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Safety and efficacy of microorganism DSM 11798 as a technological additive for all avian species

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Abstract

Biomin® BBSH 797 is the trade name for a feed additive containing viable cells of an unnamed bacterium (DSM 11798). The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) produced an opinion on the safety and efficacy of this additive when used with pigs concluding that the additive itself did not raise any safety concern. It was confirmed that the additive could reduce the trichothecene, deoxynivalenol (DON), producing the less toxic de-epoxy metabolite. The applicant is now seeking authorisation for the use of the additive in feed for all avian species and, since the current authorisation only covers DON, the amending of this authorisation to include all trichothecene mycotoxins. Chickens and turkeys for fattening and laying hens showed no adverse effects when the additive was added to diets at 1000 times the recommended dose. Consequently, the additive is considered safe for these species/categories when used at the recommended dose of 1.7×10^8 colony-forming units (CFU)/kg complete feed. This conclusion is extended to all avian species. The use of the additive in feed for all avian species is not expected to introduce concerns for consumers, users or the environment not previously considered. *In vitro* and *in vivo* studies showed that the inclusion of the additive at the recommended dose of 1.7×10^8 CFU/kg was effective in reducing contaminating DON in feed when given to avian species with a concomitant production of the less toxic de-epoxy metabolite. The additive was shown to reduce the 12,13-epoxide group of representative trichothecenes. It would be reasonable to assume a similar reaction with other mycotoxins of the same structural type independent of the animal species or category receiving contaminated feed. The additive is compatible with the coccidiostats monensin sodium, salinomycin sodium, narasin, narasin/nicarbazin, nicarbazin, robenidine hydrochloride and diclazuril.

Keywords: technological, mycotoxin binder, chickens, turkeys, hens, minor avian species, trichothecenes

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7. Article 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States.

The European Commission received a request from Biomin GmbH[2] for authorisation of the microorganism DSM 11798 Genus nov. species nov. (Biomin® BBSH 797), when used as a feed additive for all avian species (category: technological additives; functional group: substances for reduction of the contamination of feed by mycotoxins).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive) and under Article 13(3) (modification of the authorisation of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 13 April 2015.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product microorganism DSM 11798 Genus nov. species nov. (Biomin® BBSH 797), when used under the proposed conditions of use (see Section 3.1.1).

1.2. Additional information

In 2005, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) published an opinion on the bacterial strain which is the subject of this application and that was then assigned to the genus *Eubacterium* (EFSA, 2005). The strain was intended to be included in feed for poultry and pigs to reduce the adverse effects of any contaminating trichothecene mycotoxin. As there were no data on the prevalence of the strain in the digestive tract of farm animals or humans and thus no estimate of natural exposure, and as the tolerance studies did not provide sufficient evidence of safety, the Panel was unable to conclude on the safety of the strain for the target species. However, the Panel acknowledged that the strain was able to reduce the epoxide group of trichothecenes to produce less toxic metabolites.

Subsequently, a second application was made for the use of this additive in pigs as a technological additive (functional group: substances for reduction of the contamination of feed by mycotoxins). Safety for the target species, consumers, users of the product and the environment was assessed in relation to this application. No concerns other than a potential for respiratory sensitisation of those handling the product were identified. Efficacy was also established based on *in vitro* and *in vivo* studies made predominately with deoxynivalenol (DON) or feed naturally contaminated with DON (EFSA FEEDAP Panel, 2013).

