Australian Government

Australian Pesticides and Veterinary Medicines Authority

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Polihexanide: Proposed Regulatory Decisions

The reconsideration of products containing polihexanide and approvals of their associated labels

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FOREWARD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals in Australia. Its statutory powers are provided in the Agvet Codes scheduled to the *Agricultural and Veterinary Chemicals Code Act 1994*.

The APVMA has legislated powers to reconsider the approval of an active constituent, registration of a chemical product or approval of a label at any time after it has been registered. The reconsideration process is outlined in Part 2, Division 4 of the Agvet Codes.

A reconsideration may be initiated when new research or evidence has raised concerns about the use or safety of a particular chemical, a product containing that chemical, or its label. The scope of each reconsideration can cover a range of areas including human health (toxicology, public health, occupational health and safety), the environment (environmental fate and ecotoxicology), residues and trade, chemistry, efficacy or target crop or animal safety. However, the scope of each reconsideration is determined on a case- by-case basis reflecting the specific issues raised by the new research or evidence.

The reconsideration process includes a call for data from a variety of sources, a scientific evaluation of that data and, following public consultation, a regulatory decision about the ongoing use of the chemical or product. The data required by the APVMA must be generated according to scientific principles. The APVMA conducts science and evidence-based risk analysis with respect to the matters of concern, analysing all relevant information and data available.

In undertaking reconsiderations, the APVMA works in close cooperation with external experts including the Department of the Environment and Energy, Food Standards Australia New Zealand (FSANZ), and the state departments of agriculture, as well as other expert advisers as appropriate.

This document, *Polihexanide: Proposed Regulatory Decisions* (PRD) document, sets out the APVMA's proposed regulatory decisions relating to products containing polihexanide when used in accordance with approved label instructions.

This PRD and supporting technical reports on polihexanide are available from the APVMA website. The technical reports include:

- Polihexanide Carcinogenicity Hazard Assessment Report (published June 2011), and
- Human Health Risk Assessment of Polihexanide (published January 2018).

SUBMISSIONS FROM THE PUBLIC ARE INVITED

This proposed regulatory decision report:

- outlines the APVMA reconsideration process
- summarises the technical assessments
- outlines the proposed regulatory action to be taken.

The APVMA invites written comments on this report (from 25 January 2018 to 27 April 2018). All comments on this report will be assessed by the APVMA prior to finalisation of the reconsideration and publication of the final regulatory decision report.

Preparing your comments for submission

When making your comments:

- clearly identify the issue and clearly state your point of view
- give reasons for your comments, supporting them, if possible, with relevant scientific information and indicating the source of the information you have used
- suggest to the APVMA any alternative risk management solutions you may have.

Please structure your comments in point form, referring each point to the relevant section in the report.

All submissions to the APVMA will be acknowledged in writing via email or by post.

When making a submission please include:

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

Note that all submissions received are subject to the Freedom of Information Act 1982, the Privacy Act 1988 and the Agvet Code. All personal and confidential commercial information (CCI) material contained in submissions will be treated confidentially. (A full definition of 'confidential commercial information' is contained in the Agvet Code).

The closing date for submissions is 27 April 2018.

Submissions can be sent to:

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EXECUTIVE SUMMARY

Polihexanide is a polymer of chlorhexidine. It is used as an antimicrobial for the control of microorganisms, in swimming pools and spas. It is also used as an antimicrobial agent in veterinary products used for topical application on dogs, cats and horses (as a skin treatment and to prevent re-infestation) or to clean and reduce microorganisms in ears of dogs; and as disinfectant in surface, equipment, air space and animal housing cleaning products.

The reconsideration of registrations of products containing polihexanide and associated label approvals began in July 2005 based on the advice from the then Office of Chemical Safety (OCS) within the Department of Health, which identified polihexanide as a potential carcinogen.

