



Australian Government
**Australian Pesticides and
Veterinary Medicines Authority**

Trade Advice Notice

Australian Pesticides & Veterinary Medicines Authority

Avenge™ Pour-On Lousicide for Sheep

APVMA Product Number 62598

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This Trade Advice Notice for Avenge Pour-On Lousicide for Sheep (APVMA Product Number 62598) is published by the Australian Pesticides & Veterinary Medicines Authority.

The APVMA invites comments on this Trade Advice Notice until 4 August 2009. Submissions should be sent to:

Dr Elizabeth Milbourne
Veterinary Medicines Program
Australian Pesticides and Veterinary Medicines Authority

PO Box 6182
Kingston ACT 2604
Australia

Telephone:	61 2 6210 4734
Fax:	61 2 6210 4741
Email:	Elizabeth.Milbourne@apvma.gov.au

APMVA web site: <http://www.apvma.gov.au>

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1. INTRODUCTION

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it an application from Bayer Australia Limited (Animal Health) for the registration of a new product, *Avenge Pour-On Lousicide for Sheep*, which contains the approved active constituent imidacloprid (35 mg/mL). The new product is a pour-on formulation that is to be used off-shears in sheep, for the control and eradication of body lice (*Bovicola ovis*), and for the protection of sheep against re-infestation with lice for 4 weeks after treatment.

To date, there are no products containing imidacloprid that are registered for use on food-producing animal species, although there are numerous veterinary chemical products registered for use on companion animals (cats and dogs). Additionally, imidacloprid is registered for use in a number of horticultural crops.

The existing Australian MRLs for imidacloprid in animal commodities were established to cover the occurrence of residues as a result of animals consuming feedstuffs containing imidacloprid residues. Therefore, the current application does not involve the establishment of Australian Maximum Residue Limits (MRLs) for imidacloprid in edible sheep tissues.

However, the application does require the setting of meat and milk withholding periods (WHPs), establishment of an export slaughter interval (ESI), and approval of the proposed product label.

1.1. Proposed Use-pattern

The proposed Australian use-pattern for *Avenge Pour-On Lousicide for Sheep* is given below:

Avenge Pour-On Lousicide for Sheep (35 mg imidacloprid/mL)

Animal/Situation	Purpose	Dose Rate	Critical comments
Sheep (0-24 hours off-shears)	For the control and eradication of body lice (<i>Bovicola ovis</i>) in sheep.	<u>Maximum:</u> 70 mg imidacloprid/kg bw (when a lamb weighing 12.5 kg is administered 25 mL of product).	For sheep weighing <u>under 30 kg</u> , apply the entire dose as a single stripe from poll to tail butt. For sheep weighing <u>over 30 kg</u> , apply half the dose as a stripe either side of the mid-line from the neck to the butt of the tail. The stripes should be no further than 10 cm apart. The product can be used on all sheep, including shorn lambs over 12.5 kg up to 24 hours off-shears.

Restraints:

DO NOT USE on female sheep which are producing, or may in the future produce, milk or milk products for human consumption.

DO NOT USE on unshorn lambs or lambs weighing less than 12.5 kg.

DO NOT USE more than 24 hours after shearing.

Withholding Periods:

MEAT: DO NOT USE less than 21 days before slaughter for human consumption.

MILK: DO NOT USE on female sheep which are producing, or may in the future produce, milk or milk products for human consumption.

Trade Advice:

EXPORT SLAUGHTER INTERVAL (ESI): DO NOT slaughter for export less than 63 days (9 weeks) after treatment. The ESI on this label was correct at the time of label approval. Before using this product, confirm the correct ESI from the Bayer Website www.bayeranimal.com.au or via the APVMA website at www.apvma.gov.au/residues/ESI.shtml or by calling Bayer Australia Ltd on 1800 678 368.

1.2. Current Australian MRLs and residues definition

The current relevant entries for imidacloprid in the *MRL Standard* are listed below.

