clarify what is meant by slight increase and what is considered in the case-by-case evaluation.** It was unclear what was referred to as “tests for infections” by the applicant. **The applicant would be asked to clarify what they meant by tests for infection and provide more details of these tests.**

Members noted that no information on HACCP or control points were provided. **The applicant would be asked to provide a complete HACCP plan for the production process of the additive and critical control points as well as more information on how these points are controlled during the production process.** It was noted that the provided MSDS documents for the products were issued in 2014 and last updated in 2017. **The applicant would be asked to provide updated MSDSs for RONOZYME® WX (CT) and RONOZYME® WX (L).**

Members noted that the pelleting stability for RONOZYME® WX (CT) was only tested for 20 seconds, and therefore this should be made clear on the label as some of the uses may require longer conditioning times. **The applicant would be asked to provide pelleting stability test for a longer time, or they should include on the label that the pelleting stability was tested for only 20 seconds.**

It has been noted that in the submitted EFSA opinion on safety and efficacy of RONOZYME® WX CT/L (endo-1,4-β-xylanase) as a feed additive for sows for reproduction, a combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (OECD 422) was considered by the panel**. As this application is for the renewal, modification of an existing authorisation and a new use, the applicant would be asked to provide the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD 422).**

According to the OECD guideline No. 471 (bacterial reverse mutation test), the positive control reference substance should be selected on the basis of the type of bacterial strain used. For TA100, the positive control suggested in the guideline is sodium azide, however the guideline adds that other appropriate positive control reference substances may be used. **The applicant would be asked to provide justification of the use of 4-nitroquinoline-1-oxide (NQO) for positive control of TA100 in the bacterial reverse mutation test.** Members agreed that the product should be labelled as a dermal sensitiser in addition to being labelled as a

respiratory sensitiser as no information on skin sensitisation was provided. **The applicant would be asked to carry out a Phase I assessment for the feed additive according to EFSA's Guidance on the assessment of the safety of feed additives for the environment.**

An extension of use of the additive for all poultry species and all pigs (Suidae) is sought. However, the applicant did not provide any reproductive and developmental toxicity testing studies or information on using the feed additive during pregnancy and therefore extension of use to the pregnant animals cannot be assessed. **If the applicant seeks authorisation for pregnant animals, reproductive and developmental toxicity testing studies are required.**

10. Response to RFI: RP812 – Intellibond C

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

The Committee were satisfied with the explanation provided for why the enhanced solubility of the additive is not expected to have an effect physiologically.

The Committee reviewed the eye irritancy study and bovine corneal opacity and permeability test provided by the applicant. The applicant had referred to four unpublished studies relating to eye irritation but had only provided these two. Members determined that as no conclusion could be drawn from either of these tests and that the two remaining eye irritancy studies have not been provided, Intellibond C should be regarded as a potential eye irritant. It was noted that the original studies had not been provided for skin irritancy, therefore **the applicant would be asked to provide these skin irritancy studies with the intention of members reviewing and concluding offline.** Upon receipt of these studies, the Committee concluded no further information is required from the applicant and the dossier will move to the draft safety assessment stage of the process.

Members discussed the Phase I environmental assessment, **concluding that the data should be reviewed offline taking the guidance into consideration to determine if a Phase II environmental assessment was required.**

Addendum: *Following further analysis of the guidance and the PEC values provided by the applicant, the Committee were able to conclude that a Phase II environmental assessment was not required and that the additive remains safe when used at the proposed levels for terrestrial species and land-based aquaculture systems. However, members could not conclude on the safety of the additive for marine sediment compartment when used in sea cages.*

11. Response to RFI: RP814 – Intellibond Zinc

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

Members noted that the applicant had accepted the conclusion that in the absence of data the additive would be considered a potential eye irritant. The additional skin sensitisation studies provided were assessed by members, concluding that the additive is not a dermal sensitiser.

The Phase I environmental assessment was assessed by members noting that the PEC values appeared to be above the trigger level for a Phase II evaluation. **A decision was made to review the data further offline before a conclusion would be drawn or if a Phase II environmental assessment was required for the additive.**

Addendum: *Following further analysis of the guidance and the PEC values provided by the applicant, the Committee were able to conclude that a Phase II environmental assessment was not required and that the additive remains safe when used at the proposed levels for terrestrial species and land-based aquaculture systems. However, members could not conclude on the safety of the additive for marine sediment compartment when used in sea cages. The application will now progress to the draft safety assessment stage of the process.*

12. Response to RFI: RP1015 – *Lactococcus lactis* NCIMB30117

No conflicts of interest were declared for this item.

The applicant provided data to support the stability of the additive in water for 48 hours at ambient temperature. A complete HACCP plan was also provided, as requested, in addition to a list of the cryoprotectants used and their MSDSs. The applicant was also asked to provide an updated SDS for the additive, taking into consideration the points raised by the Committee. Members were satisfied with the applicant's response and no further questions were raised. The dossier will move to the draft safety assessment stage of the process.

13. Response to RFI: RP1039/40 – VTR-xylanase

No conflicts of interest were declared for this item.

The Committee noted that all the queries raised had been appropriately addressed by the applicant. Members noted that the pelleting process performed was not in line with industry standards and so a conclusion could only be drawn on the additive's stability at 70°C for 15 seconds which would be reflected in the labelling of the product. The safety information provided was reviewed and a conclusion was drawn that the additive should be regarded as a skin sensitiser for both forms. In its liquid form the additive is not a skin irritant and in its granular form the additive should be considered a potential irritant to the skin. It was noted following issue of the RFI that the applicant hadn't listed a carrier for the additive, **the applicant provided SDS documentation for corn starch which members would review offline and conclude upon.** No further information would be required from the applicant and the dossier would move to the draft safety assessment stage of the process.

14. Response to RFI: RP1111 PP1021 – *Bifidobacterium longum*

Due to time constraints, the Committee agreed to assess the RFI response for RP1111 offline.

Addendum: *The Committee reviewed the applicant's response offline. The applicant had been asked to further clarify the dusting potential results, as well as provide further details on the manufacturing process, including HACCP documentation. SDS documentation for the starting ingredients used in the manufacturing process were also requested, in addition to updated versions of quality assurance certificates. Clarification was needed in relation to incompatibilities and interactions, as well as on the conditions of use and mode of application of the additive. The applicant was also asked to provide clarification on how the defined dosage will be achieved by the end user and to review a number of documents for potential typos. The Committee was satisfied with the responses received, however was still unclear on how the defined dosage will be achieved by the end user. Therefore,* ***the applicant would be asked to provide the feeding instructions that will be provided with the complimentary feed.*** *Members were satisfied upon receiving the feeding instructions and therefore this application would move to the draft safety assessment phase of the process.*

15. Draft safety assessments: RP746, RP1047, RP1087 and RP709

Members were presented with draft Committee's Advice documents for applications RP746, RP1047 and RP1087. 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 application RP709. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

16. List of requests to applicants

Common shortcomings in applications have been noted by ACAF, and previously AFFAJEG. Members reviewed a paper containing proposed recommendations to applicants to improve the status of dossiers at the time of submission. Feedback was provided to be reviewed by the Secretariat.

17. Any other business

No other business was discussed.

Next ACAF meeting: 31st January 2024 on Microsoft Teams