As part of the reconsideration, the OCS completed a toxicological hazard assessment of potential carcinogenicity for polihexanide, published in 2011. The assessment identified polihexanide as a potential carcinogen in whole-of life studies in rodents via the oral route but only at high exposure levels, unlikely to be encountered in occupational or public settings. Since polihexanide did not appear to be genotoxic and clear NOAELs (no observed adverse effect levels) were demonstrated in animal carcinogenicity studies, the OCS did not regard carcinogenicity findings in rodents as a barrier to continuing registration of products containing polihexanide.

There are no Australian or Codex Maximum Residue Limits (MRLs), and no acute reference dose (ARfD) or acceptable daily intake (ADI) for polihexanide. There are no direct food uses registered for polihexanide in Australia. There is very limited potential for inadvertent contamination of food based on current Australian use patterns. On that basis, there are no grounds for establishing an acute ARfD or ADI/tolerable daily intake (TDI) for polihexanide.

A risk assessment was conducted for workers exposed to polihexanide when using pool chemicals and veterinary disinfectants. In addition, the use of domestic veterinary products was considered, as was post-application exposure for the public bathing in pools/spas treated with polihexanide products. Both qualitative and quantitative risk assessments were undertaken.

After consideration of the hazards associated with the products, along with the exposure and risks expected with use of the products, it was concluded that all product registrations can continue to be supported after varying the labels to update the first aid instructions and safety directions.

1 INTRODUCTION

Polihexanide or poly(hexamethylene) biguanide hydrochloride or PHMB is a polymer of chlorhexidine and a member of the guanidine family. Two CAS numbers (27083-27-8 and 32289-58-0) are currently used for polihexanide, both relating to the hydrochloride salt, the former relating to the technical material and the latter to the pure polymer (minus monomers). Polihexanide is a cationic biocide and binds to the negatively charged phosphate head groups of phospholipids on the bacterial cell wall, resulting in a disruption of the membrane culminating in cell death.

1.1 Current use patterns

Polihexanide is widely used in Agricultural and Veterinary (Agvet) products as a biocide for control of micro-organisms, and algae in swimming pools and spas, as a disinfectant for veterinary hospitals and animal accommodations, and antiseptic in veterinary products (Table 2). These products are regulated by the APVMA.

Polihexanide is also used in non-agricultural and veterinary situations such as a biocide (disinfectant) in medical equipment, medical procedures, contact lens cleansers, food preparation surfaces, and industrial uses. Other authorities are responsible for regulating those uses.

Table 1: Uses of polihexanide products registered in Australia (includes only those products regulated by the APVMA)

Situation	Polihexanide content	Other active constituents
Swimming pools and spas sanitisers	20–200 g/L	None
Veterinary products used as surface, equipment, air space and animal housing disinfectants	4 g/L 1 g/L	Benzalkonium chloride Benzalkonium chloride Didecyl dimethyl ammonium chloride
Veterinary products—germicidal products for topical application	0.3 g/L 2 g/L	Benzalkonium chloride Disodium edetate

1.2 Current regulatory status of polihexanide in Australia

Polihexanide is currently listed as an exempt active constituent by the APVMA, meaning that active constituent approval is not required.

Polihexanide is currently listed in Schedule 6 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), except when in preparations at a concentration of 5% or less polihexanide.

As of January 2018, nineteen products containing polihexanide are registered (Table 1), and are included in this review.