This product is currently authorised for use in pigs as a substance for the reduction of the contamination of feed by DON.[3]

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Biomin GmbH. Industriestraße 21, A-3130 Herzogenburg, Austria.
[3] Commission Implementing Regulation (EU) No 1016/2013 of 23 October 2013 concerning the authorisation of a preparation of a microorganism strain DSM 11798 of the Coriobacteriaceae family as a feed additive for pigs. OJ L 282 24.10.2013 p.36.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[4] in support of the authorisation request for the use of the bacterium DSM 11798 Genus nov. species nov. from the family Coriobacteriaceae as a feed additive. The technical dossier was prepared following the provisions of Article 7 of Regulation (EC) No 1831/2003 and the applicable EFSA guidance documents.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies and peer-reviewed scientific papers to deliver the present opinion.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[5]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of the microorganism DSM 11798 from the family Coriobacteriaceae is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents produced by EFSA: Guidance on technological additives (EFSA FEEDAP Panel, 2012a), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011), Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008), Guidance for establishing the safety of additives for the consumer (EFSA FEEDAP Panel, 2012b) and Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012c).

3. Assessment

The active agent is a presently unnamed strain of bacterium isolated from the bovine rumen and intended to degrade trichothecene mycotoxins present in feed. The unnamed strain is deposited in the Deutsche Stammsammlung von Mikroorganismen und Zellkulturen with the accession number (DSM 11798). The applicant is seeking authorisation for the use of the additive in feed for all avian species. In addition, since the authorisation for use in feed for pigs introduced by Regulation (EU) 1016/2013 restricts the use of the additive to feed contaminated primarily with DON, the applicant is seeking recognition that the additive can also detoxify other trichothecene mycotoxins.

3.1. Characterisation

The additive which is the subject of the present application has the same formulation and method of manufacture as that considered in the previous opinion (EFSA FEEDAP Panel, 2013). Thus, the data pertaining to composition, impurities, physical properties, shelf life and stability in feed still apply.

In order to establish an identity for the strain under application, a phylogenetic analysis was made and submitted with the application made for use in feed for pigs (EFSA FEEDAP Panel, 2013). These data suggested the assignment of the strain to a new taxonomic unit within the family Coriobacteriaceae, probably warranting the establishment of a new genus. In the interim, the Panel considered that the deposition of the bacterium in the European culture collection was sufficient to ensure that any authorisation would apply only to the additive under application.

3.1.1. Conditions of use

The additive is intended to be used in feed for all avian species at a minimum inclusion level of 1.7×10^8 colony-forming units (CFU)/kg complete feed. It is intended for use in the presence of the authorised coccidiostats: monensin sodium, salinomycin sodium, narasin, narasin/nicarbazin,

[4] FEED dossier reference: FAD-2015-0003.

[5] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2012-0024_Biomin%20BBSH%20797.doc.pdf

[6] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

nicarbazin, robenidine hydrochloride and diclazuril. It is recommended that the additive is incorporated into the final feed via a premixture. No maximum level or withdrawal period are proposed.

3.2. Safety

3.2.1. Safety for target species

3.2.1.1. Chickens for fattening

A total of 750 1-day-old Ross 308 (mixed sex) chickens were allocated to one of three treatments.[7] Birds were fed maize/soybean diets in mash form without the additive or the same diets supplemented with either 2.2×10^9 CFU/kg feed (10× minimum recommended dose) or 2.2×10^{11} CFU/kg feed (1,000× minimum recommended dose) of the additive for 35 days. The concentrations of the active agent in feeds were confirmed by analysis. Each treatment consisted of 10 replicate pens of 25 birds. Feeds were shown to be essentially free of trichothecene contamination (DON < limit of detection (LOD) of 20 μg/kg feed).

Animals were monitored throughout the trial for signs of ill health. Body weights were measured on days 1 and 14 on a group basis and individually on day 35. Average feed intake (per pen) was measured for the whole period and used with the average body weight per pen to calculate the feed to gain ratio. Data were analysed by an analysis of variance (ANOVA) followed by a Tukey's test for multiple comparisons of means.

Birds reached around 1.7 kg by the end of the study with no significant differences between treatments. Mortality was around 3% and not treatment related. Similarly, feed intake and feed to gain ratio (between 1.70 and 1.77) did not differ significantly between groups.

