Eighty first Advisory Committee on Animal Feedingstuffs meeting

9th December 2022 – Online meeting

ACAF	FSA
Nicholas Jonsson (Chair)	Nathan Allen
Martin Briggs	Mark Bond
Katrina Campbell	Aaron Bradshaw
Matthew Fisher	Michael Dickinson
Christine McAlinden	Donal Griffin
Susan MacDonald	Emily Hudson
Donald Morrison	Kaitlyn Jukes
Derek Renshaw	Francisco Matilla
Mike Salter	Barry Maycock
Adam Smith	Shila Sultana
Helen Warren	Katie Schulz

1. Apologies

Nick Wheelhouse extended his apologies for the meeting.

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 Donal Griffin gave an update on the status of feed additive applications currently being processed by the Regulated Products Risk Assessment Team. Currently fourteen applications are undergoing suitability checks and forty-six are ready to commence the assessment process. Eighteen applications are currently under assessment by the Committee. Lastly, sixteen applications have been completed or are going through opinion completion.

4. Policy Update

Feed Additives Senior Policy Advisor, Mark Bond, briefed the group on the status of applications. Since the previous AFFAJEG meeting, fourteen new applications had been received, for a total of 164. The first set of authorisations for applications that went through the Tranche-1 were submitted to parliament and approved, entering into force at the end of November. The second set of feed additives going through risk management review will be going out for consultation in the new year. A further eleven additives will have now entered the third tranche of authorisation. The

Committee was updated on the proposed bill on retained EU law, for which no changes have been reported so far.

5. Minutes from 80th Meeting

The Committee reviewed the minutes from the 80th ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP709 – ProAct 360

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

An application was evaluated for the additive ProAct 360 (Subtilisin protease). The application seeks a new authorisation under the category “zootechnical additive”, functional group “digestibility enhancer”, for its use in all growing poultry (poultry for fattening).

The Committee evaluated the identity and characterisation information within the dossier including the applicant’s claim that *Bacillus licheniformis* should be assessed as a QPS organism owing to history of safe use. Members concluded that whilst the production strain was well characterised, the applicant had not sufficiently demonstrated antimicrobial susceptibility with two of the antibiotics tested above the acceptable limits defined by EFSA. **The applicant would be asked to provide further assessment of potential AMR and toxin genes through bioinformatic interrogation of the WGS data**. The Committee noted that GLP and HACCP documentation for the manufacturing process had not been provided, with several of the MSDS documents not provided in English. **The applicant would be asked to provide HACCP documentation and quality assurance statements for the manufacturing process, along with translated copies of the relevant MSDS documents.**

The physiochemical properties were considered, with the results for dusting potential deemed inappropriate as the units presented do not allow determination of concentration in the air. **The applicant would be asked to provide the dusting potential in g/m^3 as defined by EFSA guidance.** The conditions of use of the additive were discussed and the Committee noted that the duration of exposure to high temperature during the pelleting process was not detailed. **The applicant would be asked to provide further information on the pelleting process including duration of exposure to high temperature.** The appropriate timeframe and storage conditions for stability studies were discussed, with the Committee concluding the studies provided were satisfactory, noting that whilst some individual recoveries appeared to be low the average recoveries were acceptable.

The Committee evaluated the safety of the additive, agreeing with the established NOAEL (no observed adverse effect level) of 483.6 mg total organic solids (TOS) per kilogram determined by a subchronic (90-day) oral toxicity study and concluding no tolerance studies were required for assessment. Members noted the statement ‘no

effect on gut microflora' within the application and queried the validity of this statement as no primary studies had been provided. **The applicant would be asked to clarify if any studies had been conducted to support this statement.** The Committee discussed the use of a 'less purified' batch for the toxicological studies rather than the final product. They concluded results were conclusive, as the substance tested demonstrated equivalence with the final product.