Table 2: Polihexanide products registered in Australia (includes only those products regulated by the APVMA)

APVMA product registration number	Product name	Registration holder	Associated label approval numbers
Pool and spa products			
48356	HTL Bio-Blu Swimming Pool and Spa Water Treatment and Sanitiser	HTL Pty Ltd	48356/107402 48356/01
49284	King Neptune's Ozone Clear Pool Sanitiser	Isaac Technologies Pty Ltd	49284/1098
57606	Aquafresh by Lo-Chlor Pool Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	57606/56365 57606/0603
59949	Aquaspa By Lo-Chlor Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	59949/0509 59949/0408
61106	Clark Rubber Filtrite Sanit-Eezy for Family Pools Eezy Sanitiser	Clark Rubber Franchising pty Ltd	61106/59508 61106/0606
64278	Nature Spa Spa Water Treatment & Sanitiser	Enviro Spa & Pool Pty Ltd	64278/0909
64823	Clark Rubber Filtrite Sanit-Eezy Eezy Sanitiser	Clark Rubber Franchising pty Ltd	64823/50208
66624	Crystal Waters Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	66624/56198 66624/54048
66943	Crystal Waters Pool Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	66943/57122 66943/54752
68964	Filtrite Sanit-Eezy Eezy Sanitiser for Spas Spa Sanitiser	Clark Rubber Franchising pty Ltd	68964/59507

APVMA product registration number	Product name	Registration holder	Associated label approval numbers
82162	Spa Soft Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	82162/105117
Veterinary products—surface, equipment, air space and animal housing disinfectants			
54149	F10SC Veterinary Disinfectant	Health & Hygiene Pty Ltd	54149/0502
59720	F10SCXD Veterinary Disinfectant Cleanser	Health & Hygiene Pty Ltd	59720/1105
59998	Trigene II Virucidal Disinfectant Concentrate	Ceva Animal Health Pty Ltd (formerly Delvet Pty Ltd)	59998/0906
62103	Microtech 7000 General Purpose Disinfectant	Chemetall (Australasia) Pty Ltd	62103/0508
70073	Safe4 Disinfectant Cleaner Concentrate	Safe4 All (Aust) Pty Ltd	70073/106951 70073/62442
Veterinary products—germicidal products for topical application			
58543	F10 Germicidal Treatment Shampoo	Health & Hygiene Pty Ltd	58543/0207 58543/0904
58544	F10 Germicidal Barrier Ointment	Health & Hygiene Pty Ltd	58544/1105 58544/0904
60080	Dermcare Otoflush	Dermcare-Vet Pty Ltd	60080/0407

1.3 APVMA reconsideration of polihexanide

Registrations of polihexanide products and their label approvals were placed under reconsideration in 2005, based on advice from the Office of Chemical Safety (OCS), which identified polihexanide as a potential carcinogen.

The basis for a reconsideration of the approvals and registrations of a chemical is whether the APVMA remains satisfied that the safety, efficacy and trade criteria listed in sections 5A, 5B and 5C of the Agvet Codes for continued registration and approval are being met. The requirements that are relevant to the scope of this reconsideration (toxicology and human health) are that the use of the product in accordance with instructions approved, or to be approved, by the APVMA for the product or contained in an established standard:

- would not be an undue hazard to the safety of people exposed to it during its handling or people using anything containing its residues; and
- would not be likely to have an effect that is harmful to human beings.

The APVMA also considers whether labels for containers for chemical products containing polihexanide meet the labelling criteria as defined in section 5D of the Agvet Code which requires that labels have adequate instructions relating to:

- the circumstances in which the product should be used
- how the product should be used
- the times when the product should be used
- the frequency of the use of the product
- the re-entry period after use of the product
- the withholding period after the use of the product
- disposal of the product and its container
- safe handling of the product and first aid in the event of an accident
- any matters prescribed by the regulations.

There are three possible outcomes of the reconsideration of the registration of products containing polihexanide and all associated label approvals. Based on the information evaluated by the APVMA, it may be:

- satisfied that the product registrations and associated label approvals continue to meet the safety and labelling criteria and therefore affirms the registrations and approvals
- not satisfied that the approvals and registrations meet the safety and labelling criteria but is satisfied that the relevant particulars or conditions of those registrations or approvals can be varied in such a way as to allow the approval or registration to be affirmed
- not satisfied that the relevant particulars or conditions of those registrations or approvals can be varied in such a way as to allow the approval or registration to be affirmed and thus suspends or cancels the registration and/or approvals.