3.2.1.2. Turkeys for fattening

A total of 720 1-day-old female BUT 10 turkey pullets were assigned to one of three treatment groups.[8] Birds were fed wheat/soybean diets in mash form without the additive (control group) or the same diets supplemented with either 2.2×10^9 CFU/kg feed (~ 10× recommended dose) or 2.2×10^{11} CFU/kg feed (~ 1,000× recommended dose) of the additive for 42 days. Pullets were randomly allocated to 48 floor pens with 15 birds per pen. The floor pens were spatially blocked (16 blocks) in the house with 16 floor pens per treatment. The three treatments were randomly allocated within each block. The basal diet was shown to be free from trichothecene contamination (DON < LOD of 20 μg/kg feed) and the intended concentration of the additive confirmed by analysis.

The birds were bulk weighed per pen at day 0, 21 and 42 and body weight gains were calculated. Feed was weighed per pen on day 0, 21 and 42 and average feed intake determined. Feed to gain ratio was calculated from these figures. The data obtained were subjected to an ANOVA to determine the effect of experimental diets on turkey growth performance. Pen means were the units for statistical analysis. Tukey's test was used to compare means between treatments. Significance is assumed at $p \leq 0.05$.

Mortality was low (< 2.0%) and not treatment related. Average feed intake over the experimental period per bird (3.57 kg) did not differ between treatments. No significant difference in average final body weight were seen between birds in the control group and the 10× group (2.06 vs 2.08 kg), but the higher dose group had an average final body weight of 2.14 kg. This was significantly higher than the control group birds but not than the birds from the 10× group. Feed to gain ratio, which varied between 1.72 and 1.79, was not significantly different.

3.2.1.3. Laying hens

The study with laying hens followed the protocol established for chickens and turkeys.[9] A total of 576 Dekalb White hens, 20 weeks of age at the start of the trial, were assigned to one of the same three treatment groups following a randomised complete block design. Each treatment consisted of 16 replicates of 12 birds. As in the other studies, diets were shown to be free of trichothecene (DON) contamination and to contain the expected bacterial count. The concentration of the additive was confirmed.[10] The duration of the study was 56 days. Hens were weighed at the start and end of the

[7] Technical dossier/Section III/Annex III_02.
[8] Technical dossier/Supplementary Information June 2016/Annex (i) 05.
[9] Technical dossier/Supplementary Information June 2016/Annex (i) 01.
[10] Technical dossier/Supplementary Information June 2016/Annex I (Table 5).

experimental period and feed intake measured. Eggs were collected daily from each pen and weighed. Laying rate, mean egg weight, egg mass and feed to egg mass ratio were calculated. Data were subjected to an ANOVA. Treatment means were compared using Least Significant differences after significant effects were confirmed by an ANOVA. The cage was taken as the experimental unit.

Hens remained in good health with only two removed from the trial for non-treatment-related reasons. No significant differences were seen between groups for final body weight (range 1.62–1.65 kg), average feed intake (104–105 g/hen per day), laying rate (92.8–93.1%), mean egg weight (53.2–53.3 g), egg mass (49.3–49.7 g/day) or feed to egg mass (2.18–2.19).[11]

3.2.1.4. Conclusion

Chickens for fattening, turkeys for fattening and laying hens showed no adverse effects when the additive was added to diets at either 10× or 1,000× the minimum recommended dose. Consequently, the additive is considered safe for these species/categories when used at the recommended dose of 1.7×10^8 CFU/kg complete feed.

Since the applicant proposes the use of the same dose in minor avian species and as a wide margin of safety has been established for chickens, turkeys for fattening and for laying hens, Biomin® BBSH 797 can be considered safe for all avian species at a dose of 1.7×10^8 CFU/kg complete feed without the need for additional studies.

