Trade Advice Notice

Australian Pesticides & Veterinary Medicines Authority

Halocur oral solution for treatment of calves

APVMA Product Number 57163

June 2007

This Trade Advice Notice for Halocur oral solution for treatment of calves (APVMA Product Number 57163) is published by the Australian Pesticides & Veterinary Medicines Authority.

The APVMA invites comments on this Trade Advice Notice until **3 July 2007**.

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1. INTRODUCTION

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it an application from Intervet Australia Pty Limited for the registration of a new product, *Halocur Oral Solution for Treatment of Calves* (referred to as *Halocur Oral Solution*), which contains 0.5 g/L of halofuginone (present as halofuginone lactate). The product is an oral solution that is to be administered to calves aged 1-21 days, as an aid in control and prevention of diarrhoea caused by *Cryptosporidium parvum*.

The application involves consideration of the proposal to extend the use of halofuginone to cattle, along with the establishment of Australian Maximum Residue Limits (MRLs) for halofuginone in meat and offal of cattle.

2. RESIDUES IN LIVESTOCK

In support of the application, Intervet Australia Pty Limited provided details of two residues trials conducted in calves.

2.1. Tissue residues trial

In each trial, calves were orally administered 0.10 mg halofuginone/kg bw/day for 7 consecutive days, equivalent to 0.77 × the maximum proposed label rate. Groups of calves (n=4-5) were sacrificed at specified times, ranging from 0.25 to 25 days after last dosing. Samples of liver, kidney, muscle and fat were collected and analysed for their concentrations of halofuginone residues.

Liver and kidney were identified as the critical tissues for halofuginone residues in treated calves. It is the decline of halofuginone residues in these tissues that determines the duration of the slaughter WHP and ESI that applies to use of the new product in calves.

Statistical analysis of the residues decline data for halofuginone in calf liver and kidney, and application of a correction factor of 1.3 to address the maximum 1× dose rate, shows that a period of 13 days is required for residues to decline to below the proposed halofuginone MRLs of 0.03 mg/kg for cattle liver and cattle kidney.

2.1.1. Meat WHP

Thus, a 13-day meat WHP is recommended for the use of *Halocur Oral Solution* in calves.

2.1.2. MRLs for beef tissues

The following halofuginone MRLs are recommended, to cover the occurrence of halofuginone residues in edible calf tissues after the 13 day WHP has been observed:

cattle liver: 0.03 mg/kg

cattle kidney: 0.03 mg/kg

cattle muscle: 0.01 mg/kg

cattle fat: 0.025 mg/kg.

3. RESIDUES-RELATED ASPECTS OF TRADE

3.1. Commodities exported

Australian exports of beef/veal (meat and offal) could be affected by the use of *Halocur Oral Solution.*

3.2. Destination and value of exports

3.2.1. Beef/veal exports

Australia exported ~ 914 ktonne of beef and veal during 2004, which was valued at $AUS 4.4 billion. Details of the top six export markets for Australian beef are provided below.

Beef and veal exports in 2004 (Source ABARE 2005)

Rank (by $ value)	Importing country	Quantity (ktonne)	Value ($AUS million)
1	Japan	393.5	2189.8
2	USA	347.2	1374.4
3	Korea, Rep. of	93.3	434.4
4	Chinese Taipei	25.5	119.5
5	Malaysia-Singapore	6.9	74.6
6	European Union†	6.7	62.7

†Regarded as 15 countries to May 2004, then 25 countries from June 2004.

3.3. Proposed Australian use pattern

Halocur Oral Solution for treatment of calves [Halofuginone (0.5 mg/mL)]

Animal/ Situation	Purpose	Dose Rate	Critical Comments
New born calves	An aid in control and prevention of scours caused by Cryptosporidium parvum.	**Nominal** 2 mL product/10 kg bw (equiv. 0.1 mg halofuginone/kg bw) **Maximum** 0.13 mg halofuginone/ kg bw (when a 45 kg calf receives 12 mL of product).	For the treatment of new born calves up to 21 days of age. For the control of diarrhoea, treatment should be commenced within 24 hours of onset of diarrhoea. For the prevention of diarrhoea due to a confirmed diagnosis of Cryptosporidium parvum, on properties with a history of cryptosporidiosis, treatment should be commenced within 24-48 hours after birth. Administer to calves after feeding. Administer once daily for 7 consecutive days.