2 INTERNATIONAL REGULATORY STATUS

United States

Polihexanide was first registered in the United States in 1982 as an active ingredient.

Polihexanide products are registered for use as a fungicide, algicide and sanitizer in swimming pools, preservative for cut flowers; materials preservative; bacteriostat in industrial processes and water systems, and hard surface disinfectant. About 95% of the use of polihexanide is said to be for pools and spas. Surface disinfectant uses include uses on food and non-food contact surfaces, in agricultural premises and equipment, commercial and industrial premises and equipment, and medical premises and equipment.

Polihexanide was reviewed by the US EPA in 2004 and noted as having very low aggregate risk of adverse health effects to the public or environment.

Polihexanide is exempt from the registration of a tolerance for residues on all foods when the residues arise from its use as a surface sanitizer and therefore there is no requirement to set maximum permissible levels for residues of polihexanide.

European Union

Polihexanide as an active constituent is supported under Directive 98/8/EC for uses as a disinfectant.

Biocidal products containing polihexanide are allowed for several types of application. Uses include disinfection of surfaces, materials, equipment and furniture which are not used for direct contact with food or feeding stuffs; air conditioning systems; walls and floors in private, public and industrial areas; as algaecides for treatment of swimming pools, aquariums, bathing and other waters; veterinary hygiene purposes and to disinfect the materials and surfaces associated with the housing or transportation of animals; disinfection of equipment, containers, consumption utensils, surfaces or pipework associated with the production, transport, storage or consumption of food or feed to control algae, microbes and mussels in water or other liquids used in cooling and processing systems.

In 2007, the agency responsible for regulation of biocides in the EU scheduled polihexanide for a review. In February 2010, France, the rapporteur member state submitted a proposal for harmonised classification and labelling (CLH). This report considered all human health and environmental endpoints. It concluded that polihexanide is not genotoxic *in vitro* and *in vivo* and a classification as carcinogenic category 3 (agent is not classifiable as to its carcinogenicity to humans), R40 (limited evidence of carcinogenic effect) is warranted.

EU determined that polihexanide is not safe for consumers when used as a preservative in cosmetic products up to the maximum concentration of 0.3%. At this concentration or above, polihexanide is not allowed for products used for application on skin.

3 SUMMARY OF ASSESSMENTS AND PROPOSED FINDINGS

3.1 Toxicology

In June 2011, the APVMA published the polihexanide toxicology assessment entitled *Polihexanide Carcinogenicity: Analysis of Human health Risk*. The assessment was conducted by the then Office of Chemical Safety (OCS–within the Department of Health). The OCS assessed toxicology data submitted to the reconsideration, together with information from its toxicological database and relevant published data.

Toxicokinetics

The gastrointestinal absorption of polihexanide ranged from 2.6 to 7.8%, with 90% of an oral dose of polihexanide excreted via the faeces with <1% biliary excretion. Very small quantities were excreted in the urine (2–3%). There were no percutaneous absorption studies available for evaluation. However, it is generally considered that the level of dermal absorption would not exceed the level of gastrointestinal absorption.

Acute toxicity

Repeat-dose oral studies in mice, rats and dogs demonstrated that the target organ was the liver.

Polihexanide has low acute oral toxicity in rats. Clinical signs included slight salivation, lacrimation and piloerection and in some cases a subdued appearance. At the highest dose, there was also wheezing and staining around the mouth.

In an acute dermal toxicity study in rats, where moistened solid polihexanide was applied to the skin and resulted in no deaths at up to 5000 mg/kg bw. OCS concluded that dermal LD50 of polihexanide is greater than 5000 mg/kg bw.

Polihexanide is regarded as a slight skin irritant, severe eye irritant and mild to moderate skin sensitiser.