3.2.2. Safety for the consumer

The safety for consumers arising from exposure to the active agent, the additive or to metabolites of trichothecene mycotoxins were considered in the context of the scientific opinion for use in feed for pigs, where no concerns were identified. Use of the additive in feed for all avian species will not introduce concerns for consumers not previously considered (EFSA FEEDAP Panel, 2013). Therefore, the use of the additive in poultry diets under the recommended conditions is considered safe for the consumer.

3.2.3. Safety for the user

In the previous opinion, the FEEDAP Panel concluded that 'the additive was non-irritant to eyes and skin and was not a skin sensitiser. Although the additive is formulated to minimise exposure by inhalation some exposure of the respiratory tract remains possible and the potential for respiratory sensitization cannot be excluded' (EFSA FEEDAP Panel, 2013). The FEEDAP Panel concludes that the use of the additive in feed for all avian species will not introduce concerns for users of the product not previously considered.

3.2.4. Safety for the environment

In the previous opinion, the FEEDAP Panel stated that 'The active agent in the additive is a strictly anaerobic strain originally isolated from bovine rumen. It would appear to naturally occur in the digestive tract but, as a potentially new genus, no data on its prevalence is available. However, as the strain has a very limited capability to survive in aerobic conditions, its use in animal production is unlikely to introduce an environmental concern' (EFSA FEEDAP Panel, 2013). Therefore, the use of the additive in feed for all avian species will not introduce concerns for the environment not previously considered.

3.3. Efficacy

3.3.1. *In vitro* and *ex vivo* studies

A number of *in vitro* and *ex vivo* studies on the effects of the additive to demonstrate the activity of the active agent against DON (taken as a representative trichothecene) have been considered in the previous opinion (EFSA FEEDAP Panel, 2013).

A series of incubation studies with the additive and buffered solutions containing the mycotoxin DON confirmed that the additive was able to fully degrade DON under anaerobic conditions at 37°C and physiologically relevant pH values, with the de-epoxy form de-epoxy-deoxynivalenol-1 (DOM-1) as the sole resulting metabolite.[12] A series of parallel studies were made using rumen fluid or digesta

[11] Technical dossier/Supplementary Information June 2016/Annex I.
[12] Technical dossier/Section IV/Annexes IV-06–08.

obtained from pigs, artificially contaminated with DON.[13] Incubation of rumen fluid alone showed some activity towards DON (about 25% reduction), but addition of 10^8 CFU/mL of the active agent resulted in the total transformation of DON to DOM-1 as the sole identified metabolite.

A study was made to determine the effects of DON-contaminated diets on the electrophysiological parameters of the chicken gut.[14] The effect of DON on the electrophysiological parameters of the jejunum was studied using an isolated gut mucosa in Ussing chambers. Basal and glucose stimulated transmural potential difference, short-circuit current (Isc) and electrical resistance were measured. The presence of DON in the diet impaired the Na^+-D-glucose cotransport in the jejunum of broilers. Addition of the additive counteracted this effect.

Short-term *in vivo* studies

3.3.1.1. Chickens for fattening

A total of 45 mixed sex Ross 308 was used for a 2-day study.[15] Birds were allocated to one of three treatment groups, a control group fed a mash diet free from mycotoxin contamination, a group given the same basal diet contaminated with 2 mg/kg DON[16] and a third group given the contaminated diet supplemented with the additive at 1.7×10^8 CFU/kg feed. The concentration of DON and the additive were confirmed by analysis of feeds. Each treatment consisted of five pens housing three animals per pen. Although birds were housed in their final pens from day one, treatment began only when birds were 4-weeks-old. During the trial period, faeces were collected per pen five times a day for two consecutive days and the pooled samples per pen analysed for DON, DOM (de-epoxy-DON) and their sulfate conjugates.

Total excreted DON-3-sulfate of each experimental day was compared across groups using the ANOVA/Welch test preceded by tests for normal distribution (Kolmogorov–Smirnov test) and Levene's test for homogeneity of variances. Since variances were not homogeneous, multiple comparisons were carried out using the Tamhane's T-2 test. As DOM-3-sulfate was only measurable (> limit of quantification (LOQ)) in the treated group, only a non-parametric comparison (Mann–Whitney *U*) between the contaminated group and the treated group was made.

