Commonwealth of Australia

Gazette

No. APVMA 24, Tuesday, 2 December 2014

Published by The Australian Pesticides and Veterinary Medicines Authority

AGRICULTURAL AND VETERINARY CHEMICALS

Australian Government

Australian Pesticides and Veterinary Medicines Authority

The *Agricultural and Veterinary Chemical Code Act 1994* (the Act) commenced on 15 March 1995. The Agricultural and Veterinary Chemicals Code (the Agvet Code) scheduled to the Act requires notices to be published in the *Gazette* containing details of the registration of agricultural and veterinary chemical products and other approvals granted by the Australian Pesticides and Veterinary Medicines Authority. The Agvet Code and related legislation also requires certain other notices to be published in the *Gazette*. A reference to Agvet Codes in this publication is a reference to the Agvet Code in each state and territory jurisdiction.

ISSN 1837 - 7629

The Manager, Public Affairs and Communications
The Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Email: communications@apvma.gov.au
Website: www.apvma.gov.au.

GENERAL INFORMATION

The *APVMA (Australian Pesticides and Veterinary Medicines Authority) Gazette* is published fortnightly and contains details of the registration of agricultural and veterinary chemicals products and other approvals granted by the APVMA, notices as required by the Agricultural and Veterinary Chemicals Code (the Agvet Code) and related legislation and a range of regulatory material issued by the APVMA.

Pursuant to section 8J(1) of the Agvet Code, the APVMA has decided that it is unnecessary to publish details of applications made for the purpose of notifying minor variations to registration details. The APVMA will however report notifications activity in quarterly statistical reports.

DISTRIBUTION AND SUBSCRIPTION

The *APVMA Gazette* is published in electronic format only and is available from the APVMA website, www.apvma.gov.au/publications/gazette/.

If you would like to receive email notification when a new edition is published, please subscribe on the APVMA website.

APVMA CONTACTS

For enquiries regarding the publishing and distribution of the *APVMA Gazette*: Telephone: +61 2 6210 4870

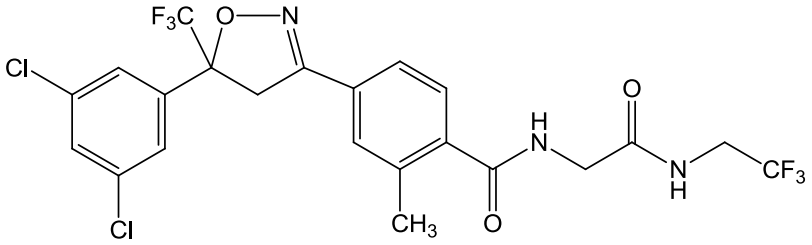
For enquiries on the *APVMA Gazette* content, please refer to the individual APVMA contacts listed under each notice.

CONTENTS

Fluralaner (active) in the products Bravecto 1400 mg Fluralaner Chewable Tablets for Very Large Dogs, Bravecto 1000 mg Fluralaner Chewable Tablets for Large Dogs, Bravecto 500 mg Fluralaner Chewable Tablets for Medium Dogs, Bravecto 250 mg Fluralaner Chewable Tablets for Small Dogs and Bravecto 112.5 mg Fluralaner Chewable Tablets for Very Small Dogs

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has before it and application from Intervet Australia Pty Limited for the approval of a new active constituent fluralaner. The APVMA also has before it applications from the same applicant for the registration of five new products containing the new active constituent. The products are Bravecto 1400 mg Fluralaner Chewable Tablets for Very Large Dogs, Bravecto 1000 mg Fluralaner Chewable Tablets for Large Dogs, Bravecto 500 mg Fluralaner Chewable Tablets for Medium Dogs, Bravecto 250 mg Fluralaner Chewable Tablets for Small Dogs and Bravecto 112.5 mg Fluralaner Chewable Tablets for Very Small Dogs.