Table 1

Compound	Food	MRL (mg/kg)
Imidacloprid	MO 0105	Edible offal (mammalian) 0.2
	MM 0095	Meat (mammalian) 0.05

The existing imidacloprid MRLs for meat (mammalian) of 0.05 mg/kg and edible offal (mammalian) of 0.2 mg/kg are based on a maximum anticipated exposure of 200 mg/animal/day, from the consumption of cereal and sweet corn fodder and forage containing residues of 10 mg/kg.

Table 3

Compound	Residue
Imidacloprid	Sum of imidacloprid and metabolites containing the 6-chloropyridinyl-methylene moiety, expressed as imidacloprid.

For full details of current imidacloprid MRLs, please refer to the APVMA website <http://www.apvma.gov.au> and follow the Residues link.

2. WITHHOLDING PERIODS AND MAXIMUM RESIDUE LIMITS

In support of their application, Bayer submitted details of two (2) residues trials conducted in sheep, and one (1) supplementary residues decline study. All residues trials were conducted with *Avenge Pour-On Lousicide for Sheep*.

2.1. Meat

2.1.1. Residues in sheep tissues

Trial 1: (Summer study in Orange, NSW in 2006)

Sheep (n=72; 36 × Merinos, and 36 × 2nd cross Merino/Border Leicester × Poll Dorset lambs) were topically treated, off-shears, with *Avenge Pour-On Lousicide for Sheep* at a rate of 105 mg imidacloprid/kg bw (equivalent to 1.5 × the maximum proposed label rate). Groups of sheep (n=8; 4 × Merinos and 4 × 2nd cross lambs) were sacrificed at 1, 3, 7, 14, 21, 28, 42, 57 and 70 days after treatment. Samples of kidney, peri-renal fat, subcutaneous fat (within 100 mm of the dorsal line), liver and muscle (semimembranosus/semitendinosus muscle) were collected and stored frozen until analysed for their concentrations of imidacloprid residues.

Trial 2: (Winter study in Orange, NSW in 2006)

Sheep (n=72; 36 × Merinos and 36 × 2nd cross Merino/Border Leicester × Poll Dorset lambs) were topically treated, off-shears, with *Avenge Pour-On Lousicide for Sheep* at a rate of 140 mg imidacloprid/kg bw (equivalent to 2 × the maximum proposed label rate). Groups of sheep (n=8; 4 × Merinos and 4 × 2nd cross lambs) were sacrificed at 1, 3, 7, 14, 21, 28, 42, 56 and 70 days after treatment. Samples of kidney, peri-renal fat, subcutaneous fat (within 100 mm of the dorsal line), liver and muscle (semimembranosus/semitendinosus muscle) were collected and stored frozen until analysed for their concentrations of imidacloprid residues.

Trial 3: (Supplementary Summer study in Orange, NSW in 2007)

