

MOXIDECTIN

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ADDENDUM

to the Moxidectin residue monograph prepared by
the 45th meeting of the Committee and published in
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Introduction

Moxidectin was evaluated at the 45th JECFA and the Committee recommended MRLs for cattle, sheep and deer of 500 µg/kg in fat, 100 µg/kg in liver, 20 µg/kg in muscle and of 50 µg/kg for kidney expressed as parent drug. The MRL for deer were temporary. Since then the sponsors have carried out further analytical work on their large study in sheep which has highlighted that the residues in sheep muscle can exceed the MRL if the recommended dosing schedule for psoroptic mange is used. They determined the residues of moxidectin in muscle, liver, kidney and at the injection sites (data for fat was submitted to 45th meeting) at various times following two injections of moxidectin 1.0% injectable, ten days apart, at the recommended rate of 0.2 mg moxidectin/kg body weight.

Residue Study

Thirty-nine Blackface x Cheviot x Suffolk lambs, aged approximately nine months and weighing 38 to 64 kg on Day 0, were used. Five groups of six lambs, three castrated males and three females each were treated with moxidectin 1.0% injectable solution on Day 0. The remaining animals served as controls or back-up animals. Six treated plus two untreated lambs were euthanized on Day +10 after treatment and samples of back fat, loin muscle, kidney, liver and injection site muscle were removed and frozen for residue analysis. At the same time the remaining twenty-four lambs were given a second injection of moxidectin on the opposite side of the neck. All animals were euthanized in groups of six on Days +20, +30, +40 and +50 respectively. On each slaughter occasion, samples were collected from the same sites as were taken from lambs on Day +10. All the samples collected were divided in half before freezing. At the end of the experiment half were transferred for analysis and the remainder were retained frozen. To accurately quantify the moxidectin residue levels at the injection site, the frozen injection site retention samples were analysed (Parker, 1995). The results for analysis of tissues are summarized in Table 1.

Three main points emerge from this study:

1. The residues in muscle exceed the MRL proposed at the 45th JECFA. The maximum value at any time was 63 µg/kg at 10 days post dosing but thereafter (20-50 days) no value exceeded 40 µg/kg even though two doses were administered;
2. The levels in liver, kidney and fat did not exceed the recommended MRL; and
3. There were very high and persistent residues at the injection sites.

In the submissions to the 45th JECFA residues of moxidectin were not measurable (< 10 µg/kg) in the muscles of sheep by 28 days. However in this study it was clear that residues persisted for at least 50 days. That there are residues in ovine muscle compared with no detectable levels in bovine or deer muscle was probably due to the high fat content in sheep muscle and the lipophilic nature of moxidectin.

Table 1. Residues of Moxidectin ($\mu\text{g}/\text{kg}$) in edible tissues and at the injection sites after one or two injections of moxidectin at a dose of 0.2 mg/kg body weight

Days post dose	Muscle	Liver	Kidney	Fat	Injection Site 1	Injection Site 2
10	16-63 [41 \pm 20]	14-36 [21 \pm 8]	<10-18 [NA]	167-314 [222]	819-2985 [1582 \pm 700]	no 2nd injection
20*	22-40 [29 \pm 6]	15-41 [29 \pm 8]	11-25 [21 \pm 5]	197-433 [324 \pm 89]	159-2159 [652 \pm 697]	409-3734 [1353 \pm 1176]
30*	<10-32 [NA]	<10-25 [NA]	<10-17 [NA]	183-284 [234 \pm 41]	202-1345 [551 \pm 377]	217-963 [660 \pm 234]
40*	<10-15 [NA]	<10-13 [NA]	<10 [NA]	91-223 [139 \pm 42]	67-177 [125 \pm 41]	106-424 [207 \pm 106]
50*	<10-22 [NA]	<10-12 [NA]	<10-16 [NA]	91-290 [164 \pm 69]	87-379 [177 \pm 96]	79-451 [185 \pm 127]

* Sheep received 2nd injection on day 10. NA is not applicable because some values were below the limit of determination of the method. No residues were detected in control tissues.

Maximum Residue Limits

The established ADI is 120 μg for a 60-kg person (45th JECFA). The MRL previously proposed used up 79 μg of this daily allowance. In view of the observed residues in sheep muscle the Committee recommended increasing the MRL specifically for sheep muscle to 50 $\mu\text{g}/\text{kg}$. Using the same factors (i.e. moxidectin accounts for 40% of the residue of concern in muscle) this would result in a theoretical increase from 15 to 37.5 μg of moxidectin equivalents for sheep muscle and the additional intake would not exceed the ADI.

REFERENCE

Parker, L.D., (1995). Residue Depletion Study in sheep following two treatments with moxidectin 1.0% injectable, ten days apart. Report GASD 02-41.00. Cyanamid.