Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Acceptability for Continuing Registration

PACR2003-13

Re-evaluation of Atrazine

The purpose of this document is to inform registrants, pesticide regulatory officials, and the Canadian public that the Pest Management Regulatory Agency (PMRA) has completed the human health risk assessment of atrazine, as part of the re-evaluation of atrazine pursuant to Section 19 of the Pest Control Products (PCP) Regulations.

This Proposed Acceptability for Continuing Registration (PACR) document provides a summary of the data and information reviewed, and the rationale for the proposed regulatory decision.

An assessment of the environmental risks of atrazine is underway, but has not yet been completed. The outcome of the assessment will be communicated in a future document.

By way of this document, the PMRA is soliciting comments from interested parties on the proposed regulatory decision for atrazine. The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed decision. All comments should be forwarded to the Publications Coordinator at the address below.

(publié aussi en français)

November 19, 2003

This document is published by the Alternative Strategies and Regulatory Affairs Division, Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 0-662-35162-2 (0-662-35163-0)
Catalogue number: H113-18/2003-13E (H113-18/2003-13E-PDF)

Foreword

The re-evaluation of the human health risk of the active ingredient (a.i.) atrazine and its associated end-use products, registered for use on food, has been completed by the Pest Management Regulatory Agency (PMRA). The registrants of the technical grade active ingredient (TGAI) are Syngenta Crop Protection Canada Inc., I.Pi.Ci. Industria Prodotti, and Makhteshim-Agan of North America Inc.

Technical registrants have restricted their support to use of atrazine on corn only. All other uses for atrazine (e.g., lowbush blueberries and atrazine-tolerant canola) will be phased out.

Recently, the PMRA has carried out an assessment of available information and has found it sufficient, pursuant to Section 20 of the PCP Regulations, to allow a determination of the safety to human health of atrazine and associated end-use products used in corn. The Agency has concluded that the use of atrazine and its end-use products does not entail an unacceptable risk to human health pursuant to Section 20, provided that the proposed mitigation measures described in the document are implemented.

This document focuses on the risks to human health. A full environmental assessment will be communicated in a future document.

Further measures may be necessary/proposed at a future date pending completion of the environmental risk assessment and the outcome of the cumulative risk assessment for all triazine which share a common mechanism of toxicity.[1]

The PMRA will accept written comments on this proposal up to 60 days from the date of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

[1] The PMRA has determined, based on products registered in Canada, that atrizine and simazine, and their common chlorinated degradates, share a common mechanism of toxicity as has the US EPA.

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1.0 Purpose

This document describes the outcome of the Pest Management Regulatory Agency's human health assessment as part of the re-evaluation of the herbicide atrazine and its end-use products. By way of this document, the Agency is soliciting comments from interested parties on the decisions and mitigation measures proposed.

This document focuses on the risks to human health. A full environmental assessment for atrazine is underway but, has not yet been completed by the PMRA. The outcome of the environmental assessment will be communicated in a future document.

2.0 Re-evaluation of atrazine

Products containing the herbicide atrazine were first registered in 1960. Atrazine is a broad spectrum triazine herbicide registered in Canada for the control of broadleaf and grassy weeds in corn, lowbush blueberries and atrazine-resistant canola. The technical registrants of atrazine in Canada are Syngenta Crop Protection Canada, I.Pi.Ci. Industria Prodotti and Makhteshim Agan of North America Inc. The currently registered commercial products containing atrazine are listed in Appendix I.

A re-evaluation of atrazine was first announced in June 1988 by Agriculture and Agri-food Canada[2], under the authority of Section 19 of the Pest Control Products (PCP) Regulations. An outcome of that re-evaluation initiative was an industry-led Label Improvement Program (LIP) that was launched in the early 1990s. The LIP resulted in the reduction of rates of application and the deletion of some use patterns (i.e., industrial and residential use). The use rates were reduced from 4.5 kg a.i./ha to a maximum of 1.5 kg a.i./ha for corn and atrazine-tolerant canola. The maximum use rate for lowbush blueberries was reduced from 8 kg a.i./ha to 4 kg a.i./ha. Industrial weed control uses were removed from the label. Fall uses were also removed from the label and post-emergent use on corn was restricted to application prior to corn reaching 30 cm in height. The use of atrazine to control perennial weeds (Canada thistle, quack grass and nutsedge) was also discontinued. All these measures led to a drastic reduction in the amount of atrazine usage. In addition, buffer zones were introduced to further reduce the amount of atrazine getting into water bodies.

[2] Agriculture and Agri-Food Canada was the federal department responsible for administering the *Pest Control Products Act* prior to the formation of the Pest Management Regulatory Agency in April 1995.