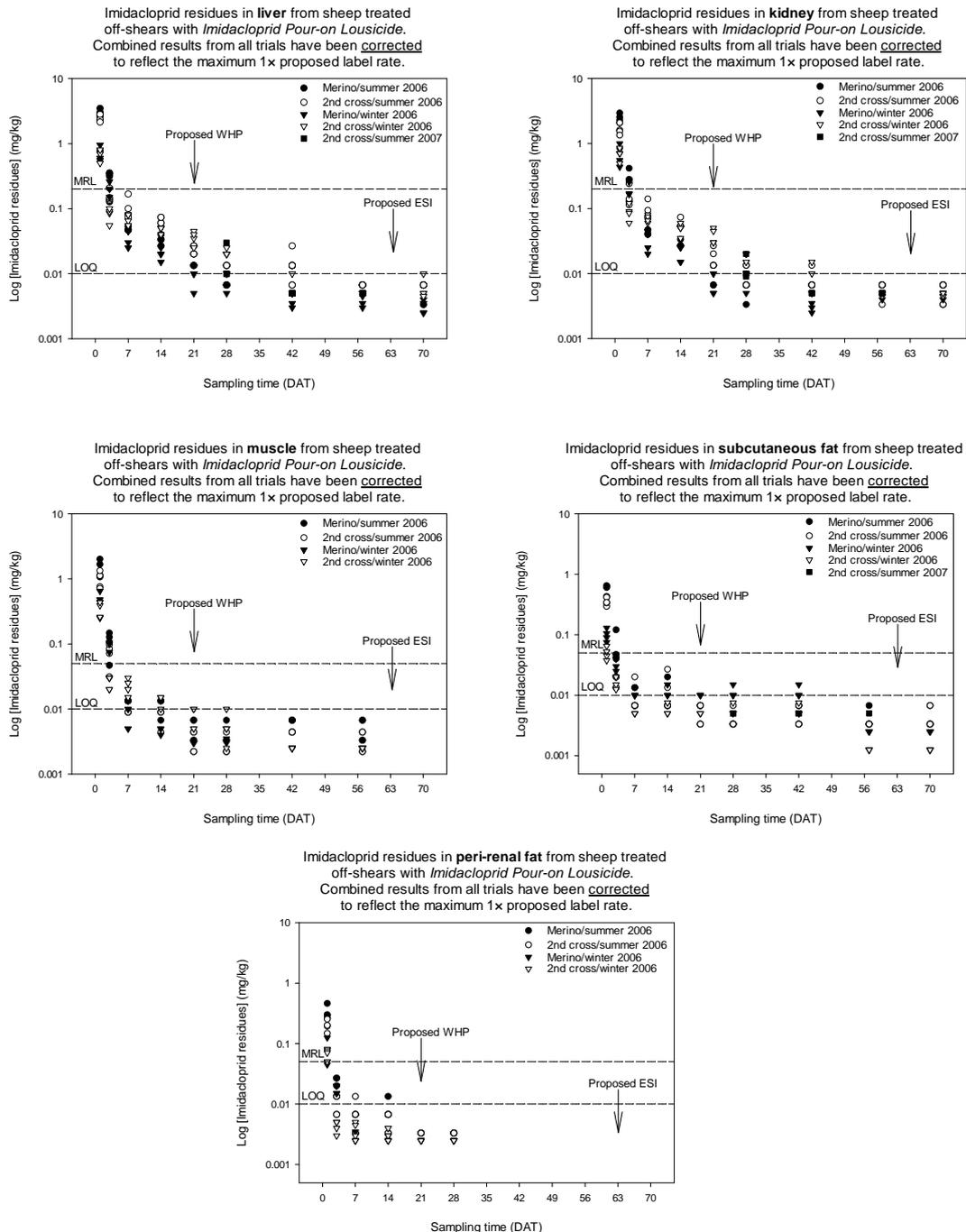
Sheep (n=30; 2nd cross Merino/Border Leicester × Poll Dorset lambs) were topically treated, off-shears, with *Avenge Pour-On Lousicide for Sheep* at a rate of 70 mg imidacloprid/kg bw (equivalent to 1 × the maximum proposed label rate). Groups of sheep (n=5) were sacrificed at 28, 42 and 56 days after treatment. Samples of kidney, subcutaneous fat (within 100 mm of the dorsal line), and liver were collected and stored frozen until analysed for their concentrations of imidacloprid residues.

The levels of imidacloprid residues (ie the sum of imidacloprid and its metabolites that are oxidised to 6-chloronicotinic acid, expressed as imidacloprid equivalents) were determined using a validated HPLC/MS/MS method. The limits of detection (LODs) for all animal tissues (muscle, liver, kidney, fat) are 0.005 mg/kg. The limits of quantification (LOQs) for all animal tissues (muscle, liver, kidney, fat) are 0.01 mg/kg.

The results from the tissue residues trials were corrected to reflect the maximum 1 × proposed label rate of 70 mg imidacloprid/kg bw (assuming a linear correlation between

dose rate and tissue residues concentrations). The residues results from all trials are presented graphically below.

Imidacloprid residues (sum of all residues oxidisable to 6-chloronicotinic acid, expressed as imidacloprid equivalents) in edible tissues from sheep that were administered a single off-shears topical treatment (results are corrected to 1x the maximum proposed label rate)



The corrected residues data from the different trials were combined, and analysed statistically using the EMEA’s ‘Meat’ program, which determines the upper 95 % confidence limit of the 95th percentile of residue concentrations.

