Proposed Re-evaluation Decision PRVD2010-06

Hexahydro-1,3,5-*tris* (2-hydroxyethyl)-s-triazine (hexahydrotriazine)

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial hexahydro-1,3,5-*tris*(2-hydroxyethyl)-s-triazine (hexahydrotriazine), Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing hexahydrotriazine in Canada.

An evaluation of available scientific information found that products containing hexahydrotriazine do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of hexahydrotriazine uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing hexahydrotriazine registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for hexahydrotriazine and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of hexahydrotriazine.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health *and* the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

Hexahydrotriazine, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (for example, the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in a 2008 RED, the USEPA concluded that hexahydrotriazine was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Hexahydrotriazine?

Hexahydrotriazine is an antimicrobial agent which acts by releasing formaldehyde.

Hexahydrotriazine is used as a material preservative and machine cleaner to control microbial activity in metalworking fluids and on machine surfaces. Hexahydrotriazine is also used as an in-can material preservative in water-based products such as paints, adhesives, resin solutions, printing inks, stuccos, joint compounds, cleaners, liquid detergents, fabric softeners, floor finishes and liquid polishes.

Health Considerations

Can Approved Uses of Hexahydrotriazine Affect Human Health?

Hexahydrotriazine is unlikely to affect your health when used according to the revised label directions.

People could be exposed to hexahydrotriazine by treating or handling products containing hexahydrotriazine; as well as consumption of food that may have come in contact with surfaces containing residues of hexahydrotriazine, or by entering sites where products containing hexahydrotriazine have been used. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that hexahydrotriazine was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Environmental Considerations

What Happens When Hexahydrotriazine Is Introduced into the Environment?

Hexahydrotriazine is unlikely to affect non-target organisms.

Hexahydrotriazine is primarily used indoors; therefore, the potential for environmental exposure is low. The USEPA concluded that reregistration of hexahydrotriazine was acceptable provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of hexahydrotriazine, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Phase out use in paint.
- Phase out manual application of machine cleaner.
- Phase out use in cleaners, liquid detergents, fabric softeners.
- Reduce application rate in metalworking fluids, hydraulic fluids, chain lubricants, and spin finish emulsions.
- Additional personal protective equipment for handlers.

Environment

Additional advisory label statements pertaining to disposing of wastewater.

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on hexahydrotriazine, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Hexahydrotriazine is an antimicrobial agent which acts by releasing formaldehyde.

Following the re-evaluation announcement for hexahydrotriazine, the registrants of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the labels of commercial end-use products in Canada.

The PMRA used recent assessments of hexahydrotriazine from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for hexahydrotriazine (Grotan), dated 27 June 2008 as well as other information on the regulatory status of hexahydrotriazine in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Hexahydro-1,3,5-*tris*(hydroxyethyl)-s-triazine Grotan (United States)	
Function	Antimicrobial	
Chemical family	Triazine	
Chemical name		
1 International Union of Pure and Applied Chemistry (IUPAC)	2,2`,2`-(1,3,5-triazinane-1,3,5-tryil)triethanol	
2 Chemical Abstracts Service (CAS)	1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol	
CAS Registry Number	4719-04-4	
Molecular formula	$C_9H_{21}N_3O_3$	
Structural formula		
Molecular weight	219.28 amu	
Purity of the technical grade active ingredient	78% nominal (limits: 76.145-80.855%)	78.5% minimum
Registration Number	25714	27854

Based on the manufacturing process used, contaminants of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	4.1×10^{-9} mm Hg
Solubility in water	soluble
***n*-Octanol–water partition coefficient**	Log K_{ow} = 0.0173

2.3 Comparison of Use Patterns in Canada and the United States

Hexahydrotriazine is a formaldehyde releasing antimicrobial agent registered in Canada as a material preservative. It is used in metalworking fluids, hydraulic fluids, chain lubricants, spin finish emulsions and in water-based products such as paints, adhesives, resin solutions, printing inks, stuccos, joint compounds, cleaners, liquid detergents, fabric softeners, floor finishes and liquid polishes. Hexahydrotriazine is formulated as a solution and incorporated into products during manufacture. For metalworking fluid uses, it is also added at regular intervals to control microbial growth.