Repeat-dose toxicity

Reduced body weight gain was the most common effect in repeat-dose animal studies. Repeat-dose oral studies in mice, rats and dogs demonstrated that the target organ was the liver. Liver effects in chronic studies in mice included hepatocyte hypertrophy, induction of hepatic DNA synthesis and increased pigmentation and increased incidence of extramedullary haematopoiesis in the spleen.

Other effects noted in repeat-dose studies include increased mortality and weight loss, reduced body weight gain in mice, rats and dogs, histopathological changes in the kidney, spleen and gall bladder of mice and in the testes of dogs.

In a 28–d repeat dose inhalation study in rats, a NOAEL of 0.024 mg/m3 was established based on histopathological changes in the larynx (squamous metaplasia).

In a short term dermal study in mice (21–d), doses up to 200 mg/kg bw/d did not result in any systemic toxicity, although local dermal effects (erythema, oedema and scabbing) were noted from 60 mg/kg bw/d. A chronic dermal study in mice showed irritation to the skin, hyperkeratosis and desquamation only at much higher doses (30 mg/mouse, approximately 1500 mg/kg bw/d). Systemic effects were noted at this dose, including increased mortality, hepatotoxicity, bilateral protrusion of the eyes, and reduced body weight gain. It can be concluded that the dermal NOAEL for systemic effects in both short- and long-term studies in rats and mice is greater than 300 mg/kg bw/d.

Neurotoxicity

No specific neurotoxicity studies were submitted for the review. In single-and repeat-dose toxicity studies conducted, no evidence of neurotoxicity was observed.

Reproductive and developmental effects

In a two-generation reproduction conducted in rats there was no evidence that polihexanide caused reproductive toxicity. There was no evidence that polihexanide was teratogenic in rats or rabbits. Increased incidence of extra ribs and skeletal variations of the sternebrae occurred in rat and rabbit studies respectively, but only at maternotoxic doses.

Genotoxicity

There was no evidence that polihexanide is genotoxic *in vitro* or *in vivo*.

Carcinogenicity

In carcinogenicity assessment, polihexanide was identified as a potential carcinogen in chronic oral rodent studies. In a chronic study in mice, haemangiosarcoma in the liver and squamous cell carcinoma at the recto-anal junction were noted at high exposure levels (approximately 700–850 mg/kg bw/d). The squamous cell carcinoma was considered to be a consequence of chronic irritation and subsequent inflammation. In a chronic rat study, 1/128 females had haemangiosarcoma in the liver and 4/128 had haemangioma in the liver at doses of approximately 120–160 mg/kg bw/d. As these tumours are rare in this strain of rat, it was considered possible that these tumours were treatment related. An expert review however, concluded that these were only sporadic and not related to treatment, given the absence of pre-neoplastic findings for example.

Polihexanide is therefore associated with cancer in rodents but only at high doses, which are considered unlikely to be encountered in an occupational or public setting. In addition, polihexanide does not appear to be genotoxic, and a clear threshold for effect (NOAEL) was demonstrated in carcinogenicity studies. Therefore the OCS does not consider the observed tumours as a likely health risk to humans from the continued use of polihexanide containing products.

First aid instructions

The current first aid instruction for polihexanide—If poisoning occurs, contact a doctor or Poisons Information Centre—remains appropriate.

Scheduling

The current Scheduling of polihexanide in the SUSMP remains appropriate. It is currently listed in Schedule 6, except when in preparations at a concentration of 5% or less polihexanide.

Some of the currently registered products contain other active constituents. The signal headings and first aid and safety directions for products (see Section 4 of this document) are formulated taking all the active constituents and excipients into account.

The OCS recommended that there were no objections on toxicological grounds to affirm the registration of polihexanide products included in this reconsideration, once the labels are varied to update the signal headings, first aid instructions and safety directions.

3.2 Human health: exposure and risk assessment

The APVMA's assessment of risk to human health from polihexanide products considered the:

- potential exposure during handling or use of the product by users;
- potential post-application exposure to the public; and
- adequacy of the safety directions and need for any additional label warnings or engineering controls.