Statistical analysis of the corrected combined residues data suggested that imidacloprid residues in all edible sheep tissues would be below the relevant Australian MRLs within 14 days of treatment. However, it is considered appropriate to incorporate a “safety factor” in the meat WHP as: (i) the quality of the residues data is diminished due to the use of elevated dosing regimens in the trials; and (ii) the possibility of sheep being exposed to imidacloprid through both direct and indirect routes needs to be covered. Therefore, a meat WHP of 21 days is recommended for the new product.

2.1.2. Meat WHP

The following meat WHP is recommended for the use of *Avenge Pour-On Lousicide for Sheep*:

DO NOT USE less than 21 days before slaughter for human consumption.

2.1.3. MRLs

No changes to the existing Australian MRLs for imidacloprid are required to cover the use of *Avenge Pour-On Lousicide for Sheep*.

2.2. Milk

2.2.1. Residues in sheep milk

No milk residues data were for the use of *Avenge Pour-On Lousicide for Sheep* in lactating sheep.

2.2.2. Milk WHP

In the absence of any milk residues data for treated sheep, the following milk WHP is recommended for *Avenge Pour-On Lousicide for Sheep*:

DO NOT USE on female sheep which are producing, or may in the future produce, milk or milk products for human consumption.

3. TRADE CONSIDERATIONS

3.1. Commodities exported

Australian exports of sheep meat and offal, and live sheep could be affected by the use of *Avenge Pour-On Lousicide for Sheep*.

3.2. Destination and value of exports

3.2.1. Mutton/lamb exports

Australia exported ~321 ktonne of mutton and lamb during 2007, which was valued at \$AUS 1.3 billion. Details of the top ten export markets for Australian lamb/mutton are provided below.

Mutton and lamb exports in 2007 (Source: ABARE 2008)

Rank (by \$ value)	Importing country	Quantity (ktonne)	Value (\$AUS million)	Cumulative total (%)
1	USA	60.5	371.6	28.3
2	EU [§]	22.3	122.5	37.6
3	Japan	15.6	85.9	44.1
4	Saudi Arabia	23.2	58.9	48.6
5	United Arab Emirates	12.6	56.3	52.9
6	Papua New Guinea	15.9	30.3	55.2
7	South Africa	19.6	29.3	57.4
8	CIS	8.1	23.5	59.2
9	Chinese Taipei	7.9	23.2	61.0
10	Malaysia	6.4	21.8	62.6
Total		321.0	1314.5	

[§] Regarded as 25 countries

3.2.2. Live sheep exports

Australia exported approximately 3.77 million head of live sheep during 2007, which were valued at \$AUS 261 million. Details of the top export markets for Australian live sheep are provided below.

Live sheep exports 2007 (Source: ABARE 2008)

Rank (by \$ value)	Importing country	Quantity (× 1000)	Value (\$AUS million)	Cumulative total (%)
1	Saudi Arabia	1,032	76	29.1
2	Kuwait	930	59	51.7
3	Oman	540	40	67.0
4	Bahrain	562	38	81.6
5	Jordan	268	18	88.5

Rank (by \$ value)	Importing country	Quantity (× 1000)	Value (\$AUS million)	Cumulative total (%)
6	Qatar	192	13	93.5
Total		3,773	261	

3.3. Overseas registrations

Bayer Australia Limited (Animal Health) has advised that there are no registrations or impending registrations for *Avenge Pour-On Lousicide for Sheep* overseas.

3.4. Comparison of the (proposed) Australian MRLs with Codex and overseas MRLs.

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. Codex CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Imidacloprid has been considered by Codex (JMPR), and the relevant CXLs are tabulated below, along with imidacloprid MRLs/tolerances that have been established by other overseas countries.