The American and Canadian use patterns were compared. Based on this comparison of use patterns, it was concluded that the 2008 USEPA RED for hexahydrotriazine (Grotan) is an adequate basis for the re-evaluation of uses of hexahydrotriazine in Canada. The PMRA is aware that the USEPA assessment of formaldehyde releasing active ingredients is ongoing and may re-assess, as required.

All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of hexahydrotriazine. Appendix II lists all hexahydrotriazine products that are registered as of 20 December 2009, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2008 RED, the USEPA concluded that the end-use products formulated with hexahydrotriazine met the safety standard under the American *Federal Insecticide, Fungicide, and Rodenticide Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Hexahydrotriazine is a formaldehyde releaser. When assessing the risks associated with the use of hexahydrotriazine, exposure to formaldehyde must also be considered. The USEPA has classified formaldehyde as a B1 probable human carcinogen; however, is currently reviewing this position. In the interim, risk mitigation measures outlined in the RED were considered to reduce exposure such that cancer risk due to exposure to formaldehyde would not be of concern. The USEPA's toxicological endpoints for assessing risk of hexahydrotriazine and formaldehyde are summarized in Appendix III.

Exposure to hexahydrotriazine and/or formaldehyde may occur through treating products during their manufacture, or by handling products containing hexahydrotriazine (i.e. professionals or homeowners may be exposed during application of treated products such as paint or cleaners). Additionally exposure to hexahydrotriazine and/or formaldehyde may occur by consumption of food that has come in contact with residue on surfaces (i.e: from use of treated cleaning products on food preparation surfaces), or post-application when entering sites where treated products have been used. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to hexahydrotriazine and/or formaldehyde when treating or handling products containing hexahydrotriazine.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Among the scenarios assessed in the RED, the following exposure scenarios were considered relevant to the Canadian situation:

- mixing/loading hexahydrotriazine for use as a material preservative in paint;
- mixing/loading hexahydrotriazine for use as a material preservative in metalworking fluids;
- application of hexahydrotriazine-treated paint by professional painter;
- application of hexahydrotriazine-treated products by professional cleaners; and
- handling of hexahydrotriazine treated metal working fluid by machinist.

The occupational exposure scenarios selected by the USEPA were considered to be of short- and intermediate-term duration, representative of all other material preservative uses, and provided high-end estimates of dermal and inhalation exposure.

Exposure to hexahydrotriazine
Hexahydrotriazine handler exposure analyses were performed using data from the Chemical Manufacturers Association (CMA) and the Pesticide Handlers Exposure Database (PHED) and were based on application rates of 0.16–0.24%.

The USEPA reported acceptable short- and intermediate-term inhalation MOEs for all handler scenarios. As there were no adverse effects noted at the limit dose (21-day dermal study), a short-term dermal end-point was not defined. Acceptable intermediate-term dermal MOEs were reported for all handler scenarios with the exception of mopping in medical facilities by professional cleaners.

Exposure to formaldehyde from use of hexahydrotriazine-treated products
Based on the use pattern, and formaldehyde's high vapour pressure, the USEPA assessed only exposure to formaldehyde via the inhalation route.

Exposure to formaldehyde from the use of hexahydrotriazine-treated metalworking fluid was assessed using personal breathing zone formaldehyde air-sampling data from the metalworking industry. Many occupational tasks involving hexahydrotriazine-treated metalworking fluid resulted in inhalation exposure exceeding the 0.1 ppm inhalation no observed adverse effect level (NOAEL). The USEPA determined that the only effective way to reduce exposure to formaldehyde from metalworking fluids and chain lubricants was to reduce the application rate of hexahydrotriazine.