The results presented in Table 1 show that virtually all unchanged DON and its de-epoxy metabolite DOM was excreted as the sulfate conjugate. Values for unconjugated DON were all below the LOD or LOQ. Inclusion of the additive resulted in a clear and significant shift in the pattern of excretion with amounts of DON decreasing and a corresponding increase in DOM.

Table 1: Average amount of DON-3-sulfate and DOM-3-sulfate (μg/day) in excreta of chickens for fattening

Compound	Control	Contaminated	Treated	p-value Contaminated *vs* treated
Day 1				
DON-3 sulfate	84.2	337.3	68.4	0.001
DOM-3 sulfate	2.8	3.0	259.2	
Day 2				
DON-3 sulfate	117.1	780.0	124.3	< 0.001
DOM-3 sulfate	5.1	5.5	616.3	

DON: deoxynivalenol; DOM: de-epoxy-deoxynivalenol.

3.3.1.2. Turkeys for fattening

A second study with a protocol essentially the same as that for chickens for fattening was made with 15 female turkeys (hybrid converter).[17] Birds were brought in when 10-weeks-old and acclimatised for 6 days before the start of the study. The five birds used for each treatment were housed in a single pen during acclimatisation and then were separately housed for the 2-day-treatment period to allow faeces collection.

[13] Technical dossier/Section IV/Annexes IV-16–17.
[14] Technical dossier/Section IV/Annex IV_13.
[15] Technical dossier/Section IV/Annex IV_29.
[16] Guidance value of deoxynivalenol in complete feed for poultry is 5 mg/kg complete feed (commission recommendation 2006/576/EC).
[17] Technical dossier/Section IV/Annex IV_18.

The treatments were those described for chickens for fattening except for the lower level of contamination with DON (1.5 mg/kg feed) and the same protocol for faecal collection and analysis was applied. The results are summarised in Table 2.

Table 2: Average amount of DON-3-sulfate and DOM-3-sulfate (μg/bird per day) in excreta of turkeys for fattening

Compound	Control	Contaminated	Treated	p-value Contaminated *vs* treated
Day 1				
DON-3 sulfate	33.0	162.5	31.3	0.009
DOM-3 sulfate	1.0	1.5	152.1	
Day 2				
DON-3 sulfate	34.7	173.3	29.6	< 0.001
DOM-3 sulfate	1.2	1.3	137.4	

DON: deoxynivalenol; DOM: de-epoxy-deoxynivalenol.

The Panel has some concerns about the number of birds used in this study. However, the pattern of results duplicated those seen with chickens for fattening with evidence that the addition of the additive resulted in a significant increase in the amounts of the de-epoxy metabolite excreted at the expense of the parent compound.

3.3.1.3. Laying hens

A third study with a protocol essentially the same as that for chickens and turkeys for fattening was made with 120 female 28-weeks-old Lohmann Brown laying hens over 3 days.[18] Each treatment consisted of ten pens housing four animals per pen.

The treatments were those described for chickens and turkeys for fattening except for the lower level of contamination with DON (1.2 mg/kg feed) and the same protocol for faecal collection and analysis was applied. Results are summarised in Table 3.

Table 3: Average amount of DON-3-sulfate and DOM-3-sulfate (μg/bird per day) in excreta of laying hens

Compound	Control	Contaminated control	Treated	p-value Contaminated *v* treated
Day 1				
DON-3 sulfate	243.5	593.3	182.1	< 0.001
DOM-3 sulfate	29.6	25.0	539.5	< 0.001
Day 2				
DON-3 sulfate	207.9	675.0	190.5	< 0.001
DOM-3 sulfate	19.8	21.7	691.1	0.001
Day 3				
DON-3 sulfate	98.7	334.4	75.8	< 0.001
DOM-3 sulfate	8.0	10.8	302.6	< 0.002

DON: deoxynivalenol; DOM: de-epoxy-deoxynivalenol.