PARTICULARS OF THE ACTIVE CONSTITUENT

Common name:	Fluralaner
IUPAC name:	4-[5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4-H-isoxazol-3-yl]-2-methyl-*N*-[2-oxo-2-(2,2,2-trifluoroethylamino)ethyl]benzamide
CAS name:	Benzamide, 4-[5-(3,5-dichlorophenyl)-4,5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-2-methyl-*N*-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl]
CAS registry number:	864731-61-3
Manufacturer's codes:	Carbamoyl Benzamide Phenyl Isoxazoline CBPI AH252723 A1443
Molecular formula:	$C_{22}H_{17}Cl_2F_6N_3O_3$
Molecular weight:	556.3
Structure:	
Chemical family:	Isoxazoline-substituted benzamide derivatives

SUMMARY OF THE APVMA'S EVALUATION OF FLURALANER ACTIVE CONSTITUENT

Fluralaner is a new active constituent and there is no compendial specification available.

The APVMA has evaluated the chemistry and manufacturing aspects of fluralaner and is satisfied that criteria (including the physico-chemical properties, spectral identification, manufacturing and quality control aspects, impurity formation, active constituent specification, stability, batch analysis, analytical methods and packaging information) necessary for the approval of this new active constituent have been met.

The Office of Chemical Safety (OCS) in the Department of Health has conducted a toxicological assessment of fluralaner and advised that there are no objections on human health grounds to the approval of the active constituent fluralaner. Based on the data provided fluralaner has low acute oral and dermal toxicity, is not a skin and eye irritant and not a skin sensitiser. Fluralaner is not genotoxic, is unlikely to be carcinogenic and does not appear to affect reproductive parameters. First Aid Instructions and Safety Directions are required for these products and will be included on the product labels.

An Acceptable Daily Intake (ADI) and Acute Reference Dose (ARfD) were not established as the products are intended for use in non-food-producing animals.

The Delegate to the Secretary of the Department of Health for scheduling has included fluralaner in Schedule 5 of the Standard for the Uniform Scheduling of Medicines and Poisons.

The APVMA accepts the findings and recommendations of its advisors on these criteria. The APVMA is satisfied that the proposed use of fluralaner would not be an undue hazard to the safety of people exposed to it during its handling and use.

PARTICULARS OF THE PRODUCT APPLICATIONS

Proposed product name(s):	Bravecto 1400 mg Fluralaner Chewable Tablets for Very Large Dogs Bravecto 1000 mg Fluralaner Chewable Tablets for Large Dogs Bravecto 500 mg Fluralaner Chewable Tablets for Medium Dog Bravecto 250 mg Fluralaner Chewable Tablets for Small Dogs Bravecto 112.5 mg Fluralaner Chewable Tablets for Very Small Dogs
Applicant company:	Intervet Australia Pty Limited
Name of active constituent:	Fluralaner
Signal heading:	Schedule 5
Summary of proposed use:	For the treatment and prevention of flea infestations and ticks on dogs and puppies.
Pack sizes:	1 tablet, 2 tablets, 4 tablets

Summary of the APVMA's evaluation of Bravecto 1400 mg Fluralaner Chewable Tablets for Very Large Dogs, Bravecto 1000 mg Fluralaner Chewable Tablets for Large Dogs, Bravecto 500 mg Fluralaner Chewable Tablets for Medium Dogs, Bravecto 250 mg Fluralaner Chewable Tablets for Small Dogs and Bravecto 112.5 mg Fluralaner Chewable Tablets for

Very Small Dogs (the products) in accordance with the requirements of section 14(1)(c) of the Agricultural and Veterinary Chemicals Code (the 'Agvet code'), scheduled to the *Agricultural and Veterinary Chemicals Code act 1994*

1. The APVMA has evaluated the applications and in its assessment in relation to human and environmental safety under section 14(3)(e) of Agvet Code, and proposes to determine that:

   (i) The APVMA is satisfied that the proposed use the products would not be an undue hazard to the safety of people exposed to them during their handling (section 14(3)(e)(i)).

   The Office of Chemical Safety (OCS) in the Department of Health has conducted a risk assessment on the products and found that the submitted data supports the safe use of the products from a toxicological perspective.

   The acute toxicity of the products were estimated based on information provided for the active constituent and information available on the product formulation excipients. Based on the toxicity profile of the active constituent and those of the product excipients, the products are expected to be slight skin and eye irritants but not skin sensitisers. The products are expected to have low acute oral and dermal toxicity. Although an inhalational toxicity study was not presented, its omission was not considered critical because the likelihood of significant inhalation exposure from the tablet formulations is expected to be low.