Exposure to formaldehyde from hexahydrotriazine-treated paint was assessed using emission data from an environmental chamber study and the Wall Paint Exposure Model (WPEM) for the professional painter. For all time-points assessed, the inhalation MOEs were below the target MOE of 1; therefore, the USEPA required that the use of hexahydrotriazine in paints, stains and coatings to be terminated.

The RED adequately addressed exposure scenarios associated with the uses of products containing hexahydrotriazine in Canada, and conclusions derived from the RED apply to the Canadian situation. Based on this, the PMRA requires the following mitigations measures to protect workers:

- remove use of hexahydrotriazine in paint from label;
- remove manual application of hexahydrotriazine as a machine cleaner to surfaces not reached by circulating machine coolant;
- reduce the maximum application rate of hexahydrotriazine in metalworking fluids, hydraulic fluids, chain lubricants and spin finish emulsions to 500 ppm;
- all handlers must wear long-sleeved shirt and long pants, shoes plus socks, chemical resistant gloves and goggles or face shield; and
- standard labelling requiring use of NIOSH-approved respiratory protection in situations where the formaldehyde air concentration exceeds the levels established by health and safety authorities in the jurisdiction of use.

Additional instructions concerning good hygiene practices are also required on labels. The proposed label amendments are listed in Appendix IV.

The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act* to demonstrate the efficacy of the reduced application rate in metalworking fluids. Appendix I lists data requirements.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach described in Section 3.1.1. The hexahydrotriazine and formaldehyde toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix III.

There are no registered hexahydrotriazine products for homeowner use in the United States; however, homeowners can be exposed to hexahydrotriazine and/or formaldehyde when handling products that contain hexahydrotriazine as a material preservative.

Among the scenarios assessed in the RED, the following exposure scenarios were considered relevant to the Canadian situation:

- application of hexahydrotriazine-treated paint by homeowner;
- application of hexahydrotriazine-treated cleaning products by homeowner; and
- application of hexahydrotriazine-treated laundry detergent by homeowner.

The residential exposure scenarios selected by the USEPA were considered to be short-term duration and representative of all other material preservative uses.

Exposure to Hexahydrotriazine
Hexahydrotriazine handler exposure analyses were performed using data from the CMA, the PHED and USEPA residential standard operating procedures using application rates from 0.16–0.24%.

Acceptable short-term inhalation MOEs were reported for all handler scenarios. As there were no adverse effects noted at the limit dose (21-day dermal study), no short-term dermal end-point was defined; therefore no dermal assessment was conducted for residential exposure to hexahydrotriazine.

Exposure to formaldehyde from use of hexahydrotriazine-treated products
Based on the use pattern, and formaldehyde's high vapour pressure, the USEPA only assessed only exposure to formaldehyde via the inhalation route. Exposure to formaldehyde from hexahydrotriazine-treated paint was assessed using emission data from an environmental chamber study and the Wall Paint Exposure Model (WPEM) for the do-it-yourself painter. Formaldehyde air concentrations resulting from the use of hexahydrotriazine-treated all-purpose cleaning products and laundry detergents were estimated using the Consumer Exposure Model (CEM).

For all residential handler scenarios, the inhalation MOEs were below the target MOE of 10. Based on this assessment, the USEPA required the use of hexahydrotriazine in paint[3], stains, coatings, all-purpose cleaning products and laundry detergents to be terminated.

The RED adequately addressed exposure scenarios associated with the residential uses of products containing hexahydrotriazine in Canada; thus, the conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires the following mitigation measures with respect to residential exposure:

- remove use of hexahydrotriazine in paint from label (also required based on occupational risk assessment); and
- remove use of hexahydrotriazine in cleaning products, laundry detergents and fabric softeners.

Additional instructions concerning good hygiene practices are also required on labels. The proposed label amendments are listed in Appendix IV.

[3] The USEPA also terminated use of hexahydrotriazine in paints, stains and coatings based on the occupational risk assessment (refer to Section 3.1.1).