Comparison of Australian and Overseas Imidacloprid MRLs/tolerances

Commodity	Overseas MRLs/tolerances (mg/kg)				Proposed Australian MRLs (mg/kg)
	Codex (JMPR)	EU (Ag)	USA (EPA)	Japan [†]	
Edible offal (mammalian)	0.05	--	--	--	0.2
Meat (from mammals other than marine mammals)	*0.02	--	--	--	--
Meat (mammalian)	--	--	--	--	0.05
Sheep, fat	--	*0.05	0.3	--	--
Sheep, meat byproducts	--	--	0.3	--	--
Sheep, meat	--	*0.05	0.3	--	--
Sheep liver	--	*0.05	--	--	--
Sheep kidney	--	*0.05	--	--	--
Sheep, edible offal of	--	*0.05	--	--	--
Muscle (terrestrial mammals, except cattle and pigs)	--	--	--	0.02	--
Fat (terrestrial mammals, except cattle and pigs)	--	--	--	0.02	--
Liver (terrestrial mammals, except cattle and pigs)	--	--	--	0.02	--

Commodity	Overseas MRLs/tolerances (mg/kg)				Proposed Australian MRLs (mg/kg)
	Codex (JMPR)	EU (Ag)	USA (EPA)	Japan [†]	
Kidney (terrestrial mammals, except cattle and pigs)	--	--	--	0.02	--
Edible offal (terrestrial mammals, except cattle and pigs)	--	--	--	0.02	--

[†]Provisional MRLs

* MRL set at or about the limit of quantification for the analytical method

3.5. Potential Risk to Trade

Export of treated produce containing finite (measurable) residues of imidacloprid may pose a risk to Australian trade in situations where: (i) no residue tolerance (import tolerance) is established in the importing country; or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

Lamb/mutton exports: Of the 10 main export markets for Australian lamb/mutton (listed in section 5.2 of this report), the top three (USA, EU and Japan) have established MRLs/tolerances to cover the occurrence of imidacloprid residues in edible sheep tissues. Further, Codex CXLs have been established for imidacloprid residues in mammalian meat and offal, and these Codex CXLs are likely to be adopted as the import standards by Saudi Arabia, the United Arab Emirates, Papua New Guinea and South Africa. However, the CIS (Russia), Chinese Taipei (Taiwan) and Malaysia have not established MRLs for imidacloprid residues in sheep tissues.

Live sheep exports: Australia's export markets for live sheep are primarily Middle Eastern countries. AQIS has advised that these countries default to Codex MRLs for their food import standards.

3.5.1. Identification of the appropriate ESI "endpoint"

In the absence of import standards for imidacloprid residues in edible sheep tissues in the CIS (Russia), Chinese Taipei (Taiwan) and Malaysia, it is concluded that the appropriate "endpoint" for determination of the ESI for *Avenge Pour-On Lousicide for Sheep* is the LOQ of the validated analytical method (ie 0.01 mg/kg).

3.5.2. Estimation of the ESI

Statistical analysis (using the EMEA's 'Meat' program, which determines the upper 95 % confidence limit of the 95th percentile of residue concentrations) of the combined residues data corrected to reflect the maximum 1× proposed label rate revealed that imidacloprid residues in liver, kidney, fat and muscle from treated sheep are likely to be below the method LOQ (<0.01 mg/kg) at 63 days (9 weeks) after treatment. Therefore,

an ESI of 63 days (9 weeks) has been recommended for the use of *Avenge Pour-On Lousicide for Sheep*.

3.5.3. Trade Advice Statements

The following trade advice statement is to be included on the product label:

EXPORT SLAUGHTER INTERVAL (ESI): DO NOT slaughter for export less than 63 days (9 weeks) after treatment. The ESI on this label was correct at the time of label approval. Before using this product, confirm the correct ESI from the Bayer Website www.bayeranimal.com.au or via the APVMA website at www.apvma.gov.au/residues/ESI.shtml or by calling Bayer Australia Ltd on 1800 678 368.

4. CONCLUSIONS

The APVMA has considered whether use of *Avenge Pour-On Lousicide for Sheep*, in accordance with the label instructions, could potentially unduly prejudice trade and commerce between Australia and places outside Australia, as per Section 14(3)(e)(iv) of the Agvet Codes.

The risk to Australia's export trade in sheep meat and live sheep is considered to be low when the recommended ESI of 63 days (9 weeks) is observed for *Avenge Pour-On Lousicide for Sheep*, as residues in all tissues are expected to be below the method LOQ (<0.01 mg/kg).

The APVMA is seeking comment from relevant industry groups and stakeholders in relation to the perceived level of risk to Australia's export trade in sheep meat and live sheep.

The APVMA also welcomes comment on any residues aspects of trade.