Values for unconjugated DON were below the LOQ. Inclusion of the additive resulted in a clear and significant shift in the pattern of excretion with amounts of DON decreasing and a corresponding increase in DOM.

3.3.1.4. Conclusions

In all three species/categories, the addition of DON to otherwise uncontaminated feed resulted in a significant increase in the sulfate conjugate of DON. Inclusion of the additive at the recommended dose of 1.7×10^8 CFU/kg feed returned the concentration of DON to or below the level seen in the uncontaminated control with a concomitant production of the de-epoxy metabolite.

[18] Technical dossier/Supplementary Information August 2016/Annex_01 Trial report.

Since the applicant proposes the use of the same dose in minor avian species and as the mode of action will the same as seen in chickens and turkeys for fattening and for laying hens, Biomin® BBSH 797 can be considered efficacious for all avian species at a dose of 1.7×10^8 CFU/kg complete feed without the need for additional studies.

3.3.2. Compatibility with coccidiostats

As a preliminary screen, the current EFSA Guidance on establishing the compatibility of a microbial additive with coccidiostats advises determining the minimum inhibitory concentration (MIC) for each coccidiostat. Where the MIC is more than four times greater than the maximum permitted concentration in feed, then compatibility is assumed.

In this case, the principle underlying this *in vitro* preliminary screen has been followed, but rather than examining growth, the additive is tested for its activity against DON in the presence of a fourfold concentration of the individual coccidiostat.[19] Retention of the ability to degrade > 90% of the DON initially present after incubation under anaerobic conditions at 37°C is taken to indicate the functionality of the active agent. When monensin sodium, salinomycin sodium, narasin, narasin/nicarbazin, nicarbazin, robenidine hydrochloride and diclazuril were tested under these conditions, > 90% of the DON was reduced to the de-epoxide after 24 h and 100% after 48 h.

3.3.3. Effect on trichothecenes other than deoxynivalenol

Microbial metabolism of trichothecenes generally involves the enzymatic reduction of the 12,13-epoxide group to the corresponding de-epoxy metabolites (Figure 1), although other reactions can occur (Binder et al., 1998; Wu et al., 2010).

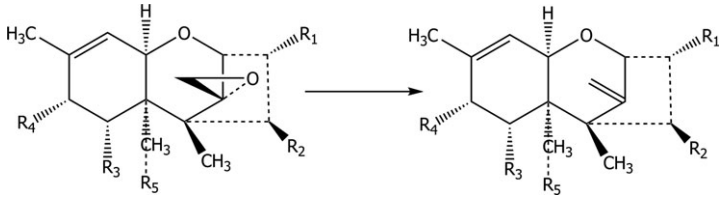

Figure 1: Reduction of the epoxide group

The strain DSM 11798 was selected because of particular capacity to metabolise trichothecenes to the corresponding de-epoxy metabolites. The *in vitro* transformation by strain DSM 11798 of five other Type A trichothecenes (scirentriol, T-2 triol, T-2 tetraol, T-2 toxin and HT-2 toxin) has been confirmed and the metabolites identified (Fuchs et al., 2002). As was found for DON, all gave rise to a single de-epoxy metabolite by a one- or two-step route. Other Group B trichothecenes similarly examined include nivalenol, fusarenon X and 3- and 15-acetyldeoxynivalenol. In these cases, deacetylation preceded de-epoxidation (Fuchs et al., 1999).

The reduced toxicity of the de-epoxy metabolites of T-2 tetraol, T-2 toxin and nivalenol has been confirmed in a variety of cell-based toxicity assays (Eriksen et al., 2004; Bretz et al., 2005; Abbas et al., 2013). Such studies have established that the double bond between C-9 –C-10 and the 12,13 epoxide ring are the essential structural features for trichothecene toxicity (Wu et al., 2013). Removal of both results in complete loss of toxicity, while reduction of the epoxide alone substantially reduces but does not eliminate toxicity.