3.1.2.2 Post-application Exposure and Risk

The post-application residential risk assessment considered exposure from floors cleaned with hexahydrotriazine-treated cleaners and exposure from clothing laundered with hexahydrotriazine-treated detergent. Exposure analyses were performed using data from the USEPA standard operating procedures for residential exposure assessments and an application rate of 0.16%. The representative exposure scenarios were considered to be of short- and intermediate-term duration; however, as there was no short-term dermal end-point defined, no short-term dermal assessment was conducted.

Children crawling or playing on floors cleaned with hexahydrotriazine-treated products have the potential for dermal exposure and "hand-to-mouth" or "object-to-mouth" incidental oral exposure from cleaner residue. Children can also be exposed to hexahydrotriazine from wearing or ingestion/mouthing of clothing that is laundered using treated detergent. Adults can be exposed via the dermal route from wearing laundered clothing. Using conservative assumptions the intermediate-term dermal and short- and intermediate-term oral MOEs for all post-application exposure scenarios were not of concern. The USEPA did not require mitigation measures with respect to post-application exposure.

The Canadian application rate of hexahydrotriazine in cleaning products and laundry detergents is higher (0.24%) than the United States rate (0.16%). However, the higher Canadian rate does not change the outcome of the risk assessments; therefore, the RED adequately addressed post-application exposure scenarios associated with the Canadian uses of hexahydrotriazine, and conclusions derived from the RED are considered to be applicable to the Canadian situation. Based on this, the PMRA does not require additional mitigation measures.

3.1.2.3 Exposure From Food and Drinking Water

There are no direct food or feed uses registered in United States or Canada for hexahydrotriazine; however, products containing hexahydrotriazine may be used in such a way that indirect food contact might occur (for example, in adhesives and inks and dyes used for food packaging and cleaners used on food contact surfaces). Existing Canadian end-use product labels include a precautionary statement prohibiting the use of hexahydrotriazine in adhesives that could have either direct or indirect food contact.

An acute and chronic dietary (food) risk assessment was conducted for hexahydrotriazine, resulting in exposures of 0.14% to 80% of the acute/chronic population adjusted dose for children (the most sensitive subpopulation). The acute/chronic risk assessments were based on "worst-case" dietary concentration values, maximum application rates in treated materials, and the United States Food and Drug Administration's default assumptions. No dietary endpoint was identified by the USEPA for formaldehyde. On this basis, no dietary risk assessment for exposure to formaldehyde was conducted.

The USEPA determined that based on the use pattern, and the short half-life of hexahydrotriazine and formaldehyde in water, the potential for hexahydrotriazine to impact drinking water sources was negligible. Hexahydrotriazine is not registered in Canada for outdoor use, therefore it is not expected that the use of this active ingredient will impact Canadian water sources significantly.

The RED adequately addressed dietary exposure associated with the uses of products containing hexahydrotriazine in Canada, and conclusions derived from the RED apply to the Canadian situation. Based on this, no mitigation measures are required.

3.1.2.4 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to hexahydrotriazine (i.e. from food, water and residential exposures). Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure.

In the case of hexahydrotriazine, there are no dietary or drinking water concerns, therefore, the short-term aggregate risk assessments were based on post-application indirect oral exposures in children, and inhalation exposures in adults. The intermediate-term aggregate risk assessments were based on post-application indirect oral and dermal exposures in children only.

For each of the hexahydrotriazine exposure scenarios the aggregate risks were not of concern.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of hexahydrotriazine in Canada. No further mitigation measures are required.

3.1.3 Cumulative Effects

The USEPA has not determined whether hexahydrotriazine has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that hexahydrotriazine does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

The USEPA determined that based on the primarily indoor use pattern, the potential for hexahydrotriazine to be released into the environment at exposure levels of concern would be low. Based on hexahydrotriazine and formaldehyde's log *n*-octanol-water partition coefficient (K_{ow}), bioaccumulation is not expected.

The USEPA conducted an environmental hazard assessment for all uses and determined that hexahydrotriazine is practically non-toxic to moderately toxic to non-target species. Based on this, the USEPA required advisory label statements pertaining to effluent discharge.