The risks were evaluated using a Margin of Exposure (MOE) approach, where estimated exposures are compared to a toxicological threshold (the No Observed Adverse Effect Level-NOAEL) for the most sensitive adverse effect relevant to humans. The larger the MOE, the lower the risk. Typically, an MOE of 100 is considered an adequate margin of safety based on non-cancer effect in laboratory animals while an MOE of 10 is considered appropriate based on human data.

In assessing the risk, any other active constituents in the products were also taken into account. Where chemical specific worker exposure data was unavailable, surrogate exposure data (the Pesticide Handler Exposure Database, PHED) were used to estimate exposure during mixing/loading and application.

Based on the risk assessment, risk management measures are then recommended to reduce human exposure to an acceptable level. Those measure may include engineering controls, safety directions (including PPE), use restraints, re-entry intervals, and scheduling recommendations.

A summary of the risk assessment is given below. For detailed risk assessment, see the *Human Health Risk Assessment of Polihexanide*.

Currently nineteen products containing polihexanide are registered (ie products regulated by the APVMA). These products fall into two groups based on their use patterns—pool and spa products and veterinary products.

Pool and spa products

Workers treating pools and spas may be exposed to polihexanide through dermal or ocular contact with the undiluted product when adding it either directly into the pool/spa water or into a bucket of water before addition to pool/spa water.

Professional worker in the pool industry may be employed to perform maintenance, including tasks such as cleaning and adding pool chemicals to domestic pools. Allowing for the time taken to travel between properties and to conduct other activities other than adding pool chemicals, it is estimated up to five pools could be treated in a day. A worker treating five pools may handle 0.6 kg of polihexanide. Workers employed by public pools and home pool owners may also handle the product, but this is expected to result in lower exposure as it would only be weekly application of the chemical.

It is assumed that workers involved in pool maintenance would not routinely be wearing long pants and long sleeves. Dermal exposure is considered unacceptable when gloves are not used (MOE=17). When gloves are used, even without long pants and long sleeves, the dermal exposure is deemed acceptable (MOE=169).

Repeated exposure through the inhalation route is not of concern for these products. Due to the small quantity of product handled (around 1 L for a large pool) and the low vapour pressure of polihexanide, inhalational exposure is expected to be minimal.

As home pool owners and workers employed by public pools are expected to handle the product only weekly, the risk is expected to be much lower when compared to that for professional workers. Hence the risk is acceptable.

For swimmers exposed to treated water

The use of polihexanide containing pool/spa sanitisers will result in public exposure to polihexanide while bathing or swimming in treated pools and spas.

The public exposure assessment is based on the SWIMODEL developed by the US EPA as a screening tool to conduct exposure assessments of chemicals found in swimming pools and spas. Exposure assessments were conducted for adults and children 7–10 years and children 11–14 years using exposure (swimming/bathing) times up to 5 hours.

The estimated exposure from swimming pools and spas is not of concern. The MOEs for estimated dermal exposure range from 117 to 716 for children and adults for competitive and non-competitive swimming scenarios. MOEs for estimated oral exposure, for children and adults computed for both competitive and non-competitive scenarios range from 2,500 to 40,000. Therefore, dermal and oral exposure are acceptable. As the estimated MOE's for both routes ae sufficiently large, the combined exposure (ie dermal + oral) is not of concern.

Veterinary disinfectants

Workers using the veterinary disinfectant products are likely to be exposed via the dermal and inhalation routes, as the products are diluted and used as wash or soaker, as well as a spray or fogger, although at this stage the product is diluted with water. Eye contact is also possible from splashes when pouring the concentrated product, or when using the diluted product as a spray or wash.