Subchronic oral toxicity was assessed by the Committee, highlighting concerns around the dose analysis presented. The study reported formulations to be stable based on information provided by the sponsor, however, there was no individual data presented to substantiate this claim. **The applicant would be asked to provide further information on the study and to provide evidence of stability for the formulations**. Genotoxicity studies were assessed with the Committee concluding that the additive is not mutagenic. Safety for the user was assessed, highlighting the proposed SDS document to contain multiple errors in continuity with the studies provided (no reference to genotoxicity studies and incorrect eye irritation study listed). **The applicant would be asked to clarify this information and amend the SDS accordingly, with a proposed label containing precautionary statements for skin, eye, and respiratory sensitization to be provided.**

Members evaluated the three efficacy studies presented in the dossier stating randomisation methods in one of the studies were unclear, however, the Committee concluded they demonstrated the additive is efficacious. No further information was requested from the applicant.

7. <u>Dossier for assessment: RP746 – Agal-Pro BL</u>

Adam Smith declared an indirect conflict of interest and was allowed to stay for the discussion.

An application was evaluated for Alpha-Galactosidase and Endo-1,4-betaglucanase, which are available in powder and liquid form. The applicant seeks renewal of authorisation under the category "zootechnical additives", functional group "digestibility enhancers".

The Committee evaluated the identity and characterisation section of the dossier. It was noted that there was an ambiguous phrase, where no differences from the original additive were described and no amendments or supplementing conditions of the original product were provided, however the Committee will accept this product is the same as the previous product. Members discussed the enzymes from the two different organisms. The alpha-galactosidase is obtained from a genetically modified strain of *Saccharomyces cerevisiae*. The committee noted the presence of two resistant genes in the whole genome sequence (WGS) report, but there was no evidence of these in the Alpha-galactosidase component of the final additive. The glucanase is obtained from *Aspergillus niger* in which the WGS report listed four different clusters of a significant match with some biosynthetic gene clusters, which included yanuthone D, a compound with antifungal and antibiotic activity. The

producer organism was absent from three batches of the glucanase enzyme component which is used in the final additive.

The Committee noted that the application concluded on absence of mycotoxin presence, but testing was not presented for every mycotoxin mentioned. **The applicant would have to provide further data on mycotoxin testing.** It was recognised the manufacturing process provided was sufficiently detailed, however no HACCP document was provided. **The applicant would be asked to provide the HACCP document as well as an expired FAMIQs certificate.**

The Committee noted that the additive showed shelf-life stability for up to 12 months, stability in mash and pelleted feed for 6 months and that homogeneity was demonstrated. It was noted by members the dusting potential results were not given in terms of air concentration, so it is unclear if it is a dusty product or not. **The applicant would be asked to provide dusting potential results and to provide an English translation of the test reports, which were provided in Dutch.**

The safety section of the dossier was evaluated by the Committee. The literature review carried out for the safety of the target species was considered to be a comprehensive and extensive search. It was concluded that previous conclusions drawn by EFSA could be accepted, and the additive could therefore be considered safe for the target species, the consumer, and the user/worker. No concerns were raised for environmental safety. Members questioned whether the latest guidelines on clastogenicity and aneugenicity would require further information from the applicant. It was concluded that the *in vivo* test originally provided by the applicant was sufficiently conclusive, and no further *in vitro* tests would be required. The committee stated the additive is a respiratory sensitiser, therefore data for dusting potential would need to be provided as low dusting cannot be assumed due to the product having a micro-granule formulation. It was also mentioned that the product may be a potential sensitiser to skin and eyes.

Efficacy was not evaluated for the additive, as it is a renewal of authorisation.

8. <u>Dossier for assessment: RP748 – Coxam</u>

No conflicts of interest were declared for this item.

An application was submitted for the additive Coxam® (amprolium hydrochloride) under Regulation (EC) No 1831/2003. The application seeks a new authorisation under the category “coccidiostats and histomonostats”. The application was initially processed through the risk management review approach, requiring an internal review of a previously published EFSA opinion on the safety and efficacy of the product. It was noted by the FSA risk assessors that no conclusion was reached on the safety of the additive for consumers, based on the information presented.