Overall, the United States use pattern for hexahydrotriazine encompasses the Canadian use pattern. Based on the RED, and in consideration of the Canadian situation, the PMRA requires additional advisory label statements to further protect the environment. Proposed label amendments are listed in Appendix IV.

3.3 Pest Control Product Policy Considerations

3.3.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, i.e., CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative.

During the re-evaluation process, hexahydrotriazine was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and evaluated against the Track 1 criteria for persistence and bioaccumulation. In order for hexahydrotriazine or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met.

The log *n*-octanol–water partition coefficients (log K_{ow}) of hexahydrotriazine and formaldehyde are 0.07 and 0.7, which are below the TSMP Track 1 cut-off criterion for log K_{ow} of 5.0. Therefore, hexahydrotriazine does not meet the Track 1 criteria, and is not considered a Track 1 substance.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of hexahydrotriazine, contaminants in the technical are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusion:

- Technical grade hexahydrotriazine does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

4.0 Incidence reports

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

There were no incident reports submitted for hexahydrotriazine as of 20 December 2009.

5.0 Organisation for Economic Co-operation and Development Status of Hexahydrotriazine

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the available information, hexahydrotriazine is permitted for use in the European Union as a slimicide and a material preservative in cans, fibre, leather, rubber, polymerised material, liquid-cooling and processing systems, and metalworking fluids.

As described earlier in this document, the United States, also an OECD member, assessed the registration of all uses of hexahydrotriazine in 2008 and concluded using hexahydrotriazine as a pesticide does not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the RED document were implemented.

The Canadian re-evaluation of hexahydrotriazine is largely based on the 2008 USEPA assessments. As described in Section 3.1 and 3.2 above, the PMRA has found the USEPA human health and environmental risk conclusions to be relevant to the use of hexahydrotriazine in Canada and requires measures to mitigate to further protect workers, bystanders and the environment.

6.0 Proposed Re-evaluation Decision

The PMRA has determined that hexahydrotriazine is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for hexahydrotriazine is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

a.i.	active ingredient
bw	body weight
CAS	Chemical Abstracts Service
CEM	Consumer Exposure Module
CEPA	Canadian Environmental Protection Act
CMA	Chemical Manufacturers Association
DACO	data code
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
WPEM	Wall Paint Exposure Model

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the PCPA. The registrants of this active ingredient are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA.

- DACO 10.2.3.2: Laboratory Trials (ASTM method E2275-03: Evaluating Water-Miscible Metalworking Fluid Bioresistance and Antimicrobial Pesticide Performance.

  This study must be conducted with a relevant end-use product.

Appendix II Registered Products Containing Hexahydrotriazine as of 20 December 2009

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
11691	Commercial	GRAY PRODUCTS, TROY CHEMICAL COMPANY LIMITED	GROTAN BK METAL WORKING MICRO-BIOCIDE	Solution	78.5%
11831	Commercial	GRAY PRODUCTS, TROY CHEMICAL COMPANY LIMITED	GROTANOL SR-1 DISINFECTANT MACHINE CLEANER	Solution	9.42%
14442	Commercial	STUART, D.A. INC	STUART DASCOCIDE NO.9 PRESERVATIVE	Solution	78.5%
25113	Commercial	GRAY PRODUCTS, TROY CHEMICAL COMPANY LIMITED	MERGAL 165 BROAD SPECTRUM MICRO-BIOCIDE	Solution	78.5%
25714	Technical	STEPAN COMPANY	ONYXIDE 200 BIOCIDE	Solution	78.5%
26971	Commercial	STEPAN CANADA INC.	ONYXIDE 200 PRESERVATIVE	Solution	78.5%
27089	Commercial	SURETY LABORATORIES INC.	SURCIDE P	Solution	78.5%
27292	Commercial	NALCO CANADA COMPANY	DURACOOL 6451	Solution	78.5%
27392	Commercial	STEPAN COMPANY	ONYXIDE 200 IN CAN PRESERVATIVE	Solution	78.5%
27854	Technical	GRAY PRODUCTS, TROY CHEMICAL COMPANY LIMITED	GROTAN BK BIOCIDE	Solution	78.5%