The applicant makes reference to three feeding trials with chickens for fattening in which the additive appeared to show some protective effects against T-2 toxin and 4,15-diacetoxiscirpenol (Diaz, 2002; Diaz et al., 2005; Nesic et al., 2012). However, these were of short duration (21–28 days) and monitored only performance. None of the studies attempted to determine the fate of the contaminating mycotoxin and to show evidence of the presence of the de-epoxy metabolites.

3.3.3.1. Conclusion

The trichothecenes are a large family of structurally related toxins and only those more commonly encountered in commodity crops have been examined in detail. For the type A and type B trichothecenes, the structure–toxicity relationship is well established and can be presumed to apply to

[19] Technical Dossier/Supplementary Information June 2016/Annex (ii)_01 Compatibility of BBSH with coccidiostats.pdf

those members not directly tested. It is clear that an intact epoxide ring is the major factor contributing to toxicity and that the de-epoxy metabolites are of lesser concern. The present additive has been shown to reduce the 12,13-epoxide group in a number of representative mycotoxins and it would be reasonable to assume a similar reaction with other trichothecenes of the same structural type. This effect would be independent of the animal species or category receiving contaminated feed.

4. Conclusions

Chickens for fattening, turkeys for fattening and laying hens show no adverse effects when the additive is added to diets at either 10× or 1,000× the recommended dose. Consequently, the additive is considered safe for these species/categories when used at the recommended dose of 1.7×10^8 CFU/kg complete feed. This conclusion can be extrapolated to all avian species.

The safety for consumers, users or the environment arising from exposure to the active agent or to metabolites of trichothecene mycotoxins were considered in the context of the scientific opinion for use in feed for pigs. Use of the additive in feed for all avian species is not expected to introduce concerns for consumers, user and environment not previously considered. Therefore, the FEEDAP Panel concludes that the additive is safe for the consumer and environment. The additive is a non-irritant to eyes and skin and is not a skin sensitiser, but the potential for respiratory sensitization cannot be excluded.

Inclusion of the additive at the recommended dose of 1.7×10^8 CFU/kg is effective in reducing the concentration of contaminating DON in feed when given to all avian species with a concomitant production of the less toxic de-epoxy metabolite.

The additive has been shown to reduce the 12,13-epoxide group in a number of representative trichothecenes and it would be reasonable to assume a similar reaction with other mycotoxins of the same structural type. This effect would be independent of the animal species or category receiving contaminated feed.

The additive is compatible with the coccidiostats monensin sodium, salinomycin sodium, narasin, narasin/nicarbazin, nicarbazin, robenidine hydrochloride and diclazuril.

5. Recommendation

No additional data or proposal for further establishing a taxonomy for the active agent is included in the current application. While the deposition in a culture collection offers a practical solution to the unambiguous identity of the active agent, in the view of the Panel, the applicant should be encouraged to formally complete the taxonomic description proposing, if necessary, a new genus/species.

Documentation provided to EFSA

1) Biomin® BBSH 797 – DSM 11798 for all avian species. February 2015. Submitted by Biomin GmbH.
2) Biomin® BBSH 797 – DSM 11798 for all avian species. Supplementary information. June 2016. Submitted by Biomin GmbH.
3) Biomin® BBSH 797 – DSM 11798 for all avian species. Supplementary information. August 2016. Submitted by Biomin GmbH.

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Abbreviations

ANOVA	analysis of variance
CFU	colony-forming unit
DON	deoxynivalenol
DOM	de-epoxy-deoxynivalenol
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
Isc	short-circuit current
LOD	limit of detection
LOQ	limit of quantification
MIC	minimum inhibitory concentration