The Committee evaluated a report by the Committee for Veterinary Medicinal Products (CVMP), presented as the only piece of evidence for safety for consumers. The applicant confirmed that the original documents describing the toxicological tests summarised in the CVMP report could not be retrieved nor presented to the Committee. **Members concluded that, while the report was comprehensive, the**

inability to access the original tests prevented them from carrying out an independent risk assessment on the safety of the additive for consumers.

***Addendum**: After the meeting, the secretariat consulted the Veterinary Medicines Directorate (VMD) for further information on the use of Coxam as a veterinary medicine, and the report of the CVMP as a reference for safety. The VMD described how the report was produced when the United Kingdom was still part of the European Union, and therefore it is still considered a valid reference from a safety standpoint. The VMD was not able to share any further safety information on Coxam due to confidentiality concerns*.

9. Dossier for assessment: RP791 – *Lactobacillus buchneri* and others

No conflicts of interest were declared for this item.

An application was evaluated requesting the renewal and modification of authorisations of a range of preparations of silage additives: *Lactobacillus buchneri* NCIMB 40788 CNCM I-4323, *Lactobacillus plantarum* CNCM I-3235, *Lactobacillus plantarum* CNCM MA 18/5U NCIMB 40788, *Pediococcus acidilactici* CNCM I-3237, *Pediococcus acidilactici* CNCM MA 18/5M DSM 11673, *Pediococcus pentosaceus* NCIMB 12455, *Propionibacterium acidipropionici* CNCM MA 26/4U, *Lactobacillus buchneri* NCIMB 40788 CNCM I-4323 and *Lactobacillus hilgardii* CNCM I-4785. The additives are currently authorised as feed additives for use in all animal species and categories and fall under the category “technological additives” and functional group “silage additives”. There have been taxonomic changes, but no changes to the organisms.

Members felt that the request for modification seemed logical and reasonable. The identity and characterisation of the additives were discussed, and the Committee found the dossier to be well-written throughout raising no issues with the specifications for the additives. The strains were well-characterised, with a robust report provided for whole genome sequencing. Queries were raised as to why CARD analysis found no resistance genes, when *Pediococcus* has been shown to demonstrate resistance to vancomycin. **The applicant would be asked to provide an explanation of the basis of vancomycin resistance in the absence of identified/recognised resistance genes.** Following a discussion by Committee members, it was decided that **the applicant would be asked to provide evidence demonstrating that the additives remain the same, for example through pulse field gel electrophoresis (PFGE).** Members had no other concerns with the characterisation of the additive. The manufacturing process was well described, and the stability of the additives demonstrated. All the additives are dusty products, and it needs to be assumed that they are respiratory sensitisers, and that PPE will be required. The applicant acknowledged this and referred to in both the label and the MSDS.

The safety of the additives was discussed by the Committee. Since they are silage inoculants, the applicant was only required to provide certain parts of safety information, with a focus on worker safety. The applicant performed tests on only

one of the organisms, therefore the rest could not be concluded upon. Consequently, they must be regarded as potential skin sensitisers and irritants, and eye irritants. **The applicant would be asked to accept this conclusion or carry out additional studies required to determine user safety.** Members were not able to conclude on the eye irritancy potential of *Pediococcus acidilactici* MA 18/5M, as they do not have access to the original individual data from the eye irritancy test. The organism would therefore have to be considered an eye irritant as default unless further information can be provided. **The applicant would be asked to accept this conclusion or provide the original data from the eye irritancy test.** It was questioned whether the use of silage additives could pose a risk by increasing the concentration of microorganisms above normal silage levels, and that the discussion would have to be explored further after the meeting.

Addendum: After the meeting, members concluded that at the end of the ensiling process, microorganism levels are expected to return to normal, despite the initial increase after the use of silage additives. No further concern was raised regarding this matter.

10. Response to RFI: RP1071 – Avatec (Turkeys)

No conflicts of interest were declared for this item.

The Committee re-evaluated the efficacy studies of the additive, after noting that the studies' lengths and timelines would not be a limitation to evaluating efficacy. The Committee noted that, based on the results reported, they would not be able to conclude on the efficacy of the additive in turkeys. The applicant provided a revisited efficacy section very close to the meeting, which members will be able to review at the February ACAF meeting.