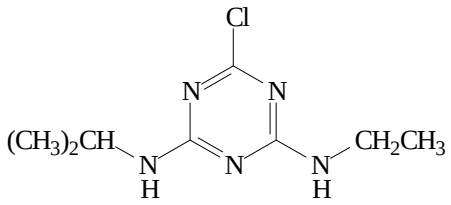
As outlined in Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, the PMRA is re-evaluating older active ingredients that were registered, or found in registered products, prior to 1995. This re-evaluation program uses a modern scientific approach to determine the continuing acceptability of older active ingredients in relation to human health and the environment. The current re-evaluation of atrazine is being conducted under this program. As indicated in Regulatory Directive DIR2001-03, the initial focus of the re-evaluation is the risk to human health with particular attention to:

a. pest control products with a common mechanism of toxicity;
b. aggregate exposure to a pesticide arising from its residues in food and in drinking water, and from non-occupational exposure, such as from treatments in and around the home;
c. susceptibility and exposure of infants and children that may be different from that of adults during critical developmental stages.

Much of the scientific information used by the PMRA in its assessment of atrazine came from reviews conducted by the United States Environmental Protection Agency (USEPA). The USEPA review of atrazine can be referenced for further details regarding scientific studies used by the PMRA. These reviews, as well as other information on the regulatory status of atrazine in the United States, can be found at the Web site of the USEPA (http://www.epa.gov/oppsrrd1/REDs/atrazine_ired.pdf).

2.1 Chemical identification

Chemical structure:



Common name:	Atrazine
Chemical names:	
International Union of Pure and Applied Chemistry (IUPAC):	6-chloro-N^2-ethyl-N^4-isopropyl-1,3,5-triazine-2,4-iamine
Chemical Abstracts Service (CAS):	6-chloro-N-ethyl-N′-(1-methylethyl)-1,3,5-triazine-2,4-diamine
Chemical family:	Triazines
CAS number:	1912-24-9
Empirical formula:	$C_8H_{14}ClN_5$

Molecular weight:	215.7
Vapour pressure:	40 µPa at 20°C
Technical registrants:	Syngenta Crop Protection Canada, Inc. I.Pi.Ci. Industria Prodotti Makhteshim-Agan of North America Inc.

2.2 Description of uses

Herbicides containing atrazine are currently registered for use on corn, triazine-tolerant canola and lowbush blueberries. Industrial and domestic vegetation control uses have or are being discontinued by registrants. Triazine-tolerant canola and lowbush blueberries uses are not being supported by registrants and will be phased out. The only use being supported by the technical registrants is corn. Therefore, this PACR is focussed on the use of atrazine on corn only.

Currently, a total of 17 commercial class products are registered for use on corn, among which nine products contain only atrazine and the remaining eight products contain at least one other active ingredient in addition to atrazine. Atrazine is formulated as a wettable powder, wettable granule, suspension, granular or an emulsifiable concentrate. Atrazine herbicides can be used on all types of corn, i.e., field corn, silage corn, sweet corn, popcorn and corn for seed production.

Atrazine herbicides are registered for control of certain broadleaf weeds and some grassy weeds. These weeds include wormseed mustard, wild buckwheat, wild mustard, lamb's-quarters, common purslane, redroot pigweed, ragweed, volunteer clover, smartweed, lady's-thumb and wild oats. Atrazine can be applied pre-plant (PP), pre-plant incorporated (PPI), pre-emergence, or post-emergence in either conventional tillage or minimum tillage programs. These products must be applied before corn plants reach 30 cm in height. A maximum of two applications per year are allowed. The maximum application rate is 1.5 kg a.i./ha for each application, therefore, the maximum amount that can be applied per year is 3 kg a.i./ha. These products are for ground application only.

Atrazine herbicides can be tank-mixed with either liquid or granular fertilizers. There are 17 herbicides and 3 adjuvants included on atrazine product labels as tank mix partners.

3.0 Effects having relevance to human health

3.1 Toxicology summary

Based on the submitted data from studies in laboratory animals, atrazine was of low to slight acute toxicity following oral exposure and of low acute toxicity by the dermal and inhalation routes of exposure. Atrazine was mildly irritating to rabbit eyes and skin and a skin sensitizer in the guinea pig. Atrazine appears to have low dermal absorption

potential. Atrazine's primary mode of action impairs hypothalamic–pituitary function in the rat. After repeated dosing (or single high doses), the most sensitive indicators of atrazine toxicity in the rat were inhibition of luteinizing hormone (LH) and prolactin, two hormones which play important roles in reproductive function and development, as well as estrous cycle alterations. Attenuation of the pre-ovulatory LH surge results in anovulation, prolonged estrus and premature reproductive aging in Sprague-Dawley (SD) female rats. Increased/prolonged exposure to estrogen from anovulated follicles leads to the development of mammary tumour in the female SD rat strain only, but atrazine itself has no direct estrogenic activity. Atrazine did not induce tumours in mice, Fischer-344 rats, ovariectomized SD rats or male SD rats, and demonstrated no genotoxic effects. Findings of delayed puberty (delays in preputial separation or vaginal opening) in rat pups, prostatitis in adult rat offspring exposed via lactation during postnatal days 1 through 4, and increased pregnancy loss in rats, are consistent with atrazine's neuroendocrine mode of action. There was no evidence of increased sensitivity of rat or rabbit offspring, following in utero and/or postnatal exposure to atrazine. Other effects included cardiotoxicity in dogs and mice, and testicular degeneration in dogs and rats.

