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SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of monensin sodium (Coxidin®) for chickens for fattening, chickens reared for laying, turkeys for fattening and turkeys reared for breeding (Huvepharma N.V.)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of monensin sodium (Coxidin®) as a coccidiostat for chickens for fattening, chickens reared for laying, turkeys for fattening and turkeys reared for breeding. The additive currently on the market complies with the existing conditions of authorisation. The FEEDAP Panel concluded that Coxidin® remains safe for turkeys for fattening (up to 16 weeks) and extends this conclusion to turkeys reared for breeding (up to 16 weeks). The Panel was not in the position to confirm that the current maximum authorised level of 125 mg monensin sodium/kg complete feed remains safe for chickens for fattening and chickens reared for laying. The use of monensin sodium from Coxidin® at the corresponding maximum authorised/proposed use levels in the target species is safe for the consumer. The existing maximum residue levels (MRLs) for poultry tissues ensure consumer safety. No withdrawal time is necessary. Both formulations of Coxidin® pose a risk by inhalation. The formulation with wheat bran as a carrier was neither irritant to the skin nor a skin sensitiser but it was irritant to the eyes. In the absence of data, no conclusions could be made on the potential of the formulation containing calcium carbonate to be irritant to skin and eyes and to be a skin sensitiser. The use of monensin sodium from Coxidin® in complete feed for the target species poses no risk for the terrestrial compartments and for sediment. No risk for groundwater is expected. For chickens for fattening the risk for aquatic compartment cannot be excluded, but no risks are expected for the other animal categories. There is no risk of secondary poisoning. Coxidin® is efficacious in controlling coccidiosis at a level of 100 mg/kg complete feed for chickens for fattening and at 60 mg/kg complete feed for turkeys for fattening. These conclusions are extended to chickens reared for laying and turkeys reared for breeding. The Panel noted that there are signs of development of resistance of *Eimeria* spp. to monensin sodium.

KEYWORDS
chickens for fattening, chickens reared for laying, coccidostats, Coxidin®, monensin sodium, safety and efficacy, turkeys for fattening, turkeys reared for breeding

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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 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest one year before the expiry date of the authorisation and Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of feed additive shall submit an application in accordance with Article 7.

The European Commission received the following requests from Huvepharma N.V.[2] for the additive consisting of monensin sodium (Coxidin®), when used as a feed additive (category: coccidiostats and histomonostats):

- Coxidin® (carrier wheat bran)
  - renewal for chickens for fattening and turkeys for fattening,[3]
  - authorisation for chickens reared for laying and turkeys reared for breeding;[4]
- Coxidin® (carrier calcium carbonate),
  - renewal for chickens for fattening, chickens reared for laying and turkeys for fattening.[5]
  - authorisation for turkeys reared for breeding.[6]

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the applications to the European Food Safety Authority (EFSA) as an application under Article 14(1) (renewal of the authorisation) and under Article 4(1) (authorisation of a feed additive or new use of a feed additive).

The dossiers were received between 2016 and 2020. The general information and supporting documentation are available at OpenEFSA.[7] The particulars and documents in support of the applications were considered valid by EFSA on 9 December 2016, 8 January 2021, 5 August 2020 and 8 February 2021, respectively.

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 feed additive consisting of monensin sodium (Coxidin), when used under the proposed conditions of use (see **Section 3.1.6**).

1.2 | Additional information

The additives monensin sodium (Coxidin®, carrier wheat bran) and monensin sodium (Coxidin®, carrier calcium carbonate) are currently authorised (authorisation number 51701) for use in feed for chickens for fattening and turkeys up to 16 weeks of age.[8] Monensin sodium (Coxidin®, carrier calcium carbonate) is also authorised for chickens reared for laying up to 16 weeks of age.[9]

EFSA issued several opinions on the safety and efficacy of this additive when used in feed for chickens for fattening and turkeys (EFSA, 2005, 2006, 2007, 2008a; EFSA FEEDAP Panel, 2011a, 2013), and when used in feed for chickens reared for laying (EFSA FEEDAP Panel, 2011b, 2013).

Monensin sodium is also present in the additive Elancoban® from another holder of the authorisation; the FEEDAP Panel adopted five opinions related to this product (EFSA, 2004b, 2006, 2008b; EFSA FEEDAP Panel, 2019, 2023). In addition, the safety and efficacy of monensin sodium in combination with nicarbazin (Monimax®) as a coccidiostat for chickens for fattening, chickens reared for laying and for turkeys for fattening was also evaluated by the FEEDAP Panel (EFSA FEEDAP Panel, 2017d, 2018c, 2019c).

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2]Uitbreidingstraat 80, 2600, Antwerpen (Berchem), Belgium.
[3]FAD-2016-0009 received on the 4 February 2016.
[4]FAD-2020-0091 received on the 26 November 2020.
[5]FAD-2020-0036 received on the 26 May 2020.
[6]FAD-2020-0111 received on the 8 February 2021.
[7]https://open.efsa.europa.eu/questions/EFSA-Q-2016-00643; https://open.efsa.europa.eu/questions/EFSA-Q-2020-00837; https://open.efsa.europa.eu/questions/EFSA-Q-2020-00405; https://open.efsa.europa.eu/questions/EFSA-Q-2021-00074.
[8]Commission Implementing Regulation (EU) No 495/2011 of 20 May 2011 amending Regulation (EC) No 109/2007 as regards the composition of the feed additive monensin sodium. OJ L 134, 21.5.2011, p.6–8.
[9]Commission Implementing Regulation (EU) No 140/2012 of 17 February 2012 concerning the authorisation of monensin sodium as a feed additive for chickens reared for laying (holder of authorisation Huvepharma NV Belgium). OJ L 47, 18.2.2012, p. 18–19.

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of technical dossiers[10] in support of the authorisation request for the use of monensin sodium (Coxidin®) as a feed additive.

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, peer-reviewed scientific papers, other scientific reports and to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the active substance in animal feed/marker residue in tissues for FAD-2016-0009.[11] The EURL considered that the conclusions and recommendations reached in this assessment regarding the methods used for the control of the monensin sodium in animal feed/marker residue in tissues are valid and applicable for FAD-2020-0036, FAD-2020-0091 and FAD-2020-0111.

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of monensin sodium (Coxidin®) is in line with the principles laid down in Regulation (EC) No 429/2008[12] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017a), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018a), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018b), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019a), EFSA statement on the requirements for whole genome sequence analysis of microorganisms intentionally used in the food chain (EFSA, 2021) and Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2021).

3 | ASSESSMENT

The additive monensin sodium (Coxidin®) is a coccidiostat currently available in two formulations, one with wheat bran as a carrier authorised for use in feed for chickens for fattening, turkeys (up to 16 weeks), and one with calcium carbonate as a carrier, authorised for chickens for fattening, chickens reared for laying and turkeys (up to 16 weeks). The applicant requested the renewal of the above authorisations, and the extension of the authorisations to cover also turkeys reared for breeding; for the formulation with wheat bran the applicant requested to extend the authorisation to chickens reared for laying.

3.1 | Characterisation

3.1.1 | Characterisation of the production microorganism

Monensin sodium is produced by fermentation with a non-genetically modified strain of *Streptomyces* spp. The production strain was originally identified as *Streptomyces cinnamonensis* (correct name *Streptomyces virginiae*, Komaki and Tamura 2021) and is deposited in the BCCM/LMG Bacteria Collection (Belgium) with the accession number LMG S-19095.

The whole genome sequence (WGS) data of the production strain were used for taxonomical identification.[13] [redacted] This suggests that strain LMG S-19095 may belong to a new *Streptomyces* species. [redacted] Therefore, the FEEDAP Panel considers that the data submitted to taxonomically identify the strain do not allow to assign LMG S-19095 to any described microbial species.

[10]Dossier reference: FAD-2016-0009, FAD-2020-0036, FAD-2020-0091, FAD-2020-0111. Most of the information submitted in the four dossiers are identical or cross-referenced from one dossier to the other, therefore the footnotes make reference solely to FAD-2016-0009 or otherwise the relevant dossier is specified. When the other dossiers are indicated.

[11]Evaluation report received on 1/3/2017 and available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en.

[12]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.

[13]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_II_2_1, Annex_RTQ_II_2_2, Annex_RTQ_II_2_3 and Annex_RTQ_II_2_4.

The susceptibility of the production strain LMG S-19095 to the relevant antibiotics listed in the Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018a,) was tested [redacted][14] [redacted], the production strain LMG S-19095 is considered resistant to the antibiotics [redacted].

The WGS data of the production strain were interrogated for the presence of antimicrobial resistance (AMR) genes, [redacted][15] [redacted] All these AMR genes are considered a hazard.

The WGS data of *Streptomyces* sp. LMG S-19095 were analysed for the presence of genes coding for virulence factors, [redacted].[16] [redacted] Therefore, it can be concluded that no hits of concern were detected.

The absence of antimicrobial compounds relevant to the use of antibiotics in humans or animals, other than the monensin sodium in the processed fermentation broth, was assessed comparing the inhibitory activity of three batches of the fermentation product with one batch of pure monensin sodium.[17] [redacted] Since no differences in the inhibitory spectrum were observed between the pure and fermentation products for any of the strains tested, the product is considered free of antimicrobial activity other than monensin sodium.

3.1.2 | Characterisation of the active substance

Monensin sodium (CAS number 22373-78-0) is a polyether ionophore produced by fermentation. No changes have been introduced in the manufacturing process compared to that in the previous submission for the assessment that led to the authorisation. Monensin sodium consists of the main chemical forms of monensin A sodium, monensin B sodium and monensin C sodium (EFSA, 2005). The solubility of monensin sodium in water was determined following OECD TG 105 and resulted in 8.78 mg/L (EFSA FEEDAP Panel, 2017). [redacted][18]

The structural formula is given in Figure 1.

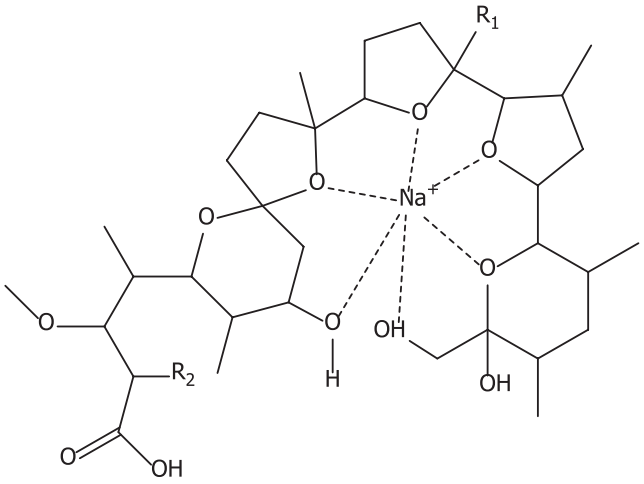
[14]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_II_2_5.

[15]Technical dossier/Supplementary information September 2021/Annex_RTQ_II_2_1_Bioinformatics Analysis Antibiotic Resistance Genes Str *cinnamonensis*.

[16]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_II_2_1_Bioinformatics Analysis Antibiotic Reistance Genes Str *cinnamonensis*.

[17]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_II_2_8_Antimicrobial production.

[18]FAD-2016-0009:Technical dossier/Section II/Reference 19.



Forms	R_1	R_2	Chemical formula	Molecular weight (g/mol)
Monensin A sodium	C_2H_5	H	$C_{36}H_{61}NaO_{11}$	693.8
Monensin B sodium	CH_3	H	$C_{35}H_{59}NaO_{11}$	679.7
Monensin C sodium	C_2H_5	CH_3	$C_{37}H_{63}NaO_{11}$	707.8

FIGURE 1 Structural formula of monensin (A, B and C) sodium.

After the fermentation process monensin sodium is not further isolated/purified and is used to formulate the additive Coxidin® as 'monensin sodium technical substance'; the latter contains dried exhausted fermentation substrate (38%–53%) and perlite (15%–20%).

'Monensin sodium technical substance' is specified to contain [redacted] ≥ 90% of monensin A, ≥ 95% of monensin A and B and 0.2%–0.3% of monensin C. [redacted][19] No information on the proportion of the three forms of monensin from recent batches was provided.

3.1.3 | Characterisation of the additive

Coxidin® is currently authorised in two different formulations, both with a content of monensin sodium technical substance equivalent to monensin activity[20] of 25% and perlite 15%–20%. The difference between the two formulations lies on the carriers used, wheat bran 55%–60% in one case, and calcium carbonate *quantum satis* 100% in the other. The applicant stated that no modifications in the manufacturing process and composition of the two formulations have been introduced since the last authorisation. Both forms of the additive are obtained by blending the 'monensin sodium technical substance' containing monensin sodium and perlite with the respective carriers.

The FEEDAP Panel notes that perlite is not authorised anymore as a feed additive[21] and is not a feed material. In its statement adopted in 2020, the FEEDAP Panel could not perform an assessment of perlite due to lack of data (EFSA FEEDAP Panel, 2020). In the absence of data in the current applications, a full assessment on the use of perlite in the formulation of Coxidin® cannot be undertaken.

The additive is specified to contain 237–262 g monensin sodium/kg. The compliance with this specification was confirmed in the batch-to-batch variation of six batches of each formulation of the additive. In the formulation with wheat bran as a carrier, monensin sodium content was on average 254.3 μg/mg (range: 251.0–261.1 μg/mg);[22] in the formulation with calcium carbonate as a carrier, monensin sodium content was on average 254.9 μg/mg (range: 251.6–259.9 μg/mg).[23]

Three batches of each formulation were analysed for the presence of chemical impurities and *Salmonella*. In the formulation with wheat bran, results showed concentrations of arsenic and mercury below their corresponding limit of quantification (LOQ), cadmium between 0.024 and 0.036 mg/kg, lead 0.1 mg/kg; levels of aflatoxins B1, B2, G1, G2 were below the LOQs.[24] Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like

[19]FAD-2016-0009: Technical dossier/Section II/Reference 26.

[20]The concentration of monensin sodium is expressed as monensin activity which includes the relative biopotency in terms of 'monensin activity' of the different monensin variants.

[21]Commission Implementing Regulation (EU) 2023/1173 of June 2023 withdrawing from the market certain feed additives, amending Regulation (EC) No 1810/2005 and repealing Regulations (EC) No 1453/2004, (EC) No 2148/2004 and (EC) No 943/2005. OJ L 155, 16.6.2023, p. 28.

[22]FAD-2016-0009:Technical dossier/Section II/Reference 5.

[23]FAD-2020-0036:Technical dossier/Section II/Annex_II_5.

[24]FAD-2016-0009:Technical dossier/Section II/Reference 10 LOQs in mg/kg were: 0.04 for arsenic and 0.005 for mercury; LOQs in μg/kg were: 1 for aflatoxins.

polychlorinated biphenyls (PCBs) were analysed and all the values were below the corresponding LOQ. The calculated upper bound (UB) concentration was 0.137 ng WHO-PCDD/F TEQ/kg for the sum of dioxins, and 0.269 ng WHO PCCD/F + PCB TEQ/kg for the sum of dioxins and dioxin-like PCBs. The UB for the sum of non-dioxin-like PCBs was 0.005 mg/kg (all values are expressed on 88% dry matter).[25] Salmonella was absent in 25 g of the additive.[26] In the formulation with calcium carbonate, results showed concentrations of arsenic between 0.293 and 0.536 mg/kg, cadmium between 0.13 and 0.143 mg/kg, lead between 1.81 and 3.04 mg/kg and mercury below 0.005 mg/kg. PCDDs, PCDFs, PCBs were analysed and all the values were below the corresponding LOQ. The calculated upper bound concentration was 0.137 ng WHO-PCDD/F TEQ/kg for the sum of dioxins, and 0.269 ng WHO PCCD/F + PCB TEQ/kg for the sum of dioxins and dioxin-like PCBs. The upper bound for the sum of non-dioxin-like PCBs was 0.005 mg/kg (all values are expressed on 88% dry matter).[27] *Salmonella* was absent in 25 g of the additive.[28]

The FEEDAP Panel considers that the amounts of the detected impurities do not raise safety concerns.

The presence of the production strain LMG S-19095 in the feed additive was investigated [redacted].[29] [redacted] No colonies were detected [redacted] in the analysed batches.

The presence of DNA of the production strain in the feed additive was investigated [redacted][30] [redacted] No DNA was detected in any of the three analysed batches [redacted]

3.1.4 | Physical properties of the additive

Both formulations of the additive appear as a light beige to brown powder with a density of 430–480 kg/m^3 (bulk) and 560–620 kg/m^3 (tapped) for the formulation containing wheat bran as a carrier[31] and 460–560 kg/m^3 (bulk) and 560–710 kg/m^3 (tapped) for the formulation containing calcium carbonate as a carrier.[32]

Dusting potential (three batches) of the formulation containing wheat bran as a carrier ranged between 95 and 100 mg/m^3.[33] The particle size distribution of the dust generated during the experiment was analysed by laser diffraction in three batches. Practically all particles were below 50 µm (99.6%) while the fraction below 10 µm was 14.0% (range: 13.6%–14.2%).[34] The mean monensin sodium content in this dust fraction was 537 mg/g.[35] The physical characteristics of the formulation containing calcium carbonate as a carrier was evaluated by the FEEDAP Panel (EFSA FEEDAP Panel, 2011a, 2011b), the same data have been resubmitted for the purpose of the current assessment. Dusting potential (three batches) ranged between 920 and 980 mg/m^3.[36] The laser diffraction analysis of the dust collected during the measurement of dusting potential showed that approximately half of the particles had a diameter of 9 µm or below. The mean monensin sodium content in this dust fraction was 235 mg/g.[37]

The applicant submitted particle size analysis data using a combination of scanning electron microscopy (SEM) and transmission electron microscopy (TEM) techniques of both formulations.[38] The descriptive SEM and TEM analysis provided demonstrated the presence of particles of variable size. The presented electron micrographs were taken at relatively low magnification (µm size scale bars) making it impossible to evaluate the presence of small/nano particles in the nano range (i.e. 1–250 nm). Moreover, the product consists of different components and the applied methodology does not allow to differentiate the particles of each component. These shortcomings did not allow the FEEDAP Panel to conclude on the absence of (a fraction of) small particles including nanoparticles in the additives. In the absence of adequate data on the decision criteria for particle size, the FEEDAP Panel considered the following elements. The active substance, pure

[25]FAD-2016-0009:Technical dossier/Section II/Reference 10 Upper bound concentrations are calculated on the assumption that all values of the different congeners below the limit of quantification are equal to the limit of quantification. TEQ = toxic equivalency factors for dioxins, furans and dioxin-like PCBs established by WHO in 2005 (van den Berg et al., 2006).

[26]FAD-2016-0009:Technical dossier/Section II/Reference 10.

[27]FAD-2020-0036:Technical dossier/Section II/Reference 10 Upper bound concentrations are calculated on the assumption that all values of the different congeners below the limit of quantification are equal to the limit of quantification. TEQ = toxic equivalency factors for dioxins, furans and dioxin-like PCBs established by WHO in 2005 (van den Berg et al., 2006).

[28]FAD-2020-0036:Technical dossier/Section II/Reference 12.

[29]FAD-2016-0009:Technical dossier/Supplementary information September 2021/Annex_RTQ_II_1_Absence strain cells and Supplementary information April 2023/Annex_RTQ_II_1–9.

[30]FAD-2016-0009:Technical dossier/Supplementary information September 2021/Annex_RTQ_II_2_2.

[31]FAD-2016-0009:Technical dossier/Section II/Reference 12.

[32]FAD-2020-0036:Technical dossier/Section II/Annex_II_13.

[33]FAD-2016-0009:Technical dossier/Section II/Reference 13.

[34]FAD-2016-0009:Technical dossier/Section II/Reference 14.

[35]FAD-2016-0009:Technical dossier/Supplementary information March 2021/Annex_RTQ_II_1_1.

[36]FAD-2020-0036:Technical dossier/Section II/Annex II.14.

[37]FAD-2020-0036§:Technical dossier/Supplementary information March 2021/Annex_RTQ_II_1_1.

[38]FAD-2016-0009:Technical dossier/Supplementary Information April 2023/Annex_RTQ_V and FAD-2020-0036/Technical dossier/Supplementary Information April 2023/Annex_RTQ and Supplementary information July 2023.

monensin sodium, is classified as insoluble[39] in water, while it is soluble in hydrocarbons and in organic solvents to some extent;[40] the log partition coefficient (n-octanol/water) varies from 3.8 to 4.5 depending on the pH (EFSA FEEDAP Panel, 2017). The test items used in the absorption, distribution, metabolism and excretion (ADME), residue and toxicological studies, including tolerance studies, were representative of the active substance (EFSA, 2005, 2007). The results from those studies are sufficient to cover nanoscale considerations since the administration mimics the actual use in animals, also in terms of the studied doses.

Considering the above and in line with the appraisal route described in Section 4 of the Guidance on technical requirements (EFSA SC, 2021), the Panel concludes that the safety of monensin sodium from Coxidin® can be adequately covered by the conventional risk assessment and any risks from particles that are potentially in the nano/small range have already been covered by the existing data.

3.1.5 | Stability and homogeneity

No new data were provided regarding the stability and homogeneously distribution of the additive in premix and/or feed. Since no changes were introduced in the additive's manufacturing process (nor in the two formulations under assessment), the data described in the previous opinions with monensin sodium from Coxidin® for the two formulations with wheat bran and calcium carbonate (EFSA, 2005; EFSA FEEDAP Panel, 2011a, respectively) are considered relevant for the present assessment.

3.1.6 | Conditions of use

The additive, in both formulations, is currently authorised as a coccidiostat in feed for chickens for fattening and turkeys (up to 16 weeks), while the formulation with calcium carbonate is also authorised for use in chickens reared for laying (up to 16 weeks). The minimum and maximum authorised use levels are 100 and 125 mg monensin sodium/kg complete feed for chickens for fattening and reared for laying, and 60 and 100 mg monensin sodium/kg complete feed for turkeys (up to 16 weeks).

The other provisions of the authorisations state:

1. Use prohibited at least 1 day before slaughter,
2. The additive shall be incorporated in compound feedingstuffs in form of a premixture,
3. Monensin sodium shall not be mixed with other coccidiostats,
4. Indicate in the instructions for use: 'Dangerous for equines. This feedingstuff contains an ionophore: avoid simultaneous administration with tiamulin and monitor for possible adverse reactions when used concurrently with other medicinal substances'.
5. Wear suitable protective clothing, gloves and eye/face protection. In case of insufficient ventilation in the premise, wear suitable respiratory equipment.

The authorisation for Coxidin® with wheat bran, in addition states:

6. Maximum permitted dose of monensin sodium in complementary feedingstuffs:
   - 625 mg/kg for chickens for fattening,
   - 500 mg/kg for turkeys.

And the authorisation for use in chickens reared for laying includes the following:

7. A post-market monitoring programme on the resistance to *Eimeria* spp. shall be planned and executed by the holder of authorisation.

Both authorisations set the following provisional maximum residue levels: 25 μg monensin sodium/kg wet skin + fat and 8 μg monensin sodium/kg wet liver, wet kidney and wet muscle.

The applicant has requested to maintain the above conditions, with the exception of the reduction of the withdrawal period to 0 days for chickens for fattening.

In addition, the applicant has requested the extension of use of both formulations to turkeys reared for breeding (up to 16 weeks) and of the formulation with wheat bran to chickens reared for laying (up to 16 weeks).

[39]For solubility terms see Table 2 of EFSA SC (2021).

[40]FAD-2016-0009/Technical dossier/Section II/Reference 19.

3.2 | Safety

The safety of the additive for the target species, consumer, user and environment was evaluated by the FEEDAP in previous opinions (EFSA, 2005, 2006, 2008a, 2008b, EFSA FEEDAP Panel, 2011b, 2013). In those opinions the FEEDAP Panel concluded that Coxidin® (both formulations, EFSA FEEDAP Panel, 2011a) was safe for chickens for fattening, turkeys for fattening (EFSA, 2005), and chickens reared for laying (EFSA FEEDAP Panel, 2011b). Additionally, monensin sodium was considered safe for the consumer (EFSA, 2006, 2008a) and the environment (EFSA FEEDAP Panel, 2011b, 2017, 2018, 2019c). Based on studies with pure monensin sodium or Coxidin® (wheat bran as a carrier), the FEEDAP Panel concluded that both formulations of the additive pose a risk by inhalation to the users, are not skin irritants or skin sensitisers but should be considered as eye irritants.

No new studies were submitted by the applicant in the context of the applications under assessment. No information was provided by the applicant on reports of adverse effects.

The applicant provided an extensive literature search to support the safety of the additive covering the period 2011–2020.[41,42,43] The literature search was conducted using two bibliographic databases (PubMed and CAB direct). The search included terms relative to the safety of monensin. The search returned a total of 577 and 724 results, on the two databases respectively, of which 19 full papers were considered relevant and submitted in relation to the safety of Coxidin®. Those papers were screened by the FEEDAP Panel and those relevant for the current evaluation are quoted below.

3.2.1 | Safety of the production microorganism

The production strain LMG S-19095 was proven to belong to the *Streptomyces* genus, however it was not possible to identify it at the species level. The WGS data provided shows that the production strain harbours several genes encoding AMR which are considered a hazard. However, viable cells and DNA of the production strain were not detected in the monensin sodium technical substance used to formulate the additives. Consequently, the FEEDAP Panel concludes that there are no safety concerns for the target species, consumers, users and the environment with regard to the production strain.

3.2.2 | Safety for the target species

In the opinion on the safety and efficacy of Coxidin® for chickens for fatting and turkeys for fattening (EFSA, 2005), the FEEDAP Panel concluded that the additive was safe at the proposed maximum concentration of 125 and 100 mg monensin sodium/kg complete feed for chickens and turkeys, respectively, with a margin of safety of less than two. In 2011, EFSA adopted an opinion on the use of Coxidin® in which the above conclusions reached in chickens for fattening were extended to chickens reared for laying (EFSA FEEDAP Panel, 2011b).

No new tolerance studies were submitted for the current applications.

In line with the requirements of the FEEDAP guidance on renewal (EFSA FEEDAP Panel, 2021), the applicant provided an extensive literature search (see Section 3.2). Only one publication was related to the safety for the target species (Zavala et al., 2011). The Panel noted that in this study an accidental overdose of approximately seven times (638–740 mg/kg feed; confirmed by analysis) was given to breeders (males and females). After 10 days of consumption of this feed, mortality reached 13.7% in hens and 70.9% in roosters and egg production decreased from 67% to 3% with affected hens/roosters displaying feed refusal, decreased water consumption and severe paralysis.[44]

The FEEDAP Panel notes that, in a recent assessment of the safety of monensin sodium from another product, the results of a tolerance trial in chickens for fattening showed a dose-related reduction of the average daily gain and the final body weight at levels of monensin sodium starting at 125 mg/kg feed. In consequence, the FEEDAP Panel could not conclude on a safe level of monensin sodium in complete feed for chickens for fattening (EFSA FEEDAP Panel, 2023). The FEEDAP Panel considers that these findings are relevant also for the product under assessment, and therefore concludes that, on the basis of the information available and for both formulations under assessment, it is not in a position to confirm that monensin sodium remains safe for chickens for fattening and chickens reared for laying under the approved conditions of use.

With regard to the safety for turkeys for fattening, considering that no adverse effects have been reported in the literature and that the manufacturing and composition of the additive have not been modified since the previous authorisation, the FEEDAP Panel concludes that monensin sodium from Coxidin® remains safe for turkeys for fattening under the authorised conditions of use. This conclusion is extended to turkeys reared for breeding (up to 16 weeks) and considered valid for both formulations.

[41]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_III_16.

[42]FAD-2016-0009: Technical dossier/Supplementary information September 2021.

[43]FAD-2020-0036: Technical dossier/Section III/Sect III/Annex_III_16_Literature review.

[44]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_V_4_1.

3.2.3 | Safety for the consumer

3.2.3.1 | *Absorption, distribution, metabolism and excretion*

Studies on ADME of monensin sodium in rat, chicken and turkey were evaluated by the FEEDAP Panel in previous opinions on Coxidin® (EFSA, 2005, 2006). The main conclusions can be summarised as follows: (i) monensin sodium is absorbed to a limited extent and this fraction is eliminated largely through bile; (ii) monensin sodium is metabolised extensively and gives rise to demethylated, oxidised and decarboxylated metabolites; (iii) unchanged monensin represents about 19% of the whole faecal excretion in chicken, up to 40% in turkey; (iv) the same metabolites have been found in the excreta and tissues where they represent each less than 10% of the total monensin derivatives and (v) the metabolic pathways in the chicken are similar to those in the turkey and rat.

Another ADME study was evaluated by the FEEDAP Panel in 2017 (EFSA FEEDAP Panel, 2017d). This study, also submitted for the current application,[45] despite some limitations[46] that prevent its use in the quantification of the relevant residue levels, confirmed the ADME profile of monensin sodium in the target animals, and provided data on the comparative metabolic profiles of monensin in tissues sampled after different withdrawal periods.

In the current dossiers, no new studies were provided, and no relevant data were retrieved from the literature search submitted by the applicant (Section 3.2). Therefore, the same conclusions, as previously reached, can be retained for the current evaluation.

3.2.3.2 | *Residues*

The residue studies in chickens (total residue and marker residue), submitted in the present dossiers,[47] were already evaluated by the FEEDAP Panel (EFSA, 2006; EFSA FEEDAP Panel, 2013). The residue studies in turkeys were evaluated in a previous FEEDAP opinion (EFSA, 2006) and were not resubmitted in the current dossiers since the studies in chickens represents a worse-case scenario and are considered relevant for the current assessment. In order to reassess the consumer exposure and perform a consumer safety assessment (Section 3.2.3.4) at the 0-withdrawal time proposed by the applicant, the main results from the chickens' studies are reported below.

Total residues were measured in tissues from chickens (three male and three females, 2-week-old) administered ^{14}C-monensin (labelling position not given) included in feed at a dose equivalent to 125 mg/kg feed (analytically confirmed), for 8 days, then slaughtered 0, 1, 2 and 3 days after the last administration.[48] Results at 0- and at 1-day withdrawal are given in Table 1.

TABLE 1 Monensin sodium total residue (mg equivalent monensin/kg wet tissues) at 0- and 24-h withdrawal time.

Withdrawal (h)	Liver	Kidney	Muscle	Skin/fat
0	1.664 ± 0.118[a] 1.900[b]	0.336 ± 0.058[a] 0.452[b]	0.087 ± 0.013[a] 0.113[b]	0.363 ± 0.049[a] 0.461[b]
24	0.791 ± 0.200 1.191	0.254 ± 0.084 0.422	0.075 ± 0.020 0.115	0.368 ± 0.092 0.552

[a]Average ± SD.
[b]Average + 2SD.

Marker residue (monensin sodium) levels relevant for the current evaluation were taken from a study already assessed by the FEEDAP Panel (EFSA FEEDAP Panel, 2013).[49] In this study, 36 one-day-old chickens for fattening (Ross 308) were fed for 42 days with a feed containing 125 mg monensin sodium from Coxidin®/kg (confirmed by analytical data). Birds were slaughtered at 0, 1, 3, 6, 12 and 24 h after withdrawal of the supplemented feed. Tissues were sampled from three male and three female birds per time point. Monensin sodium residue concentrations were determined in the tissues at 0-, 1-, 3- and 6-h withdrawal with a validated (internally) analytical method[50] with a LOQ of 0.0005 mg/kg. The results at 0- and 6-h withdrawal are given in Table 2.

TABLE 2 Monensin sodium residues (mg/kg) at 0- and 6-h withdrawal time.

Withdrawal (h)	Liver	Kidney	Muscle	Skin/fat
0	0.0165 ± 0.006[a] 0.0285[b]	0.0087 ± 0.00386[a] 0.0163[b]	0.0034 ± 0.00166[a] 0.0066[b]	0.0387 ± 0.01296[a] 0.0645[b]
6	< LOQ	< LOQ	< LOQ	3.0 ± 0.1

Abbreviation: LOQ, limit of quantification.
[a]Average ± SD.
[b]Average + 2SD.

[45]FAD-2016-0009: Technical dossier/Section III/Annex_III_5_ADME.
[46]The dose applied was 80% of the maximum authorised concentration; the labelled dose was administered via gavage which is not in accordance with the relevant EFSA Guidance on consumer safety, EFSA FEEDAP Panel (2017a).
[47]FAD-2016-0009: Technical dossier/Section III/Annexes III.5, III.6, III.7, III.10, III.12).
[48]FAD-2016-0009: Technical dossier/Section III/Annexe III.6.
[49]FAD-2016-0009: Technical dossier/Section III/Annexe III.11.
[50]FAD-2016-0009: Technical dossier/Section III/Annexe III.10.

Table 3 summarises the values of monensin sodium total residue (mg/kg), marker residue (mg/kg) and ratios marker to total residue at 0-h withdrawal time.

TABLE 3 Monensin sodium total residue (mg equivalent monensin/kg wet tissues), marker residue (mg/kg) and ratios marker to total residue at 0-h withdrawal time.

	Liver	Kidney	Muscle	Skin/fat
TR[a]	1.90	0.46	0.12	0.46
RMTR[b]	0.015	0.035	0.058	0.141
MRC[c]	0.029	0.016	0.007	0.065

[a]TR (total residue concentration) average values +2SD.
[b]RMTR (ratio marker to total residues) – (EFSA FEEDAP Panel, 2013).
[c]MRC (marker residue concentration) average values +2SD.

3.2.3.3 | *Toxicological studies*

The toxicological profile of monensin sodium was evaluated in previous FEEDAP opinions (EFSA, 2005; EFSA FEEDAP Panel, 2017d, 2018). In those opinions, the FEEDAP Panel concluded that monensin sodium is not genotoxic in an adequate set of studies and showed no structural alert for carcinogenesis, and it is not a reproductive or developmental toxin based on adequate studies in rat and rabbit. The lowest no observed effect level (NOEL) was identified in the developmental study in rabbits and it was 0.3 mg monensin sodium/kg body weight (bw) per day for maternal toxicity. The FEEDAP Panel notes that a pharmacological no observed adverse effect level (NOAEL) of 0.345 mg monensin sodium/kg bw per day was identified in a dog for acute pharmacological effects on the cardiovascular system and was considered appropriate for the establishment of an acute health-based guidance value (acute reference dose – ARfD) of 0.003 mg monensin sodium/kg bw in an EFSA opinion adopted in 2004 (EFSA, 2004a, 2004b).

For the current assessment, the applicant performed a structured literature search (see 3.2). The Panel screened the 18 papers identified as relevant for the toxicological profile of the substance and concluded that no new studies on genotoxicity, repeated dose toxicity, carcinogenicity or reproduction or developmental toxicity were identified in the literature search that would change the previous conclusions on the toxicological profile of monensin sodium.

The FEEDAP Panel confirms that a health-based guidance value (acceptable daily intake – ADI) of 0.003 mg/kg bw can be established based on the lowest NOEL identified in the developmental study in rabbits of 0.3 mg monensin sodium/kg bw per day for maternal toxicity in rabbits applying an uncertainty factor of 100.

Toxicological relevance of total monensin residues in tissues

The FEEDAP Panel notes that the toxicological relevance of total monensin residues in tissues was evaluated in an opinion adopted in 2008 (EFSA, 2008a). In that opinion, it was concluded that, taking a weight of evidence approach, monensin-derived residues of toxicological relevance represent, as a conservative estimate, not more than 50% of the total residues. This assumption is considered valid also for the present evaluation.

3.2.3.4 | *Consumer exposure and consumer safety assessment*

In the current assessment, the chronic exposure of consumers to monensin total residues in chicken tissues was calculated following the methodology described in the Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017a). The input values of total residues after 0-hour withdrawal used for the calculation are given in Table 4.

TABLE 4 Input values used to calculate consumer exposure to monensin residues (mg/kg) in poultry tissues.

	Input values (mg/kg tissue)
Birds fat tissue	0.46
Birds liver	1.90
Birds meat[a]	0.15
Birds offals and slaughtering products (other than liver)	0.46

[a]The residue concentration in muscle (0.12 mg/kg) and skin/fat (0.46 mg/kg) has been used to calculate the intake of meat at the following proportions: 90% muscle and 10% skin/fat (EFSA FEEDAP Panel, 2017b).

The results on the chronic exposure (Table 5) showed that the highest chronic exposure was for the population class 'toddlers' with 0.0014 mg/kg bw per day, corresponding to 46% of the ADI (for detailed results per age class, country and

survey see Appendix A, Table A.1). Considering that the residues of toxicological concern represent only 50% of the total residues in tissues and organs of the target animals, the exposure to residues of toxicological concern would be approximately 23% of the ADI.

TABLE 5 Chronic exposure of consumers to monensin total residues based on residue data in chicken tissues.

Population class	Highest exposure estimate[a] (mg/kg bw per day)	% ADI
Infants	0.0011	36
Toddlers	0.0014	46
Other children	0.0013	43
Adolescents	0.0007	23
Adults	0.0007	23
Elderly	0.0004	12
Very elderly	0.0004	13

Abbreviations: ADI, acceptable daily intake; bw, body weight; HRP, highest reliable percentile.

[a]HRP 95th percentile for all except for very elderly (90th percentile).

An acute exposure assessment is considered necessary considering that a pharmacological NOAEL of 0.345 mg monensin sodium/kg bw per day was identified in a dog for acute pharmacological effects (ARfD) of 0.003 mg monensin sodium/kg bw (Section 3.2.3.3).

The exposure methodology detailed in the guidance on consumer safety (EFSA FEEDAP Panel, 2017a) provides results of acute dietary exposure for each single tissue for all age classes. The tables reported in Appendix A (Tables A.2, A.3 for details) indicate that the highest exposure can be found for liver consumption of the age classes 'other children' in Romania and Bulgaria (consuming 0.0104 and 0.0031 mg/kg bw per day, respectively), of the age class 'adolescents' in Romania (consuming 0.0056 mg/kg bw per day) and of the age class 'adults' in Germany (consuming 0.006 mg/kg bw per day). All these consumptions are above the ARfD. Considering that the residues of toxicological concern represent only 50% of the total residues in tissues and organs of the target animals, acute exposure by liver of 'adolescents' and 'adults' would be at or below the ARfD. Only the levels of 'other children' from Romania would remain above the ARfD (173%). However, the data of all other countries providing data for acute exposure of 'other children' indicate an exposure below or at the level of the ARfD.

The FEEDAP Panel notes that monensin sodium is authorised in the EU also as veterinary medicine for bovines which may result in exposure of consumers to monensin residues via bovine tissues and milk of dairy cows.[51] The Committee for Medicinal Products for Veterinary Use (CVMP) of the European Medicine Agency (EMA) assessed in 2013 a residue study performed in dairy cattle (intraruminal administration with controlled release capsule, delivering approximately 335 mg monensin/day for 95 days). Tissue samples of liver, kidney, muscle and fat were collected from 10 animals 14 days after administration of the controlled release capsule (EMA-CVMP, 2013). The residue data from this study (highest values for each tissue/product as a worst-case scenario) are used by the FEEDAP Panel to assess the combined consumer exposure resulting from the use of monensin as a feed additive for poultry and as a veterinary medicine for bovine. Table 6 reports the marker residue values measured in the above-mentioned study (maximum values) and the calculated total residues applying the ratios marker to total residues reported by the CVMP.

TABLE 6 Monensin residues (mg/kg) in bovine tissues and milk after its use as veterinary medicine.[a]

	Liver	Kidney	Muscle	Skin/fat	Milk
Marker residue measured[a]	0.0263	0.00145	0.00084	0.00532	0.00048
RMTR[b]	0.05	0.05	0.05	0.05	0.027
Calculated total residues	0.526	0.029	0.017	0.106	0.018

[a]Highest value reported by CVMP.

[b]RMTR: ratio marker to total residues EMA-CVMP (2013).

Table 7 reports the input values used for the calculation of the consumer exposure to monensin residue in bovine tissues and milk.

[51]COMMISSION REGULATION (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin OJ L 15, 20.1.2010, p. 1. amended by Commission Implementing Regulation (EU) No 59/2013, OJ L 21, 24.1.2013, p. 21.

TABLE 7 Input values used to calculate consumer exposure to monensin residues (mg/kg) in bovine tissues and milk after its use as veterinary medicine.

	Input values (mg/kg tissue)
Mammals fat tissue	0.106
Mammals liver	0.526
Mammals meat[a]	0.035
Mammals offals and slaughtering products (other than liver)	0.029
Milk	0.018

[a]The residue concentration in muscle (0.017 mg/kg) and skin/fat (0.106 mg/kg) has been used to calculate the intake of meat at the following proportions: 80% muscle and 20% skin/fat (EFSA FEEDAP Panel, 2017b).

The combined chronic exposure of consumers to monensin residues originating from the consumption of chicken and bovine tissues and milk is reported in Table 8. The results showed that the highest chronic exposure was for the population class 'other children' with 0.003 mg/kg bw per day. This exposure would represent 100% of the ADI (see Appendix A, Table A.4). However, considering that the residues of toxicological concern represent only 50% of the total residues in tissues and organs of the target animals, the exposure to residues of toxicological concern would be approximately 50% of the ADI.

TABLE 8 Chronic exposure of consumers to monensin total residues based on residue data in chicken + bovine tissues/products.

Population class	Highest exposure estimate[a] (mg/kg bw per day)	% ADI
Infants	0.0029	97
Toddlers	0.0028	93
Other children	0.0030	100
Adolescents	0.0015	50
Adults	0.0010	33
Elderly	0.0007	23
Very elderly	0.0008	27

Abbreviations: ADI, acceptable daily intake; bw, body weight.

[a]HRP 95th percentile.

The FEEDAP Panel notes that the highest contribution to exposure in all age classes comes from milk consumption (see Appendix A, Table A.4).

Acute exposure calculation from both animal sources (chickens and bovines) did not lead to data essentially different to those calculated with chicken tissues and organs. Liver is again identified as the food characterising the highest risk, exceeding the ARfD as described above for 'other children', 'adolescents' and 'adults' (see Appendix A, Table A.5).

Maximum residue levels (MRLs) for monensin are in force for poultry tissues.[52] The chronic exposure calculation following the Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017a) was also performed calculating the total residue data derived from MRLs in poultry tissues (see Table 9 for TR calculated from MRLs, Table 10 for input data, Table 11 for the results).

TABLE 9 Monensin total residues calculated from MRL values[a] of poultry tissues applying the ratios marker to total residue (RMTR) for each tissue/product (mg/kg).

	Liver	Kidney	Muscle	Skin/fat
MRLs (mg/kg wet tissue)	0.008	0.008	0.008	0.025
RMTR[b]	0.015	0.035	0.058	0.146
TR_{MRL}	**0.533**	**0.229**	**0.138**	**0.171**

Abbreviation: MRL, maximum residue level.

[a]Reg. (EC) No 180/2007.

[b]RMTR: ratio marker to total residues; EFSA (2006).

[52]Reg. (EC) No 180/2007.

TABLE 10 Input values used to calculate consumer exposure to monensin residues (mg/kg) calculated from MRLs in poultry tissues.

	Input values (mg/kg tissue)
Birds fat tissue	0.171
Birds liver	0.533
Birds meat[a]	0.137
Birds offals and slaughtering products (other than liver)	0.229

Abbreviation: MRL, maximum residue level.

[a]The residue concentration in muscle (0.138 mg/kg) and skin/fat (0.171 mg/kg) has been used to calculate the intake of meat at the following proportions: 90% muscle and 10% skin/fat (EFSA FEEDAP Panel, 2017a).

TABLE 11 Chronic exposure of consumers to monensin total residues derived from MRLs in poultry tissues.

Population class	Highest exposure estimate[a] (mg/kg bw per day)	% of ADI
Infants	0.0009	30
Toddlers	0.0011	36
Other children	0.0009	30
Adolescents	0.0006	20
Adults	0.0004	14
Elderly	0.0003	10
Very elderly	0.0003	10

Abbreviations: ADI, acceptable daily intake; bw, body weight; MRL, maximum residue level.

[a]HRP 95th percentile.

The highest chronic exposure would be for the age class 'toddlers' with 0.0011 mg/kg bw per day representing 36% of the ADI (for details, see Appendix A, Table A.6).

Acute exposure calculation (for details, see Appendix A, Table A.7) indicate that all the consumptions are below the ARfD.

3.2.3.5 | *Conclusions on safety for the consumer*

The chronic exposure to monensin residues at 0 days withdrawal time resulting from the use of monensin sodium as a feed additive in chickens would amount up to 46% of the ADI (toddlers). The combined chronic exposure to monensin residues resulting from use of monensin as a feed additive in chickens and as a veterinary medicine in bovine would reach up to 100% of the ADI. However, considering that the residues of toxicological concern represent only 50% of the total residues in tissues and organs of the target animals, the exposure to residues of toxicological concern would be approximately 23% and 50% of the ADI for the chronic exposure and the combined chronic exposure, respectively.

Acute exposure estimate did not identify an intake above the ARfD for the toxicologically relevant residues for all age groups and countries and identified liver as the food providing the highest exposure. The only exception was the estimate of the acute exposure by poultry liver consumption by 'other children' in Romania (173% of the ARfD).

Overall, the FEEDAP Panel concludes that monensin sodium from Coxidin® at 125 mg/kg complete feed for chickens for fattening with 0-day withdrawal time is safe for the consumer. This conclusion is extended to the use of monensin sodium from Coxidin® to chickens reared for laying and turkeys for fattening and reared for breeding (up to 16 weeks) under the proposed conditions of use. The existing MRLs for poultry tissues ensure consumer safety. Concerns would arise for acute exposure for the age class 'other children' in those countries where dietary surveys reflect a high consumption of liver (Romania).

3.2.4 | Safety for the user

The FEEDAP Panel concluded in its previous opinions (EFSA, 2005; EFSA FEEDAP Panel, 2011a, 2011b), based on studies with either pure monensin sodium or with Coxidin® (wheat bran as a carrier), that both formulations of the additive pose a risk by inhalation, are not skin irritants or skin sensitisers but should be considered as eye irritants.

Besides new data on physical characteristics of the formulation containing calcium carbonate as a carrier (see Section 3.1.4), no new studies were submitted on the safety for the user. The outcome of the literature search did not identify papers relevant for the assessment of user safety in the present evaluation.

The FEEDAP Panel reiterates that both formulations of Coxidin® pose a risk by inhalation. The formulation with wheat bran as a carrier is not irritant to the skin, is not a skin sensitiser but it is irritant to the eyes. In the absence of data, no conclusions can be drawn on the potential of the formulation containing calcium carbonate to be irritant to skin and eyes and to be skin sensitiser.

3.2.5 | Safety for the environment

The FEEDAP Panel evaluated the safety for the environment of monensin sodium from Monimax® in three opinions (EFSA FEEDAP Panel, 2017d, 2018, 2019c). In these opinions it was concluded that 'The use of monensin sodium from Monimax® in complete feed for chickens for fattening, chickens reared for laying and turkeys for fattening poses no risk for the aquatic and terrestrial compartments or for sediment. The bioaccumulation potential of monensin sodium in the environment is low'.

The applicant submitted an updated environmental risk assessment in line with the requirements of the FEEDAP guidance to evaluate the safety of the additives for the environment (EFSA FEEDAP Panel, 2019a).[53] For the present evaluation, the Panel assumes that the safety of the worst-case scenario 'chickens for fattening' covers the safety of the additive for the other species object of this application.

3.2.5.1 | *Phase I*

Physico-chemical properties

The physical chemical properties of monensin sodium, reported in Table 12, were already reported in the FEEDAP opinion on the safety and efficacy of Monimax®) for turkeys for fattening (EFSA FEEDAP Panel, 2017a, 2017b, 2017c, 2017d) and were considered relevant for the current evaluation.

TABLE 12 Physico-chemical properties of monensin sodium.

Property	Value	Unit
Octanol/water partition coefficient (log K_{ow})[a]	4.48 (pH 5.2–5.7, 25°C) 3.82 (pH 7, 25°C) 3.82 (pH 10, 25°C)	–
Water solubility (20°C)[a]	8.78	mg/L
Vapour pressure[a]	3×10^{-28}	Pa

[a]EFSA FEEDAP Panel (2017d).

Fate and behaviour

The applicant provided the same studies already assessed in previous opinions (EFSA FEEDAP Panel, 2017d). In the present assessment, those studies were revised according to FEEDAP guidance to evaluate the safety of the additives for the environment (EFSA FEEDAP Panel, 2019a).

Fate in soil

Adsorption

The adsorption of monensin sodium was determined in two studies. In a Good Laboratory Practice (GLP)-compliant study (Study 1), following OECD guideline 106, three soils with differing properties were used to determine the adsorption/desorption behaviour of monensin sodium.[54] In another study (Study 2), derived from literature (Sassman & Lee, 2007), eight soils and a batch equilibrium methodology were used to determine the adsorption Freundlich isotherms for monensin sodium (two of the soils had the pH adjusted). In this last study, five soils were considered reliable, when the mass balance was considered. Furthermore, since the sorption endpoints in the study Sassman and Lee (2007) were calculated based on a reference concentration of 1 µmol/L or kg, they were recalculated to a reference concentration of 1 mg/L or kg, in line with the FOCUS model requirements.

The acceptable data for adsorption are reported in Table 13.

[53]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_III_15: Environmental Risk Assessment for Coxidin®.
[54]FAD-2016-0009: Technical dossier/Section III/Annex_III_22_Adsorption-desorption.

TABLE 13 Adsorption of monensin sodium in different soils.

Study	Soil	Soil pH (recalculated for H_2O)	Freundlich exponent (1/*n*)	Adsorption K_{foc} (mg/L)
Study 1	S363	6.7	0.9213	162
	S364	7.7	0.9191	74
	S369	5.4	0.9395	274
Study 2	Drummer-1	8.0	0.88	770
	Raub-12	6.8	0.97	444
	Toronto-4	4.9	0.92	3086
	Oakville-24	5.3	0.71	903
	Coloma-32	7.3	1.01	147

Since the adsorption of monensin sodium is clearly pH-dependent, the FEEDAP Panel considers that the K_{oc} of the dissociated form of monensin sodium, derived by fitting of the pH versus K_{oc} data, should be used for exposure assessment. Therefore, based on the combined data set of Study 1 and Study 2 with pH-values recalculated from 0.01 M $CaCl_2$ to water and a (fixed) pKa value of 4.5, the K_{oc} value for the dissociated form of monensin sodium is 155 mL/g. This value is used for exposure calculation.

Degradation

A study according OECD guideline 307, was performed using ^{14}C radiolabelled monensin sodium.[55] The biodegradation rate of monensin sodium was determined in three soils with differing properties at 20°C. The rate of degradation of monensin sodium at 23°C was also determined in another study (Sassman & Lee, 2007), derived from literature, in two soils using an equivalent destructive sampling incubation approach. Nevertheless, in this last study, no mass balance is reported nor single values, which may allow a recalculation of DT_{50} according to FOCUS kinetics guidance. Therefore, this study will be considered supportive only and not suitable to derive an endpoint. Since just three soils are considered appropriate for the assessment of degradation, the highest DT_{50} value of 4 days at 20°C, calculated according Single First Order (SFO) kinetics, will be considered the reference endpoint (Table 14).[56] Monensin sodium can be considered not persistent in soils (Hollis, 1991).

TABLE 14 Half-life (DT_{50}) of monensin sodium in different soils.

Soil	Temperature (°C)	DT_{50} at 20°C (SFO) (days)
S473	20	2.3
S474	20	4
S475	20	2.5

Note: The DT_{50} value, normalised to 12°C, is 8.5 days; this value will be used for further assessment.

Fate in water

No information on the biodegradation of monensin sodium in surface water or sediment was provided by the applicant.

Conclusion on fate and behaviour

A K_{oc} of 155 L/kg and a DT_{50} of 8.5 days at 12°C will be used for the assessment.

Predicted environmental concentrations (PECs)

The calculated PEC initial values for monensin sodium, in Phase I, are the following: PEC_{soil} (µg/kg) = 1889 and $PEC_{groundwater}$ (µg/L) = 146. The Phase I PEC trigger values are exceeded; therefore, a Phase II assessment is considered necessary.

[55]FAD-2016-0009: Technical dossier/Section III/Annex_III_23_Soil degradation.

[56]The temperature correction was performed according to the scientific opinion of the Panel on Plant Protection Products and their Residues on a request from EFSA related to the default Q10 value used to describe the temperature effect on transformation rates of pesticides in soil (EFSA, 2007).

3.2.5.2 | *Phase II*

Exposure assessment

PECs calculation refined in Phase II

PEC_{soil} refined for metabolism

During the calculation of $PEC_{soil\ dw}$ at Phase I, a total residue approach was used considering 100% of the additive excreted unchanged by the treated animal. A revised $PEC_{soil\ A}$ can be calculated by subtracting metabolites that represent less than 10% of the administered dose from the total dose. A study was submitted.[57] This study investigated the ADME of [^{14}C]-monensin sodium administered to chickens for fattening at a dose of 125 mg/kg complete feed for 8 days. Unchanged monensin amounted to 29.65% of the total radioactivity excreted, that confirms the results of earlier studies (Davison, 1984; Donoho et al., 1978, 1982). Moreover, 18 metabolites were separated and partly identified; each one represented less than 10% the amount excreted for a total of 58.7%. The eight major metabolites were identified as demethylated monensin, monohydroxy monensin(s), dihydroxy monensin(s) and combined demethylated/hydoxylated monensin(s). The FEEDAP Panel established formerly the conservative estimate that major monensin metabolites retain no more than 50% of the pharmacological and microbiological activity of the parent compound (EFSA, 2008a). Consequently, the active fraction (F_a) excreted is considered as the sum of monensin (29.65%) plus half the fraction corresponding to the metabolites (29.35%), i.e. 59% the amount excreted.

PEC_{soil} refined for degradation in manure

A further refinement was presented by the applicant, considering degradation in manure. A manure degradation study was performed in poultry litter using radiolabelled monensin sodium.[58]

The rate and route of degradation was determined in poultry litter at 234 mg/kg, a concentration derived according the old EFSA guidance (EFSA, 2008c). Following pre-incubation of 19 days, 50 g fresh weight replicates of poultry litter were incubated in the dark at 20 ± 2°C under aerobic conditions at a dry matter content of 60% and duplicate treated replicates were destructively sampled at 0, 1, 3, 7, 21, 41, 91 and 119 days after treatment (DAT). At appropriate time-points poultry litter samples were initially extracted with two 180 mL ammonia: methanol (0.035:99.965 v/v) extractions and subsequently with 180 mL methanol: water (3:1 v/v). All extracts were then analysed by liquid scintillation counting (LSC) and subject to radio-high-performance liquid chromatography (HPLC) analysis.

In poultry litter, monensin sodium concentrations where relatively stable to 41 DAT following which degradation was observed. Non-extractable residues were observed at the later time points peaking at 6.4% TAR (total applied radioactivity) at 119 DAT. Captured volatiles (carbon dioxide) remained below 1% TAR up to 21 DAT and then steadily increased to peak at 22.27% TAR after 119 DAT. The mass balance was higher than 90% TAR for all time points. When the sample extracts were analysed by radio-HPLC, most of the radioactivity was monensin sodium (monensin A and B) and one area of radioactivity in the latter two time points did not correspond with monensin and was labelled UNK-LD-1, which peaked at 10.09% TAR at 91 DAT. All other areas of radioactivity were less than 10% TAR throughout the incubation period. The applicant proposed a DT_{50} of 120 days derived from hockey stick (HS) kinetics, being the best fit of data. Nevertheless, the FEEDAP Panel considered more appropriate the worst-case SFO kinetic DT_{50} of 138.5 days. This value, normalised to 25°C as requested by the VICH guideline, is 86 days, which will be used for further assessment.

A storage time of 91 days was assumed to calculate the soil refinement. This value was considered closer to the real application of manure in field (even if still a worst-case situation) with respect to the 41 days used by the applicant for further assessment.

The PECs of monensin sodium in soil, groundwater, surface water and sediment refined for metabolism in livestock and degradation in manure are reported in Table 15.

TABLE 15 Predicted environmental concentrations (PECs) of monensin sodium in soil, groundwater, surface water and sediment refined for metabolism in livestock and degradation in manure.

Input	Value
Dose (mg/kg feed)	125
Molecular weight	670.87
Vapour pressure (Pa) (at 25°C)	3×10^{-28}

[57]FAD-2016-0009: Technical dossier/Section III/Annex III.5.

[58]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_III_4_1_Monensin manure degradation report.

TABLE 15 (Continued)

Input	Value
Solubility (mg/L)	8.78
K_{oc} (L/kg)	155
DT_{50} in soil at 12°C (days)	8.5
DT_{50} in manure at 25°C (days)	86
Storage time (days)	91
Fraction excreted **%** (Fa)	59
Output	
Application rate kg/ha	0.579
PEC_{soil} (µg/kg)	772
$PEC_{groundwater}$ (µg/L)	60
$PEC_{surfacewater}$ (µg/L)	19.9
$PEC_{sediment}$ (µg/kg dry weight)	380

$PEC_{groundwater}$ refinement

Considering the DT_{50} of 4 days at 20°C and the K_{oc} of 155 L/kg and applying the metamodel described in the EFSA guidance (2019a), no concern is expected for groundwater when monensin sodium is used at the proposed conditions.

$PEC_{surfacewater}$ and $PEC_{sediment}$ refined with FOCUS

Concentrations in surface waters for monensin sodium were assessed using the FOCUS Step 3 surface water models.[59] The four FOCUS scenarios that are relevant for avian use were used. Application was assumed in arable fields with winter cereals on the day of drilling. The time of drilling was estimated to be 14 days before the day of emergence in each FOCUS scenario. The test substance was applied as granular and assumed to be uniformly mixed into the top 5 cm soil layer. Uptake by plant roots was set to zero. Calculations were provided by the applicant considering application rates up to 0.671 kg/ha, which is considered a worst-case approach. The largest predicted concentration in surface water at any time is 9.563 µg/L. The largest predicted concentration in sediment at any time is 4.857 µg/kg dry weight sediment.

Conclusions

The following exposure values are used for risk assessment: PEC_{soil} of 772 µg/kg, $PEC_{surface\ water}$ of 9.563 µg/L and $PEC_{sediment}$ of 4.857 µg/kg dry weight.

Ecotoxicity studies

Toxicity to soil organisms

Effects on plants

For the current evaluation the applicant submitted three studies, two of which were previously evaluated by the FEEDAP Panel (EFSA FEEDAP Panel, 2017d, 2019c).

The first one (Study 1), already evaluated in the FEEDAP opinion adopted in 2017 (EFSA FEEDAP Panel, 2017d), was performed according to OECD guideline 208 to investigate the effect of monensin sodium on three species of terrestrial plants: monocotyledon species *Triticum aestivum*, and dicotyledon species *Sinapis alba* and *Trifolium pratense*.[60] Quartz sand was treated with monensin sodium at five concentrations. The lowest endpoint was *S. alba* fresh weight biomass EC_{50} of 4.0 mg monensin sodium/kg. The FEEDAP Panel noted that the data obtained on quartz sand may not be representative for studies with soil types containing organic matter.

In the second study (Study 2 – OECD guideline 208),[61] already evaluated in the FEEDAP opinion adopted in 2019 (EFSA FEEDAP Panel, 2019c), the effects of monensin sodium on terrestrial plants were evaluated in six plant species: monocotyledon species *Hordeum vulgare* and *Allium cepa*, and dicotyledon species *Phaseolus vulgaris, Raphanus sativus, Cucumis sativa* and *Solanum lycopersicum*. In this study, a natural sandy loam soil was treated with monensin sodium at seven concentrations. The study fulfils all validity criteria, and the results are reliable. The lowest endpoint was established based on *A. cepa* EC_{50} = 4.99 mg of monensin sodium/kg.

[59]FAD-2016-0009: Technical dossier/Supplementary information April 2023/Coxidin FOCUS surfacewater modelling output.

[60]FAD-2016-0009: Technical dossier/Section III/Annex_III_26_Plant growth.

[61]Evaluated in EFSA FEEDAP Panel (2019a).

The third study (Study 3) was conducted following OECD guideline 208 (OECD, 2006a). It was performed to investigate the chronic effects of monensin sodium on additional six species of terrestrial plants: two monocotyledon species *Zea mays* and *Triticum aestivum* and four dicotyledon species *Beta vulgaris, Glycine max, Brassica napus* and *Helianthus annus*.[62] Seeds of *B. vulgaris* and *G. max* were exposed to a nominal concentration range of 0.25, 0.5, 1.0, 2.0, 4.0 and 8.0 mg monensin sodium/kg dry soil while seeds of *B. napus*, *H. annus*, *T aestivum* and *Z. mays* were exposed to a nominal concentration range of 0.5, 1.0, 2.0, 4.0, 8.0 and 16.0 mg monensin sodium/kg dry soil. Seedlings were allowed to emerge and grow for at least 14 days following 50% emergence of the control plants under glasshouse conditions. The endpoints determined were the effects on emergence, survival, phytotoxicity, shoot length and dry weight biomass. The study was valid, control seedling emergence was ≥ 70% for all species (actual 80%–100% control and 70%–100% solvent control), the mean survival of emerged seedlings in the controls for the duration of the trial was ≥ 90% (actual 92%–100% control and 90.5%–100% solvent control) and seedlings did not exhibit visible phytotoxic effects apart from normal variation in growth and/or morphology associated with a particular species. Dry weight biomass was the most sensitive endpoint with the lowest EC_{10} value for *B. vulgaris* at 1.03 mg monensin sodium/kg.

Higher tier risk assessment

According to EMA, endpoints used to derive species sensitivity distribution (SSD) should be the same, most sensitive endpoint for all tested species. The results of the two acceptable studies described above (Study 2 and Study 3)[63,64] indicate that EC_{10} based on dry weight biomass was the most sensitive endpoint for most of the 12 species tested, so that endpoint was selected to construct the SSD. The dataset fulfils also EMA requirements on species coverage: data for minimum eight species (actual 12 species) from at least six different families (actual eight families), including at least one Brassicaceae species (actual two Brassicaceae species), at least two monocotyledonous species (actual four monocotyledonous species) and at least six dicotyledonous species (actual eight dicotyledonous species). The SSD was constructed using the USEPA CADDIS SSD generator. The derived HC_5 was 1,18 µg monensin sodium/kg and the lower confidence level (LL HC_5) of HC_5 was 884 µg monensin sodium/kg.[65]

Effect on earthworms

A study following OECD guideline 207, already evaluated by the FEEDAP Panel in 2017 (EFSA FEEDAP Panel, 2017d) was performed to investigate the effect of monensin sodium on *Eisenia foetida*.[66] Earthworms were tested in artificial soil, at 62.5, 125, 250, 500 and 1000 mg monensin sodium/kg soil (dry weight) (equivalent to 60.7, 121.4, 242.7, 485.4 and 970.9 mg monensin/kg soil (dry weight)) and mortality assessed after 7 and 14 days. The 14-day LC_{50} was determined as 112.1 mg monensin sodium/kg soil (dry weight).

The applicant submitted a new earthworm reproduction study following OECD guideline 222 (OECD, 2016) performed with the earthworm *Eisenia foetida* in an artificial soil.[67] The study was performed with a nominal concentration range of 3.125, 6.25, 12.5, 25.0, 50.0 and 100.0 mg monensin sodium/kg and earthworms were exposed for 56 days. The study was valid, adult mortality in the controls over the initial 4 weeks of the test was ≤ 10% (actual 0% in the control and 0% in the solvent control), all control replicates produced > 30 juvenile worms (actual 161–231 in the control and 125–227 in the solvent control) and the coefficient of variation of reproduction was ≤ 30% (actual 11.9% in the control and 17.4% in the solvent control). The test item did not have a statistically significant effect on adult mortality or adult biomass. There was a statistically significant effect on reproduction at the highest concentration tested; therefore, the $NOEC_{reproduction}$ was established at 50 mg monensin sodium/kg.

The FEEDAP panel notes that the most sensitive terrestrial plant (EC_{10} 0.98 mg monensin sodium/kg) is over 10 times more sensitive than the earthworms (established earthworm $NOEC_{reproduction}$ 50 mg monensin sodium/kg); therefore, in line with the requirements of the FEEDAP guidance on the environment, no additional chronic ecotoxicity testing is necessary for a second terrestrial invertebrate (EFSA FEEDAP Panel, 2019a).

Effects on soil microorganisms

A study following OECD guideline 216 (2000b) was performed to investigate the effect of monensin sodium on soil microorganisms.[68] A sandy loam soil was treated with monensin sodium at a rate of 785.5 and 7855 µg/kg soil dry weight. These concentrations represent 1x and 10x maximum PEC_{soil}. Control and treated soils were incubated for 28 days and subsamples were taken on 0, 7, 14 and 28 days after treatment and analysed for the nitrate concentration. The study was valid, variation in nitrate concentration of control replicates was less than 15% (actual ≤ 3.75%) for all timepoints. Nitrate formation

[62]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_III_4_2_Monensin plant ecotox report.

[63]Evaluated in EFSA FEEDAP Panel (2019a).

[64]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_III_4_2_Monensin plant ecotox report.

[65]FAD-2016-0009: Technical dossier/Supplementary information March 2021.

[66]FAD-2016-0009: Technical dossier/Section III/Annex_III_25_earthworms.

[67]FAD-2016-0009: Technical dossier/Supplementary information September 2021/Annex_RTQ_III_4_3_Monensin chronic earthworm report.

[68]FAD-2016-0009: Technical dossier/Supplementary information April 2023/Annex_RTQ_III_2_1_b–Monensin nitrate transformation study.

rate deviations from the controls were less than 25% for the 785.5 and 7855 µg monensin sodium/kg soil dry weight treatments calculated using the incremental and overall methods at 28 days after treatment.

Toxicity to aquatic organisms

All the studies submitted on the toxicity of monensin sodium to aquatic organisms were already evaluated in 2017 (EFSA FEEDAP Panel, 2017d), except for a newly performed study on fish. Additional data submitted by the applicant was not considered relevant for the current assessment.

A study following OECD guideline 201 was performed to investigate the effect of monensin on green algae (*Raphidocelis subcapitata*, formerly known as *Selenastrum capricornutum* and *Pseudokirchneriella subcapitata*).[69] The FEEDAP Panel in 2017 concluded that the 72-h E_rC_{50} based on growth rate was established at 3.3 mg monensin sodium/L and the 72-h E_rC_{10} at 0.91 mg monensin sodium/L.

A study following OECD guideline 202 was performed to investigate the effect of monensin sodium on aquatic invertebrates.[70] The FEEDAP Panel in 2017 concluded that the 48-h EC_{50} for immobilisation was determined to be 7.29 mg monensin sodium/L.

A study following OECD guideline 203 was performed to investigate the effect of monensin sodium on fish.[71] The FEEDAP Panel in 2017 concluded that the 96-h LC_{50} was determined to be 1.88 mg monensin sodium/L.

To investigate the chronic effects of monensin sodium on fish, a study following OECD guideline 210 (OECD, 2013) was performed.[72] Embryos of the Zebrafish (*Danio rerio*) were exposed in a dose–response nominal concentration range of 0.125, 0.25, 0.5, 1.0 and 2.0 mg monensin sodium/L for 35 days. A flow-through test design was used, and four replicates each containing 20 fertilised eggs/fish were used per test concentration and control. The study met the validity criteria. The mean measured concentration values provided the most sensitive endpoint and have been considered for this assessment. The most sensitive endpoint was the wet weight of surviving fish and the EC_{10} was established at 0.441 mg monensin sodium/L.

Effect on sediment dwelling organisms

The FEEDAP Panel noted that the effect of monensin sodium on the sediment-dwelling larvae of *Chironomus riparius* was already evaluated in 2017 (EFSA FEEDAP Panel, 2017d). In the study, following OECD guideline 218, emergence was the most sensitive endpoint and the NOEC was determined as 5.0 mg monensin sodium/kg sediment (dry weight).

The FEEDAP Panel noted that the above value will be used for the risk characterisation assessment and that the $PNEC_{sediment}$ of 35.99 µg monensim sodium/kg dry weight sediment, calculated by the applicant using the equilibrium partitioning approach (EFSA FEEDAP Panel, 2019a),[73] can be considered as supporting evidence for the present assessment.

Conclusions on the ecotoxic effect of monensin sodium on soil, water and sediment

For the terrestrial compartment, data are available for plants, earthworm and microorganisms. The risk for terrestrial compartment was evaluated based on the toxicity on plants with the application of the SSD approach, resulting in an HC_5 of 1148 µg/kg and the lower confidence level (LL HC_5) of HC_5 was 859 µg/kg. For the aquatic compartment, data are available for algae, aquatic invertebrates and fish. The most sensitive endpoint was the wet weight of surviving fish and the EC_{10} was established at 0.441 mg monensin sodium/L. Ecotoxicological data for sediment-dwelling invertebrate *Chironomus riparius* were provided for the sediment compartment resulting in an EC_{10} of 5.0 mg monensin sodium/kg.

3.2.5.3 | *Risk characterisation*

The risk characterisation ratios for terrestrial, freshwater and sediment compartments are reported in Tables 16, 17 and 18, respectively.

TABLE 16 Risk characterisation of monensin sodium (PEC/PNEC ratio) for terrestrial compartment.

Taxa	PEC_{soil} (µg/kg)	$NOEC_{rep}$/LL HC_5 (mg/kg)	AF	PNEC (µg/kg)	PEC/PNEC
Earthworm	772	50[a]	10	5000	0.15
Plants		0.88[b]	1	884	0.87

[a]$NOEC_{rep}$: no observed effect concentration for reproduction.
[b]LL HC_5: lower confidence level hazardous concentration for 5% of the species.

[69]Evaluated in EFSA FEEDAP Panel (2019c).
[70]FAD-2016-0009: Technical dossier/Section III/Annex_III_28_Daphnia.
[71]FAD-2016-0009: Technical dossier/Section III/Annex_III_29_Rainbow trout.
[72]FAD-2016-0009: Technical dossier/Supplementary information April 2023/Annex_RTQ_III_2_1_a-Monensin_Fish ELS_Final report.
[73]FAD-2016-0009: Technical dossier/Supplementary information March 2021.

TABLE 17 Risk characterisation (PEC/PNEC ratio) for freshwater compartment.

Taxa	$PEC_{surfacewater\ FOCUS}$ (μg/L)	$E_{(r)}(L)C_{50}/E_rC_{10}$/NOEC (mg/L)	AF	PNEC (μg/L)	PEC/PNEC
Algae	9.563	3.3[a]	50	8.82	1.08
Raphidocelis subcapitata		0.91[b]			
Aquatic invertebrates		7.29[c]			
Daphnia magna					
Fish		1.88[d]			
O. mykiss		0.441[e]			
Danio rerio					

[a]72-h E_rC_{50}.
[b]72-h E_rC_{10}.
[c]48-h EC_{50}.
[d]96-h LC_{50}.
[e]35-day NOEC.

The applicant proposed a refinement of PEC based on TWA concentration at 28 days. The FEEDAP Panel consider that this approach is not suitable for risk assessment.

Considering the PEC_{SW} calculated for laying hen, turkey for fattening and turkey reared for breeding, the highest PEC_{SW} value calculated is 6.245 μg/L for turkeys. When this value is compared with the PNEC of 8.82 μg/L, no concern is highlighted for the aquatic compartment. Therefore, a risk for aquatic compartment cannot be excluded just for chicken for fattening.

TABLE 18 Risk characterisation (PEC/PNEC ratio) for sediment.

Taxa	$PEC_{sediment}$ (μg/kg dry weight)	NOEC (mg/kg)	AF	$PNEC_{sed}$[a] (μg/kg)	PEC/PNEC
Sediment-dwelling invertebrates	4.857	5.0	100	50	0.097
Chironomus riparius					

[a]$PNEC_{sed}$ derived from NOEC.

3.2.5.4 | *Bioaccumulation and risk assessment for secondary poisoning*

To assess risk for secondary poisoning for worm/fish eating birds and mammals through the food chains the method proposed in the relevant Guidance from the EMA has been considered (EMA, 2016). Based on the log K_{ow} of 3.83–4.48, monensin sodium has the potential for bioaccumulation and the risk of secondary poisoning has to be assessed for this substance.

Since there were no bioaccumulation data available for fish and for terrestrial organisms, the FEEDAP Panel made an assessment on secondary poisoning of monensin sodium for aquatic and terrestrial food chains. Log K_{ow} of 4.48 was used in the assessment. The lowest NOAEL for rats was 0.4 mg monensin sodium/kg bw per day. This NOAEL was derived from a 13-week rat oral toxicity study. The NOEC value of 8.0 mg monensin sodium/kg feed was calculated using a conversion factor of 20 for rats. Using an assessment factor of 30, the corresponding $PNEC_{oral}$ was equivalent to 0.267 mg monensin sodium/kg feed. This value is higher than the estimated concentration in earthworms of 0.111 mg monensin sodium/kg based on $PEC_{gw} < 0.1$ μg monensin sodium/L and PEC_{soil} of 772 μg monensin sodium/kg. $PNEC_{oral}$ for monensin is also lower than the estimated concentration in fish based on the $PEC_{surface\ water}$, calculated as 100-day maximum time weighted average exposure concentration (TWAEC) of 0.114 μg monensin sodium/L. The FEEDAP Panel agrees that the maximum TWAEC over the longest period of 100 days most adequately represents the annual average concentration in surface water and was therefore used in the assessment. The risk of secondary poisoning to worm and fish-eating birds and mammals is unlikely. The PEC/PNEC ratios for the aquatic and terrestrial food chains are given in Table 19.

TABLE 19 The assessment of secondary poisoning for monensin sodium through the aquatic and terrestrial food chains based on the 100% of the proposed recommended dose.

	PEC_{fish}[a] (mg/kg)	PEC_{worm}[b] (mg/kg)	$PNEC_{oral}$ (mg/kg)	$PEC_{fish}/PNEC_{oral}$	$PEC_{worm}/PNEC_{oral}$
Monensin	0.146	0.111	0.267	0.55	0.42

[a]$PEC_{fish\ (oral,\ predator)}$.
[b]$PEC_{earthworm\ (oral,\ predator)}$.

3.2.5.5 | *Conclusions on the safety for the environment*

The use of monensin sodium from Coxidin® in complete feed for chickens for fattening and chickens reared for laying and turkeys for fattening and turkeys reared for breeding poses no risk for the terrestrial compartments and for sediment. No risk for groundwater is expected. For chickens for fattening the risk for aquatic compartment cannot be excluded, but no risks are expected for the other animal categories. There is no risk of secondary poisoning through the aquatic and terrestrial food chains from the use of monensin sodium.

3.3 | Efficacy

For the purpose of the renewal of the authorisation in chickens for fattening (both formulations), and the new uses in chickens reared for laying (formulation with calcium carbonate) and turkeys for fattening (both formulations), a total of six anticoccidial sensitivity tests (ASTs) were submitted; three performed in chickens for fattening[74] and other three in turkeys for fattening; the applicant also submitted the results of the post-market monitoring plan.[75]

3.3.1 | Results of the post-marketing monitoring plan

The results of a post-marketing monitoring plan (PMMP), as required in the last authorisation,[76] were submitted by the applicant. This PMMP consisted of the collection of information from farms[77] used to monitor different coccidiosis control programmes and three AST-like[78] studies.

For the monitoring of farms, data were selected from farms where either Coxidin® or another ionophore coccidiostat (not specified) were used in the period 2018–2020. The chickens for fattening reared in those farms were subject to the check of intestinal lesions as an indicator for the resistance of the *Eimeria* spp.; the scoring was done using a 5-level scoring system (0 = no lesion, 1 = very mild, 2 = mild, 3 = moderate and 4 = severe) based on Johnson and Reid (1970). The average of the individual score for *E. acervulina*, *E. maxima* and *E. tenella* were calculated for each flock as well as the average of the total mean lesion score (TMLS).

The percentage of flocks having a score higher than 1.5 for either measurement was used to compare Coxidin® to other ionophore programmes (Table 20). For *E. acervulina*, flocks receiving Coxidin® exhibited a slightly higher percent exceeding an average score of 1.5 in 2018 and 2020 compared to the other ionophores, while it was lower in 2019. For the other *Eimeria* spp., the number of farms scoring higher than 1.5 were less than 2%, with no detected average scores above 1.5 for in the years 2019 and 2020 in Coxidin®. The TMLS values were similar between Coxidin® and the other ionophores in 2018 and were below for Coxidin® in 2019 and 2020.

TABLE 20 Percentage of flocks exceeding an average intestinal lesion scores of 1.5 for individual species and total mean lesion score (TMLS) values.

Coccidiosis control treatment	Year	Number of monitored flocks	Percentage of flocks averaging ≥ 1.5 in intestinal lesion scores for individual *Eimeria* spp.[a] (%)			Percentage of flocks averaging ≥ 1.5 in TMLS[b] (%)
			E. acervulina	*E. maxima*	*E. tenella*	
Coxidin®	2018	108	20.0	1.7	2.5	27.5
	2019	72	5.9	0.0	0.0	14.1
	2020	63	15.2	0.0	0.0	16.7
Other ionophore[c]	2018	274	16.3	0.7	0.7	25.7
	2019	235	12.5	1.2	0.4	26.1
	2020	291	12.1	0.9	0.9	22.7

[a]5-level scoring system based on Johnson and Reid (1970) for lesions related to *E. acervulina*, *E. maxima* and *E. tenella*.

[b]Total mean intestinal lesions corresponding to the summatory of individual lesions of *E. acervulina*, *E. maxima* and *E. tenella*.

[c]Not specified.

Additionally, the results of three AST-like studies (2013–2019) performed in experimental facilities (in cages) were provided. The design of the studies is included in Table 21. In each study, birds were randomly allocated to three experimental groups, an uninfected untreated control (UUC) group, an infected untreated control (IUC) group and an infected treated (IT) group. Birds were orally inoculated *Eimeria* spp. inoculum on Days 15 for all three studies. The experimental period was from Day 0 to Day 22 and bird performance was measured from 1 or 2 days prior to inoculation to study end. Intestinal lesions scores and oocyst excretion (only Studies 2 and 3) were assessed on Day 22.

[74]FAD-2020-0036: Technical dossier/Section IV/Annex IV.1–3.

[75]FAD-2020-0036: Technical dossier/Section IV/Annex IV.4–6.

[76]Commission Implementing Regulation (EU) No 140/2012 of 17 February 2012 concerning the authorisation of monensin sodium as a feed additive for chickens reared for laying (holder of authorisation Huvepharma NV Belgium). OJ L 47, 18.2.2012, p. 18–19.

[77]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_V_4_1 and Annex_RQT_V_4_5.

[78]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annexes_RTQ_V_4_1, RTQ_V_4_2, RTQ_V_4_3 and RTQ_V_4_4.

TABLE 21 Experimental design of AST-like studies with chickens for fattening fed Coxidin®.

AST-like	Replicates per treatment (birds per replicate)	Inoculum characteristics				Anticoccidial treatment (days of life)	Monensin Na[3] (mg/kg feed)
		Date and country of isolation	Intended dose (number of oocysts) per bird		Day of inoculation		
1[79a]	2 (9)	07/2021 Austria	230,000	*E. acervulina*	15	13–22	100
2[80b]	6 (5)	04/2017 Italy	65,000	*E. acervulina*	15	14–22	100
			22,000	*E. maxima*			
			4000	*E. tenella*			
3[81c]	3 (6)	07/2013 France	194,700	*E. acervulina*	15	13–22	133
			12,900	*E. maxima*			
			23,000	*E. tenella*			

[a]Ross PM3 day-old birds.
[b]Ross 308 day-old birds.
[c]Analysed concentration of monensin sodium in the feed except Study 2 that was not analytically confirmed.

The results of these studies are shown in Table 22. While coccidiosis-related mortality was low and unaffected by the treatment in AST-like 1 and 2, inoculation caused a very high mortality in the IUC group in AST-like 3, which was reduced to 0 with the treatment with Coxidin®. A reduction in lesion scores were only observed in AST-like 1 for *E. acervuline*, and in AST-like 2 and 3 for *E. maxima*. No effects on total OPG were observed, with the exception of AST-like 3 where a higher oocyst excretion was observed in the IT group relative to the IUC.

TABLE 22 Intestinal lesion scores, mortality and zootechnical performance of small-scale AST-like studies with chickens for fattening.

AST-like	Group	Mean lesion scores[1]			Coccidiosis-related mortality (%)	Total OPG[2] (oocysts)
		E. acervulina	*E. tenella*	*E. maxima*		
1	UUC	0.0[c]	ns	ns	0.0	n.a.
	IUC	3.1[a]	ns	ns	0.0	n.a.
	IT	2.7[b]	ns	ns	0.0	n.a.
2	UUC	0.34*	0.10*	0.48*	3.3	257*
	IUC	1.45	0.86	1.21	3.3	203,890
	IT	1.45	0.83	0.72*	3.3	297,877
3	UUC	0.0[b]	0.0[b]	0.0[b]	0.0[b]	0[c]
	IUC	2.3[a]	1.5[a]	3.9[a]	76.5[a]	97×10^{6} [b]
	IT	1.3[a]	1.7[a]	2.6[b]	0.0[b]	210×10^{6} [a]

Abbreviation: n.a., not analysed.
[1]5-level scoring system based on Johnson and Reid (1970) for lesions related to *E. acervulina, E. maxima* and *E. tenella*.
[2]Total OPG expressed per gram in AST-like 2 and per bird in AST-like 3.
*Within each study, means with asterisk differed statistically from the IUC group ($p < 0.05$).
[a,b,c]Means with different superscript differed statistically ($p < 0.05$).

The results of the farm monitoring programme and the AST-like studies suggest that a potential resistance of the *Eimeria* strains, particularly *E. acervulina*, to monensin sodium in chickens for fattening, might be developing.

3.3.2 | Anticoccidial sensitivity tests in chickens for fattening

The three ASTs performed in chickens for fattening shared a similar experimental design using different inocula (Table 23). In each study, 1-day-old male birds (ROSS 308) were randomly allocated to three experimental groups, an UUC group, an IUC group and an IT group. The IT group received feed containing 100 mg monensin Na/kg feed from 2 days prior to inoculation until the end of the study. The intended dietary concentrations of the active substance were analytically confirmed.

[79]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_1.
[80]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_2.
[81]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_3.

All birds in the infected groups were orally inoculated via gavage with recent field isolates of *Eimeria* spp.[82] Animal health and mortality were monitored. Feed intake and body weight of the animals were measured, daily weight gain and feed to gain ratio were calculated. Samples of excreta were analysed for oocyst excretion. All birds were killed and necropsied to assess the intestinal lesions during the last 3 days of the study, corresponding to Days 5, 6 and 7 post-inoculation (PI). Lesions were scored following the method of Johnson and Reid (1970) (0 = no lesion, 1 = very mild, 2 = mild, 3 = moderate and 4 = severe).

General linear models were used for all parameters except the mortality that was analysed using the Cox's proportional hazards model. Intestinal lesion scores (ILSs) were analysed using mixed models with treatment group and study day as fixed effects. In all models, treatment groups were compared to the IUC group as reference. Significance was set at $p < 0.05$.

TABLE 23 Experimental design of ASTs with chickens for fattening fed Coxidin®.

AST	Replicates per treatment (birds per replicate)	Inoculum characteristics			Day of inoculation	Anticoccidial treatment (days of life)	Monensin Na[a] (mg/kg feed)
		Date and country of isolation	Intended dose (number of oocysts) per bird				
1[83]	10 (5)	1/2019 The Netherlands	8600	*E. acervulina*	16	14–23	102
			14,800	*E. maxima*			
			17,400	*E. tenella*			
			1400	*E. mitis*			
2[84]	10 (5)	7/2019 Italy	9300	*E. tenella*	14	12–21	88
			6400	*E. brunetti*			
3[85]	8 (5)	12/2019 Portugal	142,000	*E. acervulina*	14	12–21	96
			32,000	*E. tenella*			
			5000	*E. mitis*			

[a]Analysed concentration of monensin sodium in the feed.

The results of the three ASTs are summarised in Table 24. No coccidiosis related mortality was observed in any of the ASTs, and only few mild clinical symptoms potentially related to coccidiosis were observed. In AST-1, the mean lesion scores of *E. acervulina* and *E. maxima* were statistically lower in the IT group compared to the IUC group. In AST-3 lesions of *E. acervulina* were statistically lower in the IT group compared to the IUC group in the complete observational period (Days 5–7 PI). In AST-2, no differences in lesions were identified between the IT and the IUC group. Reductions in the oocyst excretion were only evident in the AST-2 in which the IT birds resulted in significantly lower OPG counts than those found on IUC birds on Day 6 PI. Performance parameters (daily feed intake, weight gain and feed to gain ratio) were not affected by the treatment with Coxidin® in any of the studies.

TABLE 24 Summary of anticoccidial sensitivity tests performed with Coxidin® in chickens for fattening.

AST	Group	Mean lesion scores[1]				Total oocyst excretion (OPG)[2]		
		E. acervulina	*E. tenella*	*E. maxima*	*E. brunetti*			
		Days 5–7 PI				D5 PI	D6 PI	D7 PI
1	UUC	0.27*	0.24	0.59*	ns	544	454*	24*
	IUC	0.52	0.70	1.54	ns	3904	13,359	189,093
	IT	0.10*	0.26	1.06*	ns	780	4641	70,732
2	UUC	0	0.18*	0.26	0.08	0	0*	0
	IUC	0.2	0.78	0.38	0.54	93	658	0
	IT	0	0.65	0.22	0.20	1	4*	0
3	UUC	0.03*	0.13	0.20*	ns	1*	13*	5*
	IUC	2.03	0.56	0.64	ns	27,736	739,592	327,319
	IT	1.60*	0.30	0.53	ns	7887	96,449	204,861

Abbreviations: ns, not scored; OPG, oocyst per gram faeces.

*Means significantly different from IUC ($p < 0.05$).

[1]Total mean lesion scores in IT are significantly lower than in IUC ($p < 0.05$) in all ASTs.

[2]Back log-transformed means.

[82]A dose-titration study was performed for each inoculum to establish the dose to apply in the AST.

[83]FAD-2020-0036: Technical dossier/Section VI/Supplementary information March 2021/Annex_IV_1.

[84]FAD-2020-0036: Technical dossier/Section VI/Supplementary information March 2021/Annex_IV_2.

[85]FAD-2020-0036: Technical dossier/Section VI/Supplementary information March 2021/Annex_IV_3.

3.3.3 | Anticoccidial sensitivity tests in turkeys for fattening

The applicant submitted three ASTs in turkeys for fattening. Two of them (AST-1 and AST-2) shared a similar experimental design using different inocula (see Table 22). One-day-old birds (BUT premium in AST-1 and AST-2, and Hybrid converter in AST-3) were randomly allocated to the groups (UUC, IUC and IT). The IT groups received a diet containing 60 mg monensin Na/kg complete feed starting 2 days prior to inoculation until the study end (Table 25). The intended dietary concentrations of the active substance were analytically confirmed. All birds in the infected groups were orally inoculated via gavage on study Days 15 (for AST-1 and AST-2) or 16 (for AST-3) with recent field isolates of *Eimeria*[86] spp. Animal health and mortality were monitored daily. Feed intake and body weight of the animals were measured, daily weight gain and feed to gain ratio were calculated. Samples of excreta were analysed for oocyst excretion. In AST-1 and AST-2, four birds per pen were euthanised and necropsied to assess the intestinal lesion score on Days 5 and 6 PI. In AST-3, three birds were necropsied for gut lesion scoring on Days 4, 5 and 6 PI. In AST-1 and AST-2, intestinal lesions were scored following an internal scoring system method[87] whereas in AST-3 the scoring system followed the method of El-Sherry et al. (2019) and Gadde et al. (2020), with a score from 0 (no lesions) to 4 (severe lesions) for the species relevant to turkeys described in this scoring system. Faecal droppings were scored in AST-1 and AST-2 on Days 4 and 6 PI and in AST-3 on Days 4, 5 and 6 PI (0: normal faecal droppings, 1: diarrhoea).

Statistical evaluation of AST-1 and AST-2 data was done with an ANOVA followed by Tukey test for groups comparisons for performance data; Kruskal–Wallis followed by Mann–Whitney and Bonferroni adjustment for paired comparisons for lesion scores and oocyst excretion; and Pearson chi-square or Fisher exact test for morbidity and faecal score. In AST-3, lesion scores were analysed using ordered regression model, feed intake, feed to gain ratio and OPG using general linear models, body weight and body weight gain using linear mixed regression models. In all models, treatment groups were compared to the IUC group as reference. Statistical significance was set at $p < 0.05$ using two-sided tests.

TABLE 25 Experimental design of ASTs with turkeys for fattening fed Coxidin®.

AST	Replicates per treatment (birds per replicate)	Inoculum characteristics			Day of inoculation	Anticoccidial treatment (days of life)	Monesin Na[a] (mg/kg feed)
		Date and country of isolation	Intended dose (number of oocysts) per bird and strain[b]				
1[88]	6 (12)	05/2019 France	50,000	*E. meleagrimitis*-like (85%)	15	13–21	56
				E. adenoeides-like (15%)			
2[89]	6 (12)	06/2019 France	100,000	*E. meleagrimitis*-like (65%)	15	13–21	56
				E. adenoeides-like (35%)			
3[90]	8 (9)	11/2018 UK	148,500	*E. meleagrimitis/E. meleagridis* KCH	16	14–22	61
			46,500	*E. dispersa*			
			85,500	*E. adenoeides/E. meleagridis KR/ E. gallopavonis*			

[a]Analysed concentration of monensin sodium in the feed.

[b]AST-1 and AST-2, *Eimeria* spp. identification based on morphology only; therefore, *E. meleagrimitis*-like may contain also *E. meleagridis*, and *E. adenoeides*-like may contain also *E. gallopavonis*. *Eimeria* spp. identification in AST-3 based on morphology supported by PCR.

No mortality was observed in any of the ASTs except one bird in AST-1 found dead on Day 7 PI (group not given).

In AST-1, on Day 6 PI most of the coccidiosis-related morbid birds in group IUC group scored 3 whereas the maximum score in the morbid birds of the IT group was 2, although no statistical differences were found between groups. In AST-2, on Day 6 PI morbidity scores were statistically lower in the UUC group compared to the IT group, and the latter also statistically lower than the IUC group. In AST-3, significantly less birds showed clinical signs of coccidiosis-related morbidity in the UUC group in comparison to IUC which were significantly reduced by the treatment.

In AST-1 and AST-2, intestinal lesions in the small intestine were attributed to *E. meleagrimitis* or *E. meleagridis* and, in the caecum, lesions were attributed to *E. adenoeides* or *E. gallopavonis*. In both AST studies on Days 5 and 6 PI the median ILS of UUC in the small intestine and the caecum was 0. Inoculation increased significantly the medians for those of IUC vs. IT except Day 6 PI in the small intestine (Table 26). In AST-1, on Day 5 PI, median lesions scores in the small intestine and the caecum of the IUC group were higher compared to the IT group. However, on Day 6 PI, this effect was only evident in the caecum. In AST-2, the median lesion scores were lower in the small intestine on Days 5 and 6 PI whereas in the caecum a reduction on median lesion scores was only evident on Day 6 PI.

[86]A dose-titration study was performed for each inoculum to establish the dose to apply in the ASTs.

[87]A four-point turkey coccidiosis lesions scale (from 1 [no lesions] to 4 [severe lesions]) was followed, separately for different sections of the intestinal tract (duodenum, jejunum, ileum/caecum), to score the lesions corresponding to the two different species of coccidia (*E. meleagrimitis and E. adenoeides*).

[88]FAD-2016-0009: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_4 and supplementary information September 2021/Annex_RTQ_IV_10_1.

[89]FAD-2020-0036: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_5 and supplementary information September 2021/Annex_RTQ_IV_10_2.

[90]FAD-2020-0036: Technical dossier/Supplementary information March 2021/Annex_RTQ_IV_6 and supplementary information September 2021/Annex_RTQ_IV_11.

TABLE 26 Intestinal lesion scores in AST-1 and AST-2 performed in turkeys for fattening.

		Median of the intestinal lesion scores			
		Small intestine		Caecum	
AST	Group	Day 5 PI	Day 6 PI	Day 5 PI	Day 6 PI
1	UUC	0*	0*	0*	0*
	IUC	3	4	2.5	2
	IT	1*	4	0*	0*
2	UUC	0*	0*	0	0
	IUC	2	1	2	3
	IT	1*	2*	0	1*

*Values significantly different from IUC ($p < 0.05$).

In AST-3, mean lesion scores were reported due to *E. meleagrimitis, E. meleagridis* and *E. adenoeides E. gallopavonis*. The virulence of the inoculum was shown by significant difference in the mean intestinal lesion scores between the UUC group and the IUC group for both species (Table 27). The severity of the lesions was statistically lower in the IT groups compared to IUC on Days 4, 5 and 6 PI (data not shown), and in the overall period considering the 3 days together.

TABLE 27 Intestinal lesion scores in AST-3 performed in turkeys for fattening.

	Mean intestinal lesion scores (Days 4–6 PI)		
Group	Total	*E. meleagrimitis/E. meleagridis*	*E. adenoeides/E. gallopavonis*
UUC	1.17*	0.5*	0.67*
IUC	3.22	1.04	2.18
IT	1.41*	0.65*	0.76*

*Means significantly different from IUC ($p < 0.05$).

Results of oocyst excretion and zootechnical performance parameters are reported in Table 28. Oocyst excretion in AST-1 and AST-2 was not significantly altered by the treatment. However, the differences between the infected groups IUC and IT and UUC were significant at all sampling days. Successful inoculation was demonstrated by the high number of oocysts found in the IUC group 6 days PI; oocyst excretion in the IT group was found to be significantly lower than in the IUC group (Table 28).

Zootechnical parameters were not affected by the treatment with the exception of a higher body weight gain of the IT group relative to the IUC group in AST-2 and AST-3.

TABLE 28 Oocyst excretion and zootechnical parameters in AST-s performed with Coxidin® in turkeys for fattening.

		Total oocyst excretion (OPG)[a]	
AST	Group	Day 5 PI	Day 6 PI
1	UUC	0	0
	IUC	4.82	6.74
	IT	4.67	6.60
2	UUC	0.55	0.5
	IUC	6.05	6.12
	IT	5.85	6.66
3	UUC	–	0*
	IUC	–	479,274
	IT	–	58,833*

Abbreviations: nr, not reported; OPG, oocyst per gram of excreta.

*Means significantly different from IUC ($p < 0.05$).

[a]AST-1 and AST-2 logOPGs are reported; Value 0 corresponds to no excretion whereas for AST-3 the counts are reported.

Synopsis of the efficacy

In the ASTs done in chickens, the coccidiostatic efficacy of 100 mg monensin sodium from Coxidin® per kg complete feed was confirmed in one AST (AST-1) in which the use of Coxidin® significantly reduced the intestinal lesions due to the

Eimeria spp. infection. In the other two ASTs in chickens only weak evidence concerning the reduction of lesions was observed. In one study (AST-2) a reduction on the oocyst excretion in 1 of the 3 days was identified; in the other study (AST-3) it was observed a reduction in the lesions of *E. acervulina* but not for the other *Eimeria* spp. In total, the results of the three studies could be interpreted as a symptom of a certain resistance of the *Eimeria* spp. tested to monensin, but the resistance is not considered sufficiently high that monensin at the tested dietary concentration has lost all efficacy. The results of the post-marketing monitoring plan undertaken by the applicant might also support the above conclusion on the development of some degree of resistance of *E. acervulina*.

In the ASTs done in turkeys, three ASTs with different inocula containing *Eimeria* spp. specific to turkeys, showed a significant reduction of frequency and severity of intestinal lesions by the coccidiostat.

3.3.3.1 | *Conclusions on efficacy*

The Panel concludes that monensin sodium from Coxidin® is efficacious in controlling coccidiosis at a level of 100 mg/kg complete feed for chickens for fattening and at 60 mg/kg complete feed for turkeys for fattening, the lowest proposed levels. These conclusions are extended to chickens reared for laying and turkeys reared for breeding purposes at the corresponding dietary concentrations. The Panel notes that the data in chicken for fattening might indicate that some strains of *Eimeria* are developing resistance towards monensin sodium.

3.4 | Post-market monitoring

Considering the indication that some resistance might be developing, the FEEDAP Panel considers necessary that a more exhaustive and contemporary post-market monitoring plan is put in place to monitor the development of *Eimeria* spp. resistance in chickens and turkeys during the whole period of authorisation.

4 | CONCLUSIONS

The applicant has provided evidence that the additive currently on the market complies with the existing conditions of authorisation.

The FEEDAP Panel concludes that the additive remains safe for turkeys for fattening (up to 16 weeks) under the authorised conditions of use and extends this conclusion to turkeys reared for breeding (up to 16 weeks). However, the Panel is not in a position to confirm that Coxidin® remains safe for chickens for fattening and chickens reared for laying under the approved conditions of use.

The FEEDAP Panel concludes that the use of monensin sodium from Coxidin® at the corresponding maximum authorised/proposed use levels with no withdrawal time in chickens for fattening/reared for laying and in turkeys for fattening/reared for breeding is safe for the consumer. The existing MRLs for poultry tissues ensure consumer safety.

The FEEDAP Panel concludes that both formulations of Coxidin® pose a risk by inhalation. The formulation with wheat bran as a carrier is not irritant to the skin, is not a skin sensitiser but it is irritant to the eyes. In the absence of data, no conclusions can be drawn on the potential of the formulation containing calcium carbonate to be irritant to skin and eyes and to be skin sensitiser.

The use of monensin sodium from Coxidin® in complete feed for chickens for fattening and chickens reared for laying and turkeys for fattening and turkeys reared for breeding poses no risk for the terrestrial compartments and for sediment. No risk for groundwater is expected. For chickens for fattening, the risk for aquatic compartment cannot be excluded, but no risks are expected for the other animal species/categories. There is no risk of secondary poisoning through the aquatic and terrestrial food chains from the use of monensin sodium.

The Panel concludes that monensin sodium from Coxidin® is efficacious at a level of 100 mg/kg complete feed for chickens for fattening and at 60 mg/kg complete feed for turkeys for fattening, the lowest proposed levels, in controlling coccidiosis. These conclusions are extended to chickens reared for laying and turkeys reared for breeding purposes at the corresponding dietary concentrations. The Panel notes that there are signs of development of resistance of some strains of *Eimeria* spp. to monensin sodium.

ABBREVIATIONS

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and excretion
AMR	antimicrobial resistance
ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
ARfD	acute reference dose
AST	anticoccidial sensitivity test
bw	body weight
CAS	Chemical Abstracts Service
CD	Commission Decision
CFU	colony forming unit
CV	coefficient of variation

CVMP	Committee for Medicinal Products for Veterinary Use
DAT	days after treatment
DM	dry matter
EMA	European Medicines Agency
EURL	European Union Reference Laboratory
FAO	Food Agricultural Organization
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
GLP	Good Laboratory Practice
HC	hardardous concentration
HRP	Highest Reliable Percentile
HS	hockey stick
ILS	intestinal lesion scores
Log K_{ow}	logarithm of octanol-water partition coefficient
LOQ	limit of quantification
LSC	liquid scintillation counting
MIC	minimum inhibitory concentration
MRC	marker residue concentration
MRL	maximum residue level
NOAEL	no observed adverse effect level
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OPG	oocyst per gram of excreta
PCB	polychlorinated biphenyls
PCDD	polychlorinated dibenzo-*p*-dioxins
PCDF	polychlorinated dibenzofurans
PEC	Predicted environment concentration
PMMP	post-marketing monitoring plan
PNEC	predicted no effect concentrations
RH	relative humidity
RMTR	ratio marker to total residue
SCAN	Scientific Committee on Animal Nutrition
SCF	Scientific Committee on Food
SEM	scanning electron microscopy
SSD	species sensitivity distribution
TAR	total applied radioactivity
TEM	transmission electron microscopy
TMLS	total mean lesion score
TR	total residue concentration
TWAEC	time weighted average exposure concentration
UB	upper bound
UF	uncertainty factor
WGS	whole genome sequence
WHO	World Health Organization

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CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

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APPENDIX A

Detailed results on chronic and acute exposure calculation

TABLE A.1 Chronic dietary exposure per population class, country and survey of consumers (mg/kg bw per day) to monensin total residues based on residue data in chicken tissues.

Population class	Survey's country	Number of subjects	HRP value	HRP description
Infants	Bulgaria	523	0.0010584121	95th
Infants	Germany	142	0.0001968778	95th
Infants	Denmark	799	0.0002283350	95th
Infants	Finland	427	0.0003413769	95th
Infants	Italy	9	0.0000000000	50th
Infants	United Kingdom	1251	0.0004769028	95th
Toddlers	Belgium	36	0.0005035333	90th
Toddlers	Bulgaria	428	0.0013512768	95th
Toddlers	Germany	348	0.0003275036	95th
Toddlers	Denmark	917	0.0002533493	95th
Toddlers	Spain	17	0.0004935897	75th
Toddlers	Finland	500	0.0005453188	95th
Toddlers	Italy	36	0.0004497500	90th
Toddlers	Netherlands	322	0.0005524775	95th
Toddlers	United Kingdom	1314	0.0005229049	95th
Toddlers	United Kingdom	185	0.0005309660	95th
Other children	Austria	128	0.0004361816	95th
Other children	Belgium	625	0.0006114813	95th
Other children	Bulgaria	433	0.0012563371	95th
Other children	Germany	293	0.0003538309	95th
Other children	Germany	835	0.0003432707	95th
Other children	Denmark	298	0.0002832045	95th
Other children	Spain	399	0.0006412924	95th
Other children	Spain	156	0.0008975222	95th
Other children	Finland	750	0.0005315800	95th
Other children	France	482	0.0004908936	95th
Other children	Greece	838	0.0004587769	95th
Other children	Italy	193	0.0004834117	95th
Other children	Latvia	187	0.0005209186	95th
Other children	Netherlands	957	0.0004030302	95th
Other children	Netherlands	447	0.0005075006	95th
Other children	Sweden	1473	0.0003802401	95th
Other children	Czechia	389	0.0009408426	95th
Other children	United Kingdom	651	0.0004687776	95th
Adolescents	Austria	237	0.0003013915	95th
Adolescents	Belgium	576	0.0002756807	95th
Adolescents	Cyprus	303	0.0002914525	95th
Adolescents	Germany	393	0.0002635895	95th
Adolescents	Germany	1011	0.0002162553	95th
Adolescents	Denmark	377	0.0002214812	95th
Adolescents	Spain	651	0.0003724520	95th
Adolescents	Spain	209	0.0004998289	95th
Adolescents	Spain	86	0.0004082779	95th
Adolescents	Finland	306	0.0002793909	95th
Adolescents	France	973	0.0003214667	95th
Adolescents	Italy	247	0.0002222200	95th

TABLE A.1 (Continued)

Population class	Survey's country	Number of subjects	HRP value	HRP description
Adolescents	Latvia	453	0.0003174563	95th
Adolescents	Netherlands	1142	0.0003804510	95th
Adolescents	Sweden	1018	0.0002862983	95th
Adolescents	Czechia	298	0.0007063034	95th
Adolescents	United Kingdom	666	0.0003435749	95th
Adults	Austria	308	0.0003451450	95th
Adults	Belgium	1292	0.0002805550	95th
Adults	Germany	10,419	0.0002154443	95th
Adults	Denmark	1739	0.0001443809	95th
Adults	Spain	981	0.0003474872	95th
Adults	Spain	410	0.0003469771	95th
Adults	Finland	1295	0.0002776102	95th
Adults	France	2276	0.0002837831	95th
Adults	Hungary	1074	0.0005197031	95th
Adults	Ireland	1274	0.0003422840	95th
Adults	Italy	2313	0.0001891773	95th
Adults	Latvia	1271	0.0002856668	95th
Adults	Netherlands	2055	0.0003209363	95th
Adults	Romania	1254	0.0006983569	95th
Adults	Sweden	1430	0.0002922103	95th
Adults	Czechia	1666	0.0003506455	95th
Adults	United Kingdom	1265	0.0002540710	95th
Elderly	Austria	67	0.0003040757	95th
Elderly	Belgium	511	0.0002469360	95th
Elderly	Germany	2006	0.0001716106	95th
Elderly	Denmark	274	0.0001167690	95th
Elderly	Finland	413	0.0002209825	95th
Elderly	France	264	0.0002530107	95th
Elderly	Hungary	206	0.0003751674	95th
Elderly	Ireland	149	0.0002836046	95th
Elderly	Italy	289	0.0002217424	95th
Elderly	Netherlands	173	0.0002379444	95th
Elderly	Netherlands	289	0.0002021982	95th
Elderly	Romania	83	0.0003694500	95th
Elderly	Sweden	295	0.0002721027	95th
Elderly	United Kingdom	166	0.0002172017	95th
Very elderly	Austria	25	0.0000725434	75th
Very elderly	Belgium	704	0.0002575082	95th
Very elderly	Germany	490	0.0001827832	95th
Very elderly	Denmark	12	0.0000609716	75th
Very elderly	France	84	0.0002024728	95th
Very elderly	Hungary	80	0.0002819356	95th
Very elderly	Ireland	77	0.0002831789	95th
Very elderly	Italy	228	0.0001876569	95th
Very elderly	Netherlands	450	0.0002004479	95th
Very elderly	Romania	45	0.0003893089	90th
Very elderly	Sweden	72	0.0002077802	95th
Very elderly	United Kingdom	139	0.0001566476	95th

TABLE A.2 Acute dietary exposure of consumers (mg/kg bw per day) to monensin total residues based on residue data in chicken–Summary statistics across European dietary surveys.

Raw primary commodity	Population class	Number of surveys	Maximum HRP
Birds fat tissue	Toddlers	1	0.0003434667
Birds fat tissue	Other children	4	0.0004067368
Birds fat tissue	Adolescents	2	0.0004200000
Birds fat tissue	Adults	8	0.0003026138
Birds fat tissue	Elderly	4	0.0001150000
Birds fat tissue	Very elderly	3	0.0001564000
Birds liver	Infants	2	0.0028500000
Birds liver	Toddlers	1	0.0014250000
Birds liver	Other children	7	0.0104500000
Birds liver	Adolescents	4	0.0051818182
Birds liver	Adults	12	0.0092101695
Birds liver	Elderly	6	0.0022619048
Birds liver	Very elderly	4	0.0009193548
Birds meat	Infants	5	0.0018365217
Birds meat	Toddlers	11	0.0017185117
Birds meat	Other children	20	0.0022022000
Birds meat	Adolescents	20	0.0013508637
Birds meat	Adults	23	0.0009871696
Birds meat	Elderly	16	0.0008387716
Birds meat	Very elderly	14	0.0008156296
Birds offals and slaughtering products (other than liver)	Adults	3	0.0010781250

TABLE A.3 Acute dietary exposure of consumers (mg/kg bw per day) to monensin total residues based on residue data in chicken–Summary statistics across European dietary surveys (details).

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds fat tissue	Toddlers	Bulgaria	NUTRICHILD	24	0.0003434667	75th
Birds fat tissue	Other children	Bulgaria	NUTRICHILD	45	0.0004067368	90th
Birds fat tissue	Other children	France	Individual and national study on food consumption 2	96	0.0003744186	95th
Birds fat tissue	Other children	Germany	Consumption Survey of Food Intake among Infants and Young Children	8	0.0000795062	50th
Birds fat tissue	Other children	Poland	National Food and Nutrition Institute–FAO 2000	36	0.0003846516	90th
Birds fat tissue	Adolescents	France	Individual and national study on food consumption 2	198	0.0002430189	95th
Birds fat tissue	Adolescents	Poland	National Food and Nutrition Institute–FAO 2000	61	0.0004200000	95th
Birds fat tissue	Adults	Belgium	Diet National 2004	8	0.0000606248	50th
Birds fat tissue	Adults	France	Individual and national study on food consumption 2	495	0.0001873455	95th
Birds fat tissue	Adults	Germany	National Nutrition Survey II	66	0.0001254545	95th
Birds fat tissue	Adults	Hungary	National Repr Surv	31	0.0002705882	90th
Birds fat tissue	Adults	Poland	National Food and Nutrition Institute–FAO 2000	171	0.0003026138	95th
Birds fat tissue	Adults	Romania	Dieta Pilot Adults	25	0.0002415000	75th
Birds fat tissue	Adults	Slovakia	SK MON 2008	104	0.0002308679	95th
Birds fat tissue	Adults	United Kingdom	National Diet and Nutrition Survey–Years 1–3	8	0.0000207000	50th

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds fat tissue	Elderly	France	Individual and national study on food consumption 2	48	0.0001022222	90th
Birds fat tissue	Elderly	Germany	National Nutrition Survey II	16	0.0000466216	75th
Birds fat tissue	Elderly	Hungary	National Repr Surv	11	0.0001150000	50th
Birds fat tissue	Elderly	Poland	National Food and Nutrition Institute–FAO 2000	13	0.0000978228	75th
Birds fat tissue	Very elderly	France	Individual and national study on food consumption 2	6	0.0000408889	50th
Birds fat tissue	Very elderly	Poland	National Food and Nutrition Institute–FAO 2000	7	0.0001014173	50th
Birds fat tissue	Very elderly	Romania	Dieta Pilot Adults	6	0.0001564000	50th
Birds liver	Infants	Bulgaria	NUTRICHILD	6	0.0019191919	50th
Birds liver	Infants	United Kingdom	Diet and Nutrition Survey of Infants and Young Children, 2011	9	0.0028500000	50th
Birds liver	Toddlers	Bulgaria	NUTRICHILD	29	0.0014250000	75th
Birds liver	Other children	Bulgaria	NUTRICHILD	53	0.0030962963	90th
Birds liver	Other children	Czechia	Czech National Food Consumption Survey	12	0.0003938182	75th
Birds liver	Other children	Finland	Diabetes Prediction and Prevention Nutrition Study (DIPP) 2001–2009	51	0.0013314861	90th
Birds liver	Other children	France	Individual and national study on food consumption 2	121	0.0022562500	95th
Birds liver	Other children	Germany	Consumption Survey of Food Intake among Infants and Young Children	13	0.0003518519	75th
Birds liver	Other children	Poland	National Food and Nutrition Institute–FAO 2000	38	0.0028208812	90th
Birds liver	Other children	Romania	Dieta Pilot Children	8	0.0104500000	50th
Birds liver	Adolescents	Czechia	Czech National Food Consumption Survey	7	0.0002812987	50th
Birds liver	Adolescents	France	Individual and national study on food consumption 2	228	0.0025253165	95th
Birds liver	Adolescents	Poland	National Food and Nutrition Institute–FAO 2000	66	0.0046341463	95th
Birds liver	Adolescents	Romania	Dieta Pilot Children	12	0.0051818182	75th
Birds liver	Adults	Belgium	Diet National 2004	18	0.0003953810	75th
Birds liver	Adults	Czechia	Czech National Food Consumption Survey	27	0.0002776923	75th
Birds liver	Adults	Finland	National FINDIET 2012 Survey	12	0.0002760291	75th
Birds liver	Adults	France	Individual and national study on food consumption 2	626	0.0015833333	95th
Birds liver	Adults	Germany	National Nutrition Survey II	66	0.0061750000	95th
Birds liver	Adults	Hungary	National Repr Surv	53	0.0040425532	90th
Birds liver	Adults	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	14	0.0020357143	75th
Birds liver	Adults	Netherlands	Dutch National food consumption survey 2007–2010	8	0.0013088275	50th
Birds liver	Adults	Poland	National Food and Nutrition Institute–FAO 2000	183	0.0035130971	95th
Birds liver	Adults	Romania	Dieta Pilot Adults	154	0.0092101695	95th

(Continues)

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds liver	Adults	Slovakia	SK MON 2008	109	0.0030319149	95th
Birds liver	Adults	Spain	Spanish Agency for Food Safety (AESAN)–FIAB Survey	7	0.0001980156	50th
Birds liver	Elderly	Belgium	Diet National 2004	10	0.0002435897	50th
Birds liver	Elderly	Finland	National FINDIET 2012 Survey	6	0.0001141141	50th
Birds liver	Elderly	France	Individual and national study on food consumption 2	85	0.0022619048	95th
Birds liver	Elderly	Germany	National Nutrition Survey II	13	0.0016840909	75th
Birds liver	Elderly	Hungary	National Repr Surv	7	0.0021111111	50th
Birds liver	Elderly	Poland	National Food and Nutrition Institute–FAO 2000	14	0.0005277778	75th
Birds liver	Very elderly	Belgium	Diet National 2004	20	0.0003909615	75th
Birds liver	Very elderly	France	Individual and national study on food consumption 2	13	0.0002959016	75th
Birds liver	Very elderly	Poland	National Food and Nutrition Institute–FAO 2000	8	0.0003740157	50th
Birds liver	Very elderly	Romania	Dieta Pilot Adults	11	0.0009193548	50th
Birds meat	Infants	Bulgaria	NUTRICHILD	320	0.0018365217	95th
Birds meat	Infants	Denmark	Danish National Dietary survey among infants and young children 2006–2007	1646	0.0007487665	95th
Birds meat	Infants	Finland	Diabetes Prediction and Prevention Nutrition Study (DIPP) 2001–2009	349	0.0007409035	95th
Birds meat	Infants	Germany	Consumption Survey of Food Intake among Infants and Young Children	83	0.0014075250	95th
Birds meat	Infants	United Kingdom	Diet and Nutrition Survey of Infants and Young Children, 2011	1402	0.0011380600	95th
Birds meat	Toddlers	Belgium	Regional Flanders	43	0.0011550000	90th
Birds meat	Toddlers	Bulgaria	NUTRICHILD	427	0.0017185117	95th
Birds meat	Toddlers	Denmark	Danish National Dietary survey among infants and young children 2006–2007	2887	0.0007414019	95th
Birds meat	Toddlers	Finland	Diabetes Prediction and Prevention Nutrition Study (DIPP) 2001–2009	506	0.0012326176	95th
Birds meat	Toddlers	Germany	Consumption Survey of Food Intake among Infants and Young Children	542	0.0011359091	95th
Birds meat	Toddlers	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	19	0.0010500000	75th
Birds meat	Toddlers	Netherlands	DNFCS-Young-Children	296	0.0009475115	95th
Birds meat	Toddlers	Poland	National Food and Nutrition Institute–FAO 2000	27	0.0013830097	75th
Birds meat	Toddlers	Spain	Food patterns of Spanish schoolchildren and adolescents	20	0.0008369565	75th
Birds meat	Toddlers	United Kingdom	Diet and Nutrition Survey of Infants and Young Children, 2011	2004	0.0012012000	95th

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds meat	Toddlers	United Kingdom	National Diet and Nutrition Survey–Years 1–3	304	0.0012983559	95th
Birds meat	Other children	Austria	Austrian Study on Nutritional Status 2010–12–Children	103	0.0010767480	95th
Birds meat	Other children	Belgium	Regional Flanders	764	0.0011485031	95th
Birds meat	Other children	Bulgaria	NUTRICHILD	410	0.0015246000	95th
Birds meat	Other children	Czechia	Czech National Food Consumption Survey	273	0.0018599034	95th
Birds meat	Other children	Denmark	The Danish National Dietary survey 2005–2008	1264	0.0008026388	95th
Birds meat	Other children	Finland	Diabetes Prediction and Prevention Nutrition Study (DIPP) 2001–2009	826	0.0011568076	95th
Birds meat	Other children	France	Individual and national study on food consumption 2	1172	0.0010065000	95th
Birds meat	Other children	Germany	Consumption Survey of Food Intake among Infants and Young Children	484	0.0010796923	95th
Birds meat	Other children	Germany	Eating Study as a KiGGS Module (EsKiMo)	792	0.0008160870	95th
Birds meat	Other children	Greece	Regional Crete	848	0.0010892683	95th
Birds meat	Other children	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	137	0.0012021726	95th
Birds meat	Other children	Latvia	National Dietary Survey	140	0.0010578425	95th
Birds meat	Other children	Netherlands	DNFCS-Young-Children	869	0.0007693990	95th
Birds meat	Other children	Netherlands	Dutch National food consumption survey 2007–2010	428	0.0008513044	95th
Birds meat	Other children	Poland	National Food and Nutrition Institute–FAO 2000	138	0.0016690066	95th
Birds meat	Other children	Romania	Dieta Pilot Children	109	0.0022022000	95th
Birds meat	Other children	Spain	Encuesta de nutrición 2005	311	0.0012100000	95th
Birds meat	Other children	Spain	Food patterns of Spanish schoolchildren and adolescents	136	0.0014302209	95th
Birds meat	Other children	Sweden	National Food Administration	2357	0.0009179675	95th
Birds meat	Other children	United Kingdom	National Diet and Nutrition Survey–Years 1–3	1180	0.0009618689	95th
Birds meat	Adolescents	Austria	Austrian Study on Nutritional Status 2010–12–Children	174	0.0009573533	95th
Birds meat	Adolescents	Belgium	Diet National 2004	417	0.0005284314	95th
Birds meat	Adolescents	Bulgaria	National Survey of Food Intake and Nutrition	40	0.0004613156	90th
Birds meat	Adolescents	Cyprus	Childhealth	321	0.0006126882	95th
Birds meat	Adolescents	Czechia	Czech National Food Consumption Survey	187	0.0011882716	95th
Birds meat	Adolescents	Denmark	The Danish National Dietary survey 2005–2008	1420	0.0005278318	95th
Birds meat	Adolescents	Finland	Nutrition and wellbeing of secondary school pupils	434	0.0006862745	95th
Birds meat	Adolescents	France	Individual and national study on food consumption 2	2236	0.0007056000	95th
Birds meat	Adolescents	Germany	Eating Study as a KiGGS Module (EsKiMo)	362	0.0006695652	95th

(Continues)

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds meat	Adolescents	Germany	National Nutrition Survey II	637	0.0004645409	95th
Birds meat	Adolescents	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	151	0.0006350960	95th
Birds meat	Adolescents	Latvia	National Dietary Survey	322	0.0006416667	95th
Birds meat	Adolescents	Netherlands	Dutch National food consumption survey 2007–2010	1080	0.0006570667	95th
Birds meat	Adolescents	Poland	National Food and Nutrition Institute–FAO 2000	234	0.0013508637	95th
Birds meat	Adolescents	Romania	Dieta Pilot Children	240	0.0012600000	95th
Birds meat	Adolescents	Spain	Encuesta de nutrición 2005	461	0.0007002162	95th
Birds meat	Adolescents	Spain	Food patterns of Spanish schoolchildren and adolescents	159	0.0008627451	95th
Birds meat	Adolescents	Spain	Spanish Agency for Food Safety (AESAN)–FIAB Survey	83	0.0010440678	95th
Birds meat	Adolescents	Sweden	National Food Administration	1368	0.0007437897	95th
Birds meat	Adolescents	United Kingdom	National Diet and Nutrition Survey–Years 1–3	1325	0.0006362288	95th
Birds meat	Adults	Austria	Austrian Study on Nutritional Status 2010–12–Adults	215	0.0007643173	95th
Birds meat	Adults	Belgium	Diet National 2004	928	0.0004765750	95th
Birds meat	Adults	Bulgaria	National Survey of Food Intake and Nutrition	188	0.0005223392	95th
Birds meat	Adults	Czechia	Czech National Food Consumption Survey	1057	0.0006298356	95th
Birds meat	Adults	Denmark	The Danish National Dietary survey 2005–2008	6981	0.0003733204	95th
Birds meat	Adults	Estonia	National Dietary Survey 1997	267	0.0007264151	95th
Birds meat	Adults	Finland	National FINDIET 2012 Survey	935	0.0004847550	95th
Birds meat	Adults	France	Individual and national study on food consumption 2	4731	0.0006484211	95th
Birds meat	Adults	Germany	National Nutrition Survey II	6974	0.0004620000	95th
Birds meat	Adults	Hungary	National Repr Surv	1178	0.0006895522	95th
Birds meat	Adults	Ireland	National Adult Nutrition Survey	2335	0.0006992705	95th
Birds meat	Adults	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	1212	0.0004808691	95th
Birds meat	Adults	Latvia	National Dietary Survey	969	0.0005212308	95th
Birds meat	Adults	Netherlands	Dutch National food consumption survey 2007–2010	2024	0.0005109271	95th
Birds meat	Adults	Poland	National Food and Nutrition Institute–FAO 2000	923	0.0009871696	95th
Birds meat	Adults	Romania	Dieta Pilot Adults	3953	0.0007837500	95th
Birds meat	Adults	Romania	Dieta Pilot Children	14	0.0002662000	75th
Birds meat	Adults	Slovakia	SK MON 2008	1338	0.0006995467	95th
Birds meat	Adults	Slovenia	CRP-2008	133	0.0007294737	95th
Birds meat	Adults	Spain	Spanish Agency for Food Safety (AESAN)–FIAB Survey	838	0.0008352542	95th

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds meat	Adults	Spain	Spanish Agency for Food Safety (AESAN) Survey	259	0.0006937948	95th
Birds meat	Adults	Sweden	Swedish National Dietary Survey–Riksmaten adults 2010–11	2231	0.0006825000	95th
Birds meat	Adults	United Kingdom	National Diet and Nutrition Survey–Years 1–3	2262	0.0005283019	95th
Birds meat	Elderly	Austria	Austrian Study on Nutritional Status 2010–12–Adults	49	0.0005630625	90th
Birds meat	Elderly	Belgium	Diet National 2004	368	0.0004305109	95th
Birds meat	Elderly	Bulgaria	National Survey of Food Intake and Nutrition	42	0.0003696000	90th
Birds meat	Elderly	Denmark	The Danish National Dietary survey 2005–2008	1131	0.0003261898	95th
Birds meat	Elderly	Finland	National FINDIET 2012 Survey	229	0.0004551724	95th
Birds meat	Elderly	France	Individual and national study on food consumption 2	491	0.0006246761	95th
Birds meat	Elderly	Germany	National Nutrition Survey II	1243	0.0004029667	95th
Birds meat	Elderly	Hungary	National Repr Surv	220	0.0006160000	95th
Birds meat	Elderly	Ireland	National Adult Nutrition Survey	216	0.0006229481	95th
Birds meat	Elderly	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	163	0.0004605097	95th
Birds meat	Elderly	Netherlands	Dutch National food consumption survey 2007–2010	173	0.0004240536	95th
Birds meat	Elderly	Netherlands	Dutch National Food Consumption Surveys–Older Adults	309	0.0003500702	95th
Birds meat	Elderly	Poland	National Food and Nutrition Institute–FAO 2000	108	0.0008387716	95th
Birds meat	Elderly	Romania	Dieta Pilot Adults	261	0.0007635833	95th
Birds meat	Elderly	Sweden	Swedish National Dietary Survey–Riksmaten adults 2010–11	398	0.0007560603	95th
Birds meat	Elderly	United Kingdom	National Diet and Nutrition Survey–Years 1–3	267	0.0004372240	95th
Birds meat	Very elderly	Austria	Austrian Study on Nutritional Status 2010–12–Adults	25	0.0002784653	75th
Birds meat	Very elderly	Belgium	Diet National 2004	570	0.0004095438	95th
Birds meat	Very elderly	Bulgaria	National Survey of Food Intake and Nutrition	58	0.0004180000	90th
Birds meat	Very elderly	Denmark	The Danish National Dietary survey 2005–2008	55	0.0002502680	90th
Birds meat	Very elderly	France	Individual and national study on food consumption 2	123	0.0007153548	95th
Birds meat	Very elderly	Germany	National Nutrition Survey II	315	0.0003949733	95th
Birds meat	Very elderly	Hungary	National Repr Surv	66	0.0006720000	95th
Birds meat	Very elderly	Ireland	National Adult Nutrition Survey	95	0.0006125252	95th
Birds meat	Very elderly	Italy	Italian National Food Consumption Survey INRAN-SCAI 2005–06	135	0.0004078345	95th
Birds meat	Very elderly	Netherlands	Dutch National Food Consumption Surveys–Older Adults	510	0.0003386614	95th

(Continues)

TABLE A.3 (Continued)

Raw primary commodity	Population class	Survey's country	Survey	Number of consuming days	HRP value	HRP description
Birds meat	Very elderly	Poland	National Food and Nutrition Institute–FAO 2000	42	0.0007661615	90th
Birds meat	Very elderly	Romania	Dieta Pilot Adults	136	0.0008156296	95th
Birds meat	Very elderly	Sweden	Swedish National Dietary Survey–Riksmaten adults 2010–11	97	0.0005525270	95th
Birds meat	Very elderly	United Kingdom	National Diet and Nutrition Survey–Years 1–3	201	0.0003791667	95th
Birds offals and slaughtering products (other than liver)	Adults	Czechia	Czech National Food Consumption Survey	11	0.0010781250	50th
Birds offals and slaughtering products (other than liver)	Adults	Germany	National Nutrition Survey II	10	0.0006459574	50th
Birds offals and slaughtering products (other than liver)	Adults	Hungary	National Repr Surv	14	0.0007419355	75th

TABLE A.4 Chronic combined exposure of consumers per population class, country and survey of consumers (mg/kg bw per day) to monensin total residues based on residue data in chicken and bovine tissues and milk.

Population class	Survey's country	Number of subjects	HRP value	HRP description
Infants	Bulgaria	523	0.0027970869	95th
Infants	Germany	142	0.0014562035	95th
Infants	Denmark	799	0.0021146058	95th
Infants	Finland	427	0.0015356547	95th
Infants	Italy	9	0.0006708257	50th
Infants	United Kingdom	1251	0.0013963720	95th
Toddlers	Belgium	36	0.0019628771	90th
Toddlers	Bulgaria	428	0.0026154759	95th
Toddlers	Germany	348	0.0020899796	95th
Toddlers	Denmark	917	0.0022946252	95th
Toddlers	Spain	17	0.0018177010	75th
Toddlers	Finland	500	0.0025377241	95th
Toddlers	Italy	36	0.0017933891	90th
Toddlers	Netherlands	322	0.0019744535	95th
Toddlers	United Kingdom	1314	0.0021620404	95th
Toddlers	United Kingdom	185	0.0020477545	95th
Other children	Austria	128	0.0029789788	95th
Other children	Belgium	625	0.0021104593	95th
Other children	Bulgaria	433	0.0022144434	95th
Other children	Germany	293	0.0016741325	95th
Other children	Germany	835	0.0012963476	95th
Other children	Denmark	298	0.0017778388	95th
Other children	Spain	399	0.0015626648	95th
Other children	Spain	156	0.0018885639	95th
Other children	Finland	750	0.0019652528	95th
Other children	France	482	0.0018220381	95th
Other children	Greece	838	0.0017190216	95th
Other children	Italy	193	0.0015302317	95th
Other children	Latvia	187	0.0014599587	95th

TABLE A.4 (Continued)

Population class	Survey's country	Number of subjects	HRP value	HRP description
Other children	Netherlands	957	0.0015998999	95th
Other children	Netherlands	447	0.0013998611	95th
Other children	Sweden	1473	0.0016565095	95th
Other children	Czechia	389	0.0021156587	95th
Other children	United Kingdom	651	0.0014917632	95th
Adolescents	Austria	237	0.0009339407	95th
Adolescents	Belgium	576	0.0007387547	95th
Adolescents	Cyprus	303	0.0006930656	95th
Adolescents	Germany	393	0.0009953204	95th
Adolescents	Germany	1011	0.0007020128	95th
Adolescents	Denmark	377	0.0008499553	95th
Adolescents	Spain	651	0.0008905125	95th
Adolescents	Spain	209	0.0010970320	95th
Adolescents	Spain	86	0.0008635358	95th
Adolescents	Finland	306	0.0009196508	95th
Adolescents	France	973	0.0009850036	95th
Adolescents	Italy	247	0.0008339282	95th
Adolescents	Latvia	453	0.0009815443	95th
Adolescents	Netherlands	1142	0.0009544447	95th
Adolescents	Sweden	1018	0.0009998226	95th
Adolescents	Czechia	298	0.0014714397	95th
Adolescents	United Kingdom	666	0.0007611469	95th
Adults	Austria	308	0.0007704496	95th
Adults	Belgium	1292	0.0006751782	95th
Adults	Germany	10,419	0.0006671146	95th
Adults	Denmark	1739	0.0005974358	95th
Adults	Spain	981	0.0007382862	95th
Adults	Spain	410	0.0007087374	95th
Adults	Finland	1295	0.0007870722	95th
Adults	France	2276	0.0007045041	95th
Adults	Hungary	1074	0.0007466798	95th
Adults	Ireland	1274	0.0006533933	95th
Adults	Italy	2313	0.0005549605	95th
Adults	Latvia	1271	0.0007125878	95th
Adults	Netherlands	2055	0.0007107284	95th
Adults	Romania	1254	0.0007425078	95th
Adults	Sweden	1430	0.0006575260	95th
Adults	Czechia	1666	0.0008192611	95th
Adults	United Kingdom	1265	0.0005527238	95th
Elderly	Austria	67	0.0006940741	95th
Elderly	Belgium	511	0.0006736738	95th
Elderly	Germany	2006	0.0006257813	95th
Elderly	Denmark	274	0.0005750380	95th
Elderly	Finland	413	0.0006525739	95th
Elderly	France	264	0.0006463082	95th
Elderly	Hungary	206	0.0006345909	95th
Elderly	Ireland	149	0.0006496553	95th
Elderly	Italy	289	0.0004567913	95th
Elderly	Netherlands	173	0.0005930098	95th

(Continues)

TABLE A.4 (Continued)

Population class	Survey's country	Number of subjects	HRP value	HRP description
Elderly	Netherlands	289	0.0005857721	95th
Elderly	Romania	83	0.0006284095	95th
Elderly	Sweden	295	0.0006672468	95th
Elderly	United Kingdom	166	0.0005819107	95th
Very elderly	Austria	25	0.0004532176	75th
Very elderly	Belgium	704	0.0007393619	95th
Very elderly	Germany	490	0.0006286012	95th
Very elderly	Denmark	12	0.0003889317	75th
Very elderly	France	84	0.0006125859	95th
Very elderly	Hungary	80	0.0006773768	95th
Very elderly	Ireland	77	0.0006216479	95th
Very elderly	Italy	228	0.0004579087	95th
Very elderly	Netherlands	450	0.0005814999	95th
Very elderly	Romania	45	0.0006824897	90th
Very elderly	Sweden	72	0.0007396238	95th
Very elderly	United Kingdom	139	0.0006407194	95th

TABLE A.5 Acute combined exposure of consumers per population class, country and survey of consumers (mg/kg bw per day) to monensin total residues based on residue data in chicken and bovine tissues and milk.

Raw primary commodity	Population class	Number of surveys	Maximum HRP
Birds fat tissue	Toddlers	1	0.0001276800
Birds fat tissue	Other children	4	0.0001512000
Birds fat tissue	Adolescents	2	0.0001561304
Birds fat tissue	Adults	8	0.0001124934
Birds fat tissue	Elderly	4	0.0000427500
Birds fat tissue	Very elderly	3	0.0000581400
Birds liver	Infants	2	0.0007995000
Birds liver	Toddlers	1	0.0003997500
Birds liver	Other children	7	0.0029315000
Birds liver	Adolescents	4	0.0014536364
Birds liver	Adults	12	0.0025836949
Birds liver	Elderly	6	0.0006345238
Birds liver	Very elderly	4	0.0002579032
Birds meat	Infants	5	0.0016337888
Birds meat	Toddlers	11	0.0015288058
Birds meat	Other children	20	0.0019591000
Birds meat	Adolescents	20	0.0012017424
Birds meat	Adults	23	0.0008781963
Birds meat	Elderly	16	0.0007461799
Birds meat	Very elderly	14	0.0007255926
Birds offals and slaughtering products (other than liver)	Adults	3	0.0005367188
Mammals fat tissue	Infants	4	0.0002529731
Mammals fat tissue	Toddlers	11	0.0002528779
Mammals fat tissue	Other children	20	0.0001978667
Mammals fat tissue	Adolescents	20	0.0001613394
Mammals fat tissue	Adults	23	0.0001110136
Mammals fat tissue	Elderly	16	0.0001027465
Mammals fat tissue	Very elderly	14	0.0001067586
Mammals liver	Infants	4	0.0018286894

TABLE A.5 (Continued)

Raw primary commodity	Population class	Number of surveys	Maximum HRP
Mammals liver	Toddlers	9	0.0014089286
Mammals liver	Other children	20	0.0027073529
Mammals liver	Adolescents	18	0.0014410959
Mammals liver	Adults	22	0.0019700375
Mammals liver	Elderly	15	0.0009068966
Mammals liver	Very elderly	10	0.0008547500
Mammals meat	Infants	6	0.0003666250
Mammals meat	Toddlers	11	0.0003935260
Mammals meat	Other children	20	0.0005661667
Mammals meat	Adolescents	20	0.0003948137
Mammals meat	Adults	23	0.0002568579
Mammals meat	Elderly	16	0.0002168280
Mammals meat	Very elderly	14	0.0002223337
Mammals offals and slaughtering products (other than liver)	Toddlers	5	0.0001318182
Mammals offals and slaughtering products (other than liver)	Other children	15	0.0002456944
Mammals offals and slaughtering products (other than liver)	Adolescents	16	0.0001380952
Mammals offals and slaughtering products (other than liver)	Adults	22	0.0001635897
Mammals offals and slaughtering products (other than liver)	Elderly	13	0.0001260870
Mammals offals and slaughtering products (other than liver)	Very elderly	12	0.0001111111
Milk	Infants	6	0.0024226479
Milk	Toddlers	11	0.0022779892
Milk	Other children	20	0.0032296750
Milk	Adolescents	20	0.0011446695
Milk	Adults	23	0.0006444620
Milk	Elderly	16	0.0005844022
Milk	Very elderly	14	0.0006142312

TABLE A.6 Chronic dietary exposure per population class, country and survey (mg/kg bw per day) of consumers exposure of consumers to monensin total residues derived from poultry MRLs.

Population class	Survey's country	Number of subjects	HRP value	HRP description
Infants	Bulgaria	523	0.0009313223	95th
Infants	Germany	142	0.0001649431	95th
Infants	Denmark	799	0.0002031292	95th
Infants	Finland	427	0.0003036924	95th
Infants	Italy	9	0.0000000000	50th
Infants	United Kingdom	1251	0.0004046763	95th
Toddlers	Belgium	36	0.0004479485	90th
Toddlers	Bulgaria	428	0.0010801472	95th
Toddlers	Germany	348	0.0002913506	95th
Toddlers	Denmark	917	0.0002253821	95th
Toddlers	Spain	17	0.0004391026	75th
Toddlers	Finland	500	0.0004851212	95th
Toddlers	Italy	36	0.0004001023	90th
Toddlers	Netherlands	322	0.0004914897	95th

(Continues)

TABLE A.6 (Continued)

Population class	Survey's country	Number of subjects	HRP value	HRP description
Toddlers	United Kingdom	1314	0.0004619265	95th
Toddlers	United Kingdom	185	0.0004723529	95th
Other children	Austria	128	0.0003880317	95th
Other children	Belgium	625	0.0005358592	95th
Other children	Bulgaria	433	0.0009354764	95th
Other children	Germany	293	0.0003025093	95th
Other children	Germany	835	0.0003053772	95th
Other children	Denmark	298	0.0002519416	95th
Other children	Spain	399	0.0005705004	95th
Other children	Spain	156	0.0007984451	95th
Other children	Finland	750	0.0004169893	95th
Other children	France	482	0.0003534736	95th
Other children	Greece	838	0.0004081327	95th
Other children	Italy	193	0.0004300481	95th
Other children	Latvia	187	0.0004634146	95th
Other children	Netherlands	957	0.0003585399	95th
Other children	Netherlands	447	0.0004514778	95th
Other children	Sweden	1473	0.0003382655	95th
Other children	Czechia	389	0.0008288278	95th
Other children	United Kingdom	651	0.0004170294	95th
Adolescents	Austria	237	0.0002681210	95th
Adolescents	Belgium	576	0.0002452484	95th
Adolescents	Cyprus	303	0.0002592792	95th
Adolescents	Germany	393	0.0002344919	95th
Adolescents	Germany	1011	0.0001920148	95th
Adolescents	Denmark	377	0.0001970320	95th
Adolescents	Spain	651	0.0003313371	95th
Adolescents	Spain	209	0.0004446530	95th
Adolescents	Spain	86	0.0003632082	95th
Adolescents	Finland	306	0.0002485490	95th
Adolescents	France	973	0.0002357587	95th
Adolescents	Italy	247	0.0001911137	95th
Adolescents	Latvia	453	0.0002824125	95th
Adolescents	Netherlands	1142	0.0003384532	95th
Adolescents	Sweden	1018	0.0002546939	95th
Adolescents	Czechia	298	0.0006091826	95th
Adolescents	United Kingdom	666	0.0003056478	95th
Adults	Austria	308	0.0003070445	95th
Adults	Belgium	1292	0.0002337989	95th
Adults	Germany	10,419	0.0001898361	95th
Adults	Denmark	1739	0.0001284428	95th
Adults	Spain	981	0.0003091282	95th
Adults	Spain	410	0.0003086744	95th
Adults	Finland	1295	0.0002450733	95th
Adults	France	2276	0.0002005307	95th
Adults	Hungary	1074	0.0003177686	95th
Adults	Ireland	1274	0.0003024012	95th
Adults	Italy	2313	0.0001665007	95th
Adults	Latvia	1271	0.0002530361	95th
Adults	Netherlands	2055	0.0002819798	95th

TABLE A.6 (Continued)

Population class	Survey's country	Number of subjects	HRP value	HRP description
Adults	Romania	1254	0.0003830097	95th
Adults	Sweden	1430	0.0002599534	95th
Adults	Czechia	1666	0.0003053079	95th
Adults	United Kingdom	1265	0.0002255979	95th
Elderly	Austria	67	0.0002705089	95th
Elderly	Belgium	511	0.0002046671	95th
Elderly	Germany	2006	0.0001477794	95th
Elderly	Denmark	274	0.0001038790	95th
Elderly	Finland	413	0.0001965884	95th
Elderly	France	264	0.0001670566	95th
Elderly	Hungary	206	0.0002455297	95th
Elderly	Ireland	149	0.0002522976	95th
Elderly	Italy	289	0.0001883831	95th
Elderly	Netherlands	173	0.0002116778	95th
Elderly	Netherlands	289	0.0001798776	95th
Elderly	Romania	83	0.0003209161	95th
Elderly	Sweden	295	0.0002420654	95th
Elderly	United Kingdom	166	0.0001877709	95th
Very elderly	Austria	25	0.0000645354	75th
Very elderly	Belgium	704	0.0002195580	95th
Very elderly	Germany	490	0.0001626058	95th
Very elderly	Denmark	12	0.0000542410	75th
Very elderly	France	84	0.0001801219	95th
Very elderly	Hungary	80	0.0002438993	95th
Very elderly	Ireland	77	0.0002519189	95th
Very elderly	Italy	228	0.0001669415	95th
Very elderly	Netherlands	450	0.0001728698	95th
Very elderly	Romania	45	0.0003083356	90th
Very elderly	Sweden	72	0.0001848435	95th
Very elderly	United Kingdom	139	0.0001393554	95th

TABLE A.7 Acute dietary exposure per population class, country and survey (mg/kg bw per day) of consumers exposure of consumers to monensin total residues derived from poultry MRLs.

Raw primary commodity	Population class	Number of surveys	Maximum HRP
Birds fat tissue	Toddlers	1	0.0001276800
Birds fat tissue	Other children	4	0.0001512000
Birds fat tissue	Adolescents	2	0.0001561304
Birds fat tissue	Adults	8	0.0001124934
Birds fat tissue	Elderly	4	0.0000427500
Birds fat tissue	Very elderly	3	0.0000581400
Birds liver	Infants	2	0.0007995000
Birds liver	Toddlers	1	0.0003997500
Birds liver	Other children	7	0.0029315000
Birds liver	Adolescents	4	0.0014536364
Birds liver	Adults	12	0.0025836949
Birds liver	Elderly	6	0.0006345238
Birds liver	Very elderly	4	0.0002579032
Birds meat	Infants	5	0.0016337888
Birds meat	Toddlers	11	0.0015288058

(Continues)

TABLE A.7 (Continued)

Raw primary commodity	Population class	Number of surveys	Maximum HRP
Birds meat	Other children	20	0.0019591000
Birds meat	Adolescents	20	0.0012017424
Birds meat	Adults	23	0.0008781963
Birds meat	Elderly	16	0.0007461799
Birds meat	Very elderly	14	0.0007255926
Birds offals and slaughtering products (other than liver)	Adults	3	0.0005367188