11. Response to RFI: RP226 – Xygest HT

Adam Smith declared an indirect conflict of interest and was allowed to stay for the discussion.

Members evaluated the data presented for stability under conditions of high temperature for several minutes at a minimum of 12% humidity. The study provided by the applicant was considered to be of good quality, answering the Committee's query adequately. The application would move to the opinion formulation stage.

12. Response to RFI: RP416 – Axtra XB

Adam Smith declared an indirect conflict of interest and was allowed to stay for the discussion.

The applicant provided an extensive RFI document responding to various questions posed by the Committee. A whole genome sequence was carried out to characterise the production strain, **but the applicant would be asked to identify toxin-**

generation and antimicrobial resistance genes. Further queries regarding batch testing, homogeneity, pelleting stability, and particle size distribution were satisfactorily responded to by the applicant. The safety and efficacy studies of the original application were provided by the applicant. The committee asked for confirmation that the product under renewal was identical to the one tested in the original studies. Members reviewed the efficacy studies and concluded that the additive can be considered efficacious in suckling piglets. Efficacy data was considered to be sufficiently conclusive, if not strong, to confirm efficacy at the proposed reduced minimum dose for avian species of 610 U/kg (xylanase) of feed and 76 U/kg of feed (glucanase).

13. Response to RFI: RP666

No conflicts of interest were declared for this item.

The ACAF evaluated new information presented for application RP666. Five queries were raised for the applicant. Members were satisfied with the reasoning behind offering two different formulations of sodium benzoate. The applicant had been asked to clarify the proposed conditions of use for the product, as there was some disparity in the original conditions provided. Members were happy with the clarification that the recommended dose is 4000 mg/kg of complete feed with a moisture content of 12%, as well as the clarification of the inclusion level as 4 kg/ton or 0.4%. However, given the initial confusion regarding the units and level of inclusion in the feed, **the applicant would be asked for an example of the updated label.** Lastly, there was discussion among the members relating to the extrapolation of efficacy data to “all growing *suidae*”. The efficacy data provided by the applicant only assessed efficacy in piglets, therefore it was decided that the Committee could only conclude on the efficacy of sodium benzoate in piglets (suckling), piglets (weaning) and piglets (suckling and weaned piglets). They could not conclude on the efficacy of sodium benzoate in pigs for fattening. **The applicant would be asked to accept this conclusion or carry out the additional studies required in pigs for fattening to support efficacy in all growing *suidae.***

14. Response to RFI: RP686

No conflicts of interest were declared for this item.

The Committee evaluated the applicant’s response providing three certificates of analyses for the detection of *Salmonella* spp. and concluded that these showed absence of the pathogen in 25 g of the product, in line with the specification. The application would move into the opinion formulation stage.

15. Draft opinions

Members were presented with draft opinions for applications RP597-600. Feedback was provided to be reviewed by the Secretariat.

The Committee was also presented with the final version of opinions for applications RP140-141-142-284, 641. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

16. Committee's workload and expertise survey

The ACAF took part in a survey aimed at identifying the work patters of individual members and their expertise and confidence when evaluating different sections of the application dossier. The survey provided valuable insights on member's workloads and time required to evaluate dossiers. The survey showed that for almost all areas of dossiers several members feel very or moderately confident evaluating them, but that further expertise would be useful for toxicology and efficacy, as well as for chemical substances. Environmental safety was also identified as a gap in expertise, however the Secretariat clarified that the FSA has access to various environmental risk assessors through the Register of Specialists, whose independent input can be requested as needed.

Most members agreed that having more meetings throughout the year would be of use to reduce the workload for each meeting. While results varied, eight meetings per year was the most voted option by members. The Secretariat took note of the proposal and agreed to investigate further solutions to facilitate the work of the Committee, with action in early 2023.

17. Any Other Business

No other business was discussed.

Next ACAF meeting: Wednesday 15th February 2023 on Microsoft Teams.