   To mitigate the risks associated with using these products the OCS has recommended first aid statement (a) *If poison occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26*. This First Aid Instruction will be included on the product labels. The OCS has recommended the following safety directions *May irritate the eyes and skin. Avoid contact with the eyes and skin. Wash hands after use*. These Safety Directions will be included on the product labels.

   The APVMA has considered and accepted the findings and recommendations of the OCS.

   (ii) The APVMA is satisfied that the proposed use of the products will not be an undue hazard to the safety of people using anything containing its residues (section 14(3)(e)(i))

   The products are for use in non-food-producing animals only, therefore fluralaner or its metabolites are unlikely to enter the food chain. No Acceptable Daily Intake (ADI) or Acute Reference Dose (ARfD) was established as the products will not be used in food-producing species.

   (iii) The APVMA is satisfied that the proposed use of the products is not likely to be harmful to human beings (section 14(3)(e)(ii)) if used according to the product label directions.

   The Delegate to the Secretary of the Department of Health for scheduling has included the products in Schedule 5 of the Standard for the Uniform Scheduling of Medicines and Poisons. The appropriate Signal Heading for Schedule 5 will be included on the product labels. The appropriate First Aid Instructions and Safety Directions will be included on the product labels.

2. The APVMA has evaluated the applications and in its assessment in relation to environmental safety under section 14(3)(e)(iii) of the Agvet Code it proposes to determine that:

   (i) The APVMA is satisfied that the proposed use of the products would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment if used according to the product label directions.

The Department of the Environment (DE) has advised that the products meet the criteria for the environmental risk assessment to stop at VICH Phase I (where the potential for environmental exposure is assessed based on the intended use of the product). DE has recommended to the APVMA that the use of the products in the proposed manner and with the estimated levels of use is unlikely to have an unintended effect that is harmful to the environment.

The APVMA has considered these findings and accepts the recommendations of DE. The product labels will contain a suitable disposal statement.

The APVMA has assessed the safety of the products to target animals based on data submitted by the applicant. The margin of safety data supported a 5x safety margin in healthy dogs and puppies from eight week of age. The safety margin is based on the maximum label dose rate of 30 mg/kg bodyweight orally three times at eight week intervals. The efficacy and safety data support that the product formulation has an acceptable safety profile in the target animal (dogs) when used according to the label directions.

The APVMA is satisfied that the products would not have an unintended effect that is harmful to animals. Precautions will be included on the product labels.

3. The APVMA has evaluated the applications and in its assessment in relation to whether the trade criterion has been met in accordance with section 14(3)(e)(iv) of the Agvet Code it proposes to determine that:

(ii) The APVMA is satisfied that the proposed use of the products would not unduly prejudice trade or commerce between Australia and places outside Australia as the products are for use in dogs. Dogs are not food-producing animals nor do they produce any major Australian export commodities.

4. The APVMA has evaluated the applications and in its assessment in relation to whether the efficacy criterion has been met in accordance with section 14(3)(f) of the Agvet Code, if proposes to determine that:

(iii) The APVMA is satisfied that the data from trials supporting the efficacy of the products adequately demonstrate that the products will be effective for the proposed use if used according to the product label directions.

Data from dose determination (flea & tick), dose confirmation (flea & tick), flea field efficacy, flea simulated home efficacy, flea speed-of-kill, flea *in vitro* and palatability studies were provided in support of efficacy of the products.

Dose confirmation studies for ticks (*Ixodes holocyclus*) included untreated control groups and groups treated with the product on Day 0. Dogs were infested with ticks on days -1, 14, 28, 42, 56, 70, 84, 112 and 140. Ticks were counted 24, 48 and 72 hours after treatment/reinfestation when any remaining ticks were removed. Efficacy at 72 hours after treatment or reinfestation was >95% at each time point.

The dose confirmation, field efficacy and simulated home efficacy studies submitted to support a claim against fleas (*Ctenocephalides felis*) were appropriately controlled and consistently demonstrated efficacy >95% at time points up to three months after treatment.

The palatability study included 144 healthy dogs. A palatability percentage was calculated as 91.7% (132 of 144 dogs voluntarily ingested the product when it was offered).

The data generated from the studies provided are consistent with claims: ‘treatment and prevention of paralysis tick (*Ixodes holocyclus*) for up to four months’ and ‘three monthly treatment and prevention for flea (*Ctenocephalides felis*) infestations’.

MAKING A SUBMISSION

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether fluralaner should be approved and whether the applications for registration of the products should be granted. Submissions should relate only to matters that the APVMA is required by legislation to take into account in deciding whether to approve the active or grant the registration applications for the products. These grounds include: for approval of the active constituent, the safety and trade criteria. For the registration applications for the products: the safety, efficacy and trade criteria. Submissions should state the grounds on which they are based. Comments received outside these grounds cannot be considered by the APVMA.

Submissions must be received by the APVMA within **28 days** of the date of this notice and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Flural relevant comments will be taken into account by the APVMA in deciding whether the active constituent should be approved and whether the products should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address
- the date you made the submission.

All personal and confidential commercial information (CCI) material contained in submissions will be treated confidentially.

Written submissions should be addressed in writing to:

Enquiries
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604

Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

Amendments to the APVMA MRL Standard

The Australian Pesticides and Veterinary Medicines Authority (APVMA) approves maximum residue limits (MRLs) of agricultural and veterinary chemicals in agricultural produce, particularly produce entering the food chain. The MRLs approved by the APVMA are associated with a regulatory decision to register a product, grant a permit approval, or as an outcome from a review decision and are set out in the *Agricultural and Veterinary Chemicals Code Instrument No. 4 (MRL Standard) 2012*. The *MRL Standard* lists MRLs of substances that may arise from the approved use of agricultural and veterinary chemical products containing those substances on commodities used for human consumption as well as livestock feeds. The *MRL Standard* also provides the relevant residue definitions to which these MRLs apply. There may be situations where the residue definition for monitoring and enforcement is different to the definition used for dietary risk assessment purposes.

MRLs are set at levels which are not likely to be exceeded if the agricultural or veterinary chemicals are used in accordance with approved label instructions. In considering MRLs and variation to MRLs, the APVMA takes into account studies on chemistry, metabolism, analytical methodology, residues, toxicology, good agricultural practice and dietary exposure. In approving MRLs, the APVMA is satisfied, from dietary exposure assessment, that the levels set are not an undue hazard to human health.

The APVMA has amended the *MRL Standard* with affect from 28 November 2014.

Details of the amendment can be found in the *Agricultural and Veterinary Chemicals Code Instrument No. 4 (MRL Standard)* Amendment Instrument 2014 (No. 11).

The amendments will be incorporated into the compilation of the Agricultural and Veterinary Chemicals Code Instrument No. 4 (MRL Standard) 2012.

The *MRL Standard* is accessible via the ComLaw website www.comlaw.gov.au or the links above.

For further information please contact:

MRL Contact Officer
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604

Phone: +61 2 6210 4897
Fax: +61 2 6210 4840
Email: enquiries@apvma.gov.au

Proposal to Amend Standard 1.4.2 of the Australia New Zealand Food Standards Code

In the previous notice, the APVMA gazetted that amendments which it has approved varying maximum residue limits (MRLs) for substances contained in agricultural and veterinary chemical products as set out as in the APVMA's *MRL Standard*, have been made.

Under Section 82 of the *Food Standards Australia New Zealand Act 1991* the APVMA is proposing to incorporate those variations (*Agricultural and Veterinary Chemicals Code Instrument No. 4 (MRL Standard)* Amendment Instrument 2014 (No. 11)) to MRLs into Standard 1.4.2. Maximum Residue Limits of the Australia New Zealand Food Standards Code.

MRLs contained in Standard 1.4.2 provide the limits for residues of agricultural and veterinary chemicals that may legitimately occur in foods. By this means, Standard 1.4.2 permits the sale of treated foods and protects public health and safety by minimising residues in foods consistent with the effective control of pests and diseases.

The APVMA and FSANZ are satisfied, based on dietary exposure assessments and current health standards, that the proposed limits are not harmful to public health.

The Agreement between the Government of Australia and the Government of New Zealand concerning a Joint Food Standards System, excludes MRLs for agricultural and veterinary chemicals in food from the system setting joint food standards. Australia and New Zealand independently and separately develop MRLs for agricultural and veterinary chemicals in food.

Food Standards Australia New Zealand (FSANZ) will make a Sanitary and Phytosanitary (SPS) notification to the World Trade Organization (WTO).

The APVMA invites comment on these proposals. Details on how to make a submission appear near the end of this notice, below the details of the proposed amendment.

The APVMA will consider any public comments made in response to this proposal. If the APVMA decides to proceed with the proposal, it will further notify any variations it makes to Standard 1.4.2 in the APVMA *Gazette*. The variations will take effect as from the date of that subsequent notice.

DRAFT VARIATIONS TO THE *AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE*

Note: The following amendments are in a format that accords with the proposed amending Legislative Instrument which, in turn, has to be consistent with the existing format of Standard 1.4.2 (Maximum Residue Limits) of the *Australia New Zealand Food Standards Code*.

PROPOSED AMENDMENT (*AGRICULTURAL AND VETERINARY CHEMICALS CODE INSTRUMENT NO. 4 (MRL STANDARD)* AMENDMENT INSTRUMENT 2014 (NO. 11))

Note: Subsection 82(2) of the *Food Standards Australia New Zealand Act 1991* provides that variations to standards are legislative instruments, but are not subject to disallowance or sunsetting.

To commence: on gazettal of variation

Standard 1.4.2 of the Australia New Zealand Food Standards Code is varied by –

1. *inserting in alphabetical order in* Schedule 1, *the foods and associated MRLs for each of the following chemicals*

Dimethomorph Sum of E and Z isomers of dimethomorph	
Beetroot	T0.1
Mizuna	T10
Parsley	T2
Radish	T0.1
Haloxyfop Sum of haloxyfop, its esters and conjugates, expressed as haloxyfop	
Green Elk	T0.5
Leafy vegetables [except mizuna]	T0.5
Mizuna	T0.5
Metalaxyl Metalaxyl	
Beetroot	T*0.01
Beetroot leaves	T0.1
Vegetables [except asparagus; beetroot; bulb vegetables [alliums]; fruiting vegetables, cucurbits; leafy vegetables; peppers; podded pea (young pods) (snow and sugar snap peas)]	T0.1
Pymetrozine Pymetrozine	
Leafy vegetables [except mizuna]	T5

2. *omitting from* Schedule 1 *the foods and associated MRLs for each of the following chemicals –*

Dimethomorph Sum of E and Z isomers of dimethomorph	
Brassica leafy vegetables	T2

Metalaxyl Metalaxyl	
Vegetables [except asparagus; bulb vegetables [alliums]; fruiting vegetables, cucurbits; leafy vegetables; peppers; podded pea (young pods) (snow and sugar snap peas)]	T0.1
Pymetrozine Pymetrozine	
Leafy vegetables	T5

3. *omitting from* Schedule 1, *under the entries for the following chemicals, the maximum residue limit for the food, substituting –*

Dimethomorph Sum of E and Z isomers of dimethomorph	
Leafy vegetables [except lettuce head]	T10
Pymetrozine Pymetrozine	
Fruiting vegetables, cucurbits	T1
Spirotetramat Sum of spirotetramat, and cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat	
Banana	0.3

INVITATION FOR SUBMISSIONS

Written submissions are invited from interested individuals and organisations to assist the APVMA in considering the proposal to vary Standard 1.4.2–Maximum Residue Limits of the *Australia New Zealand Food Standards Code.* Submissions should be strictly confined to relevant matters that the APVMA must consider (such as public health and safety) which are associated with the occurrence of the proposed residues in foods. Comments received outside these grounds will not be considered by the APVMA. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

Please note that FSANZ will make a SPS notification to the WTO and submissions related to impacts on international trade should be made to FSANZ in response to that notification.

Submissions must be made in writing and should be clearly marked as a 'submission on the proposed amendment to Standard 1.4.2' and quote the correct amendment number.

DEADLINE FOR PUBLIC SUBMISSIONS: **6 pm (AEDT) 12 January 2015**

SUBMISSIONS RECEIVED AFTER THIS DEADLINE WILL ONLY BE CONSIDERED BY PRIOR ARRANGEMENT

Submissions received after this date will only be considered if agreement for an extension has been given prior to this closing date. Agreement to an extension of time will only be given if extraordinary circumstances warrant an extension to the submission period.

For further information please contact:

MRL Contact Officer
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604

Phone: +61 2 6210 4897
Fax: +61 2 6210 4840
Email: enquires@apvma.gov.au