Appendix III Toxicological Endpoints for Hexahydrotriazine Health Risk Assessments

Exposure Scenario	NOAEL (mg/kg bw/day)	Study	Target MOE
Acute dietary (All populations)	500	Developmental toxicity (rat)	1000
Chronic dietary (All populations)	50	90-Day oral study (rat)	100
Short-term oral	500	Developmental toxicity (rat)	1000
Intermediate-term oral	50	90-day oral study	100
Short-term dermal	No adverse systemic effects observed in a 21-day dermal toxicity study up to 1000 mg/kg bw/day.		
Intermediate/long-term dermal	250	90-day dermal study (rat) Based on systemic NOAEL found to be greater than 250 mg/kg bw/day (the HDT)	1000
Inhalation (all durations)	50	90-day oral study	100

Exposure Scenario	NOAEL (ppm)	Study	Target MOE
Inhalation (all durations)	0.1 (human)	Horvath, E.P. et al. (1986): JAMA 259(5): 701-707. Based on complaints of eye, nose, and throat irritation in particle board workers at concentrations of formaldehyde from 0.4 - 1.0 ppm.	(Occupational) = 1 (Residential) = 10
Cancer	B1, Probable human carcinogen, Currently under review by the USEPA.		

Appendix IV Label Amendments for Products Containing Hexahydrotriazine

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of end-use products in Canada must be amended as follows to further protect workers and the environment.

I) The following uses are not eligible for continued registration and must be removed from end-use product labels:

- Machine cleaner when applied manually to machine surfaces not reached by circulating coolant/cleaner.
- Paints and related products.
- Cleaning products, liquid detergents, fabric softeners.

Labels of end use products intended for material preservation must be reworded such that hexahydrotriazine may only be used as a material preservative in the following uses: adhesives, resin solutions, printing ink, stuccos, joint compounds, floor finishes, and liquid polishes applied by liquid pour or metering pump up to a maximum rate of 0.24% active ingredient by weight.

II) The end-use product labels must be amended to indicate a maximum application rate:

- Application rate in metalworking fluids, hydraulic fluids, chain lubricants and spin finish emulsions must be reduced to 0.05% a.i. by weight.

III) The following statement must be included on the primary display panel.

CAUTION – EYE IRRITANT

The following statements must be included on the secondary display panel

Harmful or Fatal if swallowed.
May irritate eyes.

IV) The following statements must be included in a section entitled **PRECAUTIONS**.

All mixers and other handlers must wear: long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, goggles or face shield.

Formaldehyde can be released during use of this product. Ensure that formaldehyde air concentrations in the workplace do not exceed the exposure levels established by the occupational health and safety authorities in your jurisdiction (e.g., engineering controls, monitoring). If values exceed this level, wear NIOSH-approved respiratory protection.

V) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

Machine cleaner must be added by closed transfer system.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

References

Studies Considered in the Chemistry Assessment

List of Studies/Information Submitted by Registrant

PMRA Document Number 1633386
Reference: 1996, HHT-SGE-1 Hexahydro-1,3,5-*tris* (hydroxyethyl)-*s*-triazine, DACO: 2.1, 2.10, 2.11, 2.12, 2.13, 2.14, 2.15, 2.16, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9

PMRA Document Number 1618235
Reference: Part 2 Chemistry. Date of Submission: February 1984. Additional Information: August 1994 HHT-SPN-3 , DACO: 2.1, 2.10, 2.11, 2.12, 2.13, 2.14, 2.15, 2.16, 2.3, 2.4, 2.6, 2.7, 2.8, 2.9

PMRA Document Number 1618214
Reference: Part 2.12 Specifications Date of Submission: February 1984 Additional Information: December 1997 HHT-SPN-3, DACO: 2.12, 2.13