The mode of action by which atrazine induces mammary tumours in the female SD rat (LH attenuation) is not considered to be relevant to humans. Attenuation of LH in women is associated with low rather than high estrogen levels, and reproductive senescence in women is due to depletion of oocytes in the ovaries rather than LH failure. In addition, attenuation of the LH surge in normal cycling women would probably not lead to an increased incidence of mammary tumours because when LH is low (anovulation), such as in women with hypothalamic amenorrhoea, or in women using gonadotropin-releasing hormone (GnRH) analogues for therapeutic purposes, a state of low estrogen is found. Hypothalamic amenorrhoea or use of GnRH analogues is not associated with an increased risk of breast cancer in women. Although one epidemiological study suggests a possible association between atrazine exposure and prostate cancer, confounding factors make this study inconclusive.

Reference doses were based on no observed adverse effect levels (NOAEL) for the most relevant endpoints, namely attenuation of the LH surge, estrous cycle alterations and developmental effects. These reference doses incorporate uncertainty factors to account for extrapolation between rats and humans and for variability within human populations, as well as an additional safety factor to provide an extra level of protection for the potential neuroendocrine modulating effects of atrazine.

The toxicology endpoints used in the risk assessment of atrazine are summarized in Appendix II and III.

3.2 Occupational risk assessment

Occupational risk is estimated by comparing the potential exposure of persons mixing, loading and applying pesticides to the most relevant endpoints from toxicology studies to generate a margin of exposure (MOE). The risk exceeds the PMRA's level of concern if the MOE is less than the desired or target MOE.

For **short-term dermal and inhalation exposure (1–30 days)**, the toxic endpoint selected was from a 28-day oral toxicity study in female rats with a NOAEL of 5 mg/kg bw/day based on attenuation of the LH surge at the next dose level. For dermal exposure, a 6% dermal absorption factor was employed. The exposure assessment has a **target MOE of 300** for dermal and inhalation exposure, and includes the conventional uncertainty factor of 100 (10× for interspecies extrapolation and 10× for intraspecies variability) as well as an additional safety factor of 3× for the endpoint of concern (neuroendocrine modulating potential).

3.2.1 Mixer/loader/applicator exposure

Farmers and custom applicators can be exposed occupationally to atrazine through mixing, loading and applying (M/L/A) the registered products to corn during normal use. Additionally, workers can be exposed during the impregnation of dry bulk fertilizer with atrazine. Farmers, custom applicators, and workers are expected to have short-term exposure (<30 days).

Acceptable MOEs for M/L/A of products containing atrazine are reached provided the following conditions are met:

- During application, chemical resistant-gloves, and coveralls over a long-sleeved shirt and long pants are worn.
- During mixing and loading, a face shield is worn in addition to chemical resistant gloves, and coveralls over a long-sleeved shirt and long pants.
- Wettable powders (WP), and wettable granule (WG) formulations employ a closed mixing and loading system (i.e., water soluble bags).

Acceptable MOEs for workers incorporating atrazine into dry bulk fertilizers are reached provided the following conditions are met:

- The activity is restricted to commercial facilities (prohibit on-farm impregnation)
- These facilities employ a closed mix/load system.
- A maximum of 1500 kg active ingredient is incorporated per day.
- This activity occurs for no more than 30 days per year.

3.2.2 Post-application exposure

As atrazine is applied pre-emergence or early post-emergence, re-entry exposure is expected to be minimal.

3.3 Residential risk assessment

Atrazine will no longer be registered for use in any residential areas, so a residential risk assessment was not required.

3.4 Dietary risk assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested as part of the daily diet. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, assessments take into account differences in children's eating patterns, such as food preference and greater consumption of food relative to their body weight compared with adults.

Acute dietary risk is calculated by considering food consumption and residue values in food. A probabilistic statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of atrazine residues which might be eaten in a day. A value representing the high end (99.9^{th} percentile) of this distribution is compared with the acute reference dose (ARfD), which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake from residues is less than the ARfD, the expected intake is not considered to be of concern.

The chronic dietary risk is calculated by using the average consumption of different foods, and average residue values on those foods, over a 70-year lifetime. This expected intake of residues is compared to the acceptable daily intake (ADI), which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, the expected intake is not considered to be of concern.

In the risk assessments presented here, atrazine's chlorinated metabolites are considered to be equivalent in toxicity to atrazine, per se. Atrazine and its chlorinated metabolites were assessed together. The toxic effects attributed to the hydroxy–metabolites of atrazine are considered to be independent of the effects of atrazine, per se. Consequently, risks associated with exposure to these hydroxylated compounds (expressed as hydroxyatrazine) have been assessed separately.

3.4.1 Acute reference dose

Atrazine and its chlorinated metabolites
The ARfD was derived from a 4-day rat study (NOAEL of 12.5 mg/kg body weight (bw)/day) in which an increