

**APPENDIX II****MAXIMUM RESIDUE LIMITS (MRLs) FOR VETERINARY DRUGS IN FOODS****IVERMECTIN (broad-spectrum antiparasitic agent)****(PIGS, SHEEP AND GOATS – FAT, KIDNEY, LIVER AND MUSCLE)****(for adoption at Step 5/8)**

Acceptable daily intake	JECFA established an ADI of 0–10 µg/kg body weight at the eighty-first meeting.
Acute reference dose	JECFA established an ARfD of 200 µg/kg body weight at the eighty-first meeting.
Residue definition	The marker residue in sheep, pigs and goats is ivermectin B <sub>1a</sub> (H <sub>2</sub> B <sub>1a</sub> , or 22,23-dihydroavermectin B <sub>1a</sub> ).
Estimated chronic dietary exposure	<p>The GECDE for adults and the elderly is 0.72 µg/kg bw per day, which represents 7.2% of the upper bound of the ADI of 10 µg/kg bw.</p> <p>The GECDE for children and adolescents is 0.93 µg/kg bw per day, which represents 9.3% of the upper bound of the ADI of 10 µg/kg bw.</p> <p>The GECDE for infants and toddlers is 0.48 µg/kg bw per day, which represents 4.8% of the upper bound of the ADI of 10 µg/kg bw.</p>
Estimated acute dietary exposure	<p>The GEADE for cattle muscle, applicable to children and the general population, is 69 µg/kg bw, which represents 35% of the ARfD of 200 µg/kg bw.</p> <p>The GEADE for sheep muscle, applicable to children and the general population, is 73 µg/kg bw, which represents 37% of the ARfD of 200 µg/kg bw.</p> <p>The GEADE for pig muscle, applicable to children and the general population, is 30 µg/kg bw, which represents 15% of the ARfD of 200 µg/kg bw.</p>

**Recommended maximum residue limits (MRLs)**

<b>Species</b>	<b>Muscle (µg/kg)</b>	<b>Liver (µg/kg)</b>	<b>Kidney (µg/kg)</b>	<b>Fat (µg/kg)</b>
Pigs	15	30	20	50
Sheep and goats	30	60	20	100

**NICARBAZIN (coccidiostat)**  
**(CHICKEN)**  
**(For adoption at Step 5/8)**

Toxicological effects	The NOAEL was 60 mg/kg bw per day (equivalent to 42.5 mg/kg bw per day of DNC) due to prominent liver lobulation, observed in a study of developmental toxicity in the rabbit.
Uncertainty factor	When considering nicarbazin it is DNC that is the toxic component, and its absorption alone or in a mixture with HDP is substantially less (< 5%) than when formed from ingested nicarbazin. As DNC is the residue of concern and there is no nicarbazin in products from treated animals, JECFA concluded that despite limitations in the database, a reduction in the default safety factor of 100 used to account for interspecies and intraspecies variability, would be justified. JECFA was unable to quantify just how much of a reduction would be appropriate, but concluded that 50 could certainly be supported, and would still result in a conservative evaluation.
Toxicological ADI	The tADI for nicarbazin was established at 0–0.9 mg/kg bw (DNC).
Microbiological effects	Nicarbazin and/or its metabolites show no antimicrobial activity towards representative bacteria of the human intestinal microbiota.
Microbiological ADI	JECFA concluded that it was not necessary to establish an mADI for nicarbazin.
Acceptable daily intake	The ADI for nicarbazin was established at 0–0.9mg/kg bw based on toxicological effects.
Acute reference dose	JECFA concluded that it was not necessary to establish an ARfD for nicarbazin.
Residue definition	The marker residue in chickens is DNC.
Estimated dietary exposure	<p>Based on incurred DNC residues in chicken muscle, offal, and skin with fat, at 24 hours withdrawal time and 125 mg/kg feed:</p> <p>The global estimate of chronic dietary exposure (GECDE) for adults and the elderly is 120 µg/kg body weight (bw) per day, which represents 13% of the upper bound of the ADI of 900 µg/kg bw.</p> <p>The GECDE for children and adolescents is 160 µg/kg bw per day, which represents 18% of the upper bound of the ADI of 900 µg/kg bw.</p> <p>The GECDE for infants and toddlers is 210 µg/kg bw per day, which represents 23% of the upper bound of the ADI of 900 µg/kg bw.</p> <p>Based on incurred DNC residues in chicken muscle, offal, and skin with fat, at zero days withdrawal time and 50 mg/kg feed:</p> <p>The GECDE for adults and the elderly is 95 µg/kg bw per day, which represents 11% of the upper bound of the ADI of 900 µg/kg bw.</p> <p>The GECDE for children and adolescents is 120 µg/kg bw per day, which represents 14% of the upper bound of the ADI of 900 µg/kg bw.</p> <p>The GECDE for infants and toddlers is 160 µg/kg bw per day, which represents 18% of the upper bound of the ADI of 900 µg/kg bw.</p>

**Recommended maximum residue limits (MRLs)**

Species	Muscle (µg/kg)	Liver (µg/kg)	Kidney (µg/kg)	Skin with fat (µg/kg)
Chicken	4000	15 000	8000	4000

**IVERMECTIN (broad-spectrum antiparasitic agent)**  
**(SHEEP, PIGS AND GOATS – FAT, KIDNEY, LIVER AND MUSCLE)**  
**(For discontinuation)**

<b>Acceptable daily intake</b>	The ADI of 0–10 µg/kg bw established by JECFA81 (1) remains unchanged.
<b>Acute reference dose</b>	The ARfD of 0.2 mg/kg bw established by JECFA81 remains unchanged.
<b>Estimated chronic dietary exposure</b>	JECFA established a GECDE for the general population of 0.41 µg/kg bw per day, which represents 4% of the upper bound of the ADI.  JECFA established a GECDE for children of 0.59 µg/kg bw per day, which represents 5.9% of the upper bound of the ADI.
<b>Estimated acute dietary exposure</b>	JECFA established a GEADE for the general population of 87 µg/kg bw per day, which represents 43% of the ARfD, from consumption of cattle muscle, and of 1.1 µg/kg bw, which represents 0.6% of the ARfD, from consumption of sheep muscle.  JECFA established a GEADE for children of 82 µg/kg bw per day, which represents 41% of the ARfD, from consumption of cattle muscle and of 1.0 µg/kg bw, which represents 0.5% of the ARfD, from consumption of sheep muscle.
<b>Residue definition</b>	The marker residue (MR) in sheep, pigs and goats is Ivermectin B <sub>1a</sub> (H <sub>2</sub> B <sub>1a</sub> , or 22,23-dihydroavermectin B <sub>1a</sub> ).
<b>Maximum residue limits</b>	JECFA established MRLs for sheep, pigs and goats of 20 µg/kg for fat, 15 µg/kg for kidney, 15 µg/kg for liver and 10 µg/kg for muscle.

**Recommended maximum residue limits (MRLs)**

Species	Tissue	MRLs (µg/kg) recommended by JECFA88	Step	JECFA
Sheep, pigs and goats	Fat	20	7	88
Sheep, pigs and goats	Kidney	15	7	88
Sheep, pigs and goats	Liver	15	7	88
Sheep, pigs and goats	Muscle	10	7	88