3.3.1. Re-treatment interval

DO NOT expose calves to a second period of treatment.

3.3.2. Meat withholding period

DO NOT USE less than 13 days before slaughter for human consumption.

3.3.3. Trade advice

EXPORT SLAUGHTER INTERVAL (ESI): DO NOT slaughter for export for 17 days after last treatment. The ESI on this label was correct at the time of label approval. Before using this product, confirm the current ESI from Intervet Australia on 1800 033 461 (Australian callers only) or via the APVMA website at www.apvma.gov.au/residues/ESI.shtml

3.4. Overseas registrations

Intervet Australia Pty Limited indicated that *Halocur Oral Solution* is currently registered in all 25 Member States of the European Union (EU), and that the EU dossier is currently before the Canadian registration authorities for assessment of the same use-pattern as that proposed for use in Australia.

3.5. 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 employed by various countries. Some countries may accept Codex CXLs when importing foods. Halofuginone has not been considered by Codex. However, halofuginone MRLs/tolerances have been established by a number of overseas countries, and these are tabulated below along with the proposed Australian MRLs.

Comparison of Australian and Overseas Halofuginone MRLs/tolerances

Commodity	Overseas MRLs/tolerances (mg/kg)			Proposed Australian MRLs (mg/kg)
	Europe	USA	†Japan	
Cattle muscle	0.01	--	0.01	0.01
Cattle fat	0.025	--	0.03	0.025
Cattle liver	0.03	--	0.02	0.03
Cattle kidney	0.03	--	0.02	0.03
Cattle, edible offal	--	--	0.02	--

† Provisional Japanese MRLs

3.6. Potential risk to trade

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

3.6.1. Beef/veal exports

Australia's main export markets for beef/veal are Japan and the USA.

Japan has established provisional MRLs for halofuginone residues in cattle commodities. The Japanese MRLs for cattle muscle and fat are the same as, or higher than, the proposed Australian MRLs. However, the Japanese MRLs for cattle kidney and liver (0.02 mg/kg) are lower than the proposed Australian MRLs of 0.03 mg/kg.

Europe has established MRLs for halofuginone residues in cattle commodities that are identical to the proposed Australian MRLs. It is probable that some of the Asian countries, such as Singapore and Malaysia, would adopt the European MRLs as their import standards.

There are no halofuginone tolerances established for cattle commodities in the USA. Therefore, it is concluded that the appropriate endpoints for the ESI determinations for *Halocur Oral Solution* are the limits of quantification (LOQs) of the analytical method, that is 0.005 mg/kg for cattle muscle and 0.01 mg/kg for cattle kidney, liver and fat.

3.6.2. Estimation of ESIs

Liver and kidney are the target tissues. The decline of halofuginone residues in these tissues determines the duration of the ESI for *Halocur Oral Solution*.

Statistical analysis of the combined residues trial data for halofuginone in calf kidney and calf liver, and application of a correction factor of 1.3 to address the 1× maximum dose rate, shows that a period of 17 days is required for halofuginone residues in each tissue to decline to below the method LOQ of 0.01 mg/kg. At 17 days after treatment, halofuginone residues in calf muscle and calf fat are below the method LOQs of 0.005 mg/kg and 0.01 mg/kg, respectively.

Therefore, an export slaughter interval (ESI) of 17 days is recommended for *Halocur Oral Solution*.

3.6.3. Trade Advice Statements

The following trade advice statements are to be included on the product label:

> EXPORT SLAUGHTER INTERVAL (ESI): DO NOT slaughter for export for 17 days after last treatment. The ESI on this label was correct at the time of label approval. Before using this product, confirm the current ESI from Intervet Australia on 1800 033 461 or the APVMA website (www.apvma.gov.au/residues/ESI.shtml).

4. CONCLUSIONS

The risk to Australia's export trade in beef/veal, arising from the use of *Halocur Oral Solution* in calves, is considered to be low when an ESI of 17 days is observed, as halofuginone residues in edible tissues from treated calves are expected to be below the limit of quantification.

However, the APVMA is seeking comment from relevant industry groups and stakeholders in relation to whether the proposed use of halofuginone in the product *Halocur Oral Solution* poses an undue prejudice to Australia's export trade in beef/veal.

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