One litre of diluted product used for veterinary disinfection may contain up to 0.05 g (=0.00005 kg) of polihexanide. Considering the exposures previously mentioned for a pool worker handling 0.6 kg of polihexanide a day, to achieve a similar level of exposure for a worker using the veterinary disinfectants, they would need to be exposed to a large amount of the product (sufficient to make up 12,000 L). This is clearly unrealistic. Repeat exposure to polihexanide from the veterinary disinfectants is therefore not of concern.

The exposure level when using veterinary disinfectants (5 L of product for use) is acceptable with MOE computed at values greater than 100.

Veterinary topical products

Based on the presentation and use pattern of the products, and the concentration of polihexanide, the level of exposure of veterinarians or pet owners/handlers to polihexanide is likely to be extremely low. The exposures estimated for pool workers handling 0.6 kg of polihexanide a day are acceptable. To achieve a similar level of exposure for a worker using the topical products would need to be exposed to a large amount of the product. Exposure to such large amounts from use of veterinary topical products is clearly unrealistic.

4 PROPOSED RECONSIDERATION DECISIONS

Based on the toxicology and human health risk assessments, the following decisions are proposed as outcomes of the reconsideration.

4.1 Vary relevant particulars of label approvals to satisfy human health and, worker health and safety requirements

Note that where a product currently has multiple label approvals, the variations proposed below apply only to the most recently approved label (Column D, Table 3). The older label approvals (Column E, Table 3) will be cancelled, as, when the reconsideration is completed, the older labels would no longer meet the labelling criteria of the Agvet Codes.

- Vary the relevant particulars of the label approvals of the pool and spa products (48356, 49284, 57606, 61106, 64278, 64823 and 66943) to include the following signal headings, first aid instructions and safety directions.

	Instruction
Signal headings	POISON KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING
First aid instructions	If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766. If in eyes, hold eyes open, flood with water for at least 15 minutes and see a doctor.
Safety directions	May irritate the skin. Will damage the eyes. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. When opening the container and using the product, wear rubber gloves. Wash hands after use. After each day's use wash gloves.

- Vary the relevant particulars of label approvals of spa sanitising products (59949, 66624, 68964 and 82162) to delete the current signal headings and add the following signal heading, first aid instructions and safety direction.

	Instruction
Signal heading	READ SAFETY DIRECTIONS BEFORE OPENING OR USING
First aid instructions	First aid is not generally required. If in doubt, contact a Poisons Information Centre (eg phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.
Safety direction	Wash hands after use.

- Vary the particulars of the label approvals of veterinary disinfectants used for surface, equipment, air space and animal housing disinfection (54149, 59720, 62103 and 70073) to include the following statements. The signal headings on current labels for these products remain appropriate.

	Instruction
First aid instructions	If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766. If swallowed, do NOT induce vomiting. Give a glass of water.
Safety directions	Harmful if swallowed. May irritate the eyes and skin. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. When opening the container and preparing the product for use, wear elbow length chemical resistant gloves. Wash hands after use. After each day's use wash gloves.

- Vary the particulars of the label approvals of the veterinary disinfectant product 59998 used for control of microorganisms in veterinary hospitals and animal accommodation, to delete current first aid instructions and safety directions and to include the following first aid instructions and safety directions. The signal headings on current labels for this product remain appropriate.

	Instruction
First aid instructions	If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766.If swallowed, do NOT induce vomiting. Give a glass of water. If skin contact occurs, remove contaminated clothing and wash skin thoroughly. . If in eyes, hold eyes open, flood with water for at least 15 minutes and see a doctor.
Safety directions	Harmful if swallowed. Product will damage eyes, nose, throat and skin. Avoid contact with eyes and skin. When opening the container and using the product wear rubber gloves. Wash hands after use.

- For the germicidal products for topical application (58543 and 58544), benzalkonium chloride is present at less than the scheduling cut-off, and therefore does not require additional first aid instructions. Vary the particulars of the label approvals of the germicidal products (58543 and 58544) to include the following signal headings, first aid instructions and safety directions.

	Instruction
Signal headings	READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
First aid instructions	First aid is not generally required. If in doubt, contact a Poisons Information Centre (eg phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.
Safety directions	Harmful if swallowed. May irritate the eyes. Avoid contact with eyes. Repeated exposure may cause allergic disorders. Wash hands after use.

- For the product Dermacare Otoflush (60080), the current signal heading and first aid instruction remain appropriate. Vary the particulars of the label approvals of the product to include the following safety directions.

	Instruction
First aid instructions	First aid is not generally required. If in doubt, contact a Poisons Information Centre (eg phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.
Safety direction	Wash hands after use.

4.2 Affirm products with varied labels

After varying the labels as described in Section 4.1, affirm the registrations of the following currently registered products.

Table 3: Details of Polihexanide products label approvals to be varied or cancelled.

APVMA Product registration number (A)	Product name (B)	Registration holder (C)	Label approvals to be varied (D)	Label approvals to be cancelled (E)
48356	HTL Bio-Blu Swimming Pool and Spa Water Treatment and Sanitiser	HTL Pty Ltd	48356/107402	48356/01
49284	King Neptune's Ozone Clear Pool Sanitiser	Isaac Technologies Pty Ltd	49284/1098	
57606	Aquafresh by Lo-Chlor Pool Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	57606/56365	57606/0603
59949	Aquaspa By Lo-Chlor Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	59949/0509	59949/0408
61106	Clark Rubber Filtrite Sanit-Eezy for Family Pools Eezy Sanitiser	Clark Rubber Franchising pty Ltd	61106/59508	61106/0606
64278	Nature Spa Spa Water Treatment & Sanitiser	Enviro Spa & Pool Pty Ltd	64278/0909	
64823	Clark Rubber Filtrite Sanit-Eezy Eezy Sanitiser	Clark Rubber Franchising pty Ltd	64823/50208	
66624	Crystal Waters Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	66624/56198	66624/54048
66943	Crystal Waters Pool Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	66943/57122	66943/54752
68964	Filtrite Sanit-Eezy Eezy Sanitiser for Spas Spa Sanitiser	Clark Rubber Franchising pty Ltd	68964/59507	

APVMA Product registration number (A)	Product name (B)	Registration holder (C)	Label approvals to be varied (D)	Label approvals to be cancelled (E)
82162	Spa Soft Spa Sanitiser	M I International Pty Ltd T/A Lo-Chlor Chemicals	82162/105117	
54149	F10SC Veterinary Disinfectant	Health & Hygiene Pty Ltd	54149/0502	
59720	F10SCXD Veterinary Disinfectant Cleanser	Health & Hygiene Pty Ltd	59720/1105	
59998	Trigene II Virucidal Disinfectant Concentrate	Ceva Animal Health Pty Ltd (formerly Delvet Pty Ltd)	59998/0906	
62103	Microtech 7000 General Purpose Disinfectant	Chemetall (Australasia) Pty Ltd	62103/0508	
70073	Safe4 Disinfectant Cleaner Concentrate	Safe4 All (Aust) Pty Ltd	70073/106951	70073/62442
58543	F10 Germicidal Treatment Shampoo	Health & Hygiene Pty Ltd	58543/0207	58543/0904
58544	F10 Germicidal Barrier Ointment	Health & Hygiene Pty Ltd	58544/1105	58544/0904
60080	Dermcare Otoflush	Dermcare-Vet Pty Ltd	60080/0407	

4.3 Cancel older label approvals

Cancel the label approvals shown in Column E of Table 3, as these labels no longer meet the labelling criteria.

In accordance with s.45B of the Agvet Code, supply and use of products bearing cancelled labels will be allowed for a one-year period.

APVMA will determine that subsection 81(3) is to apply in respect of the pre-variation versions of varied labels (Column D, Table 3). This effectively will allow supply of product with such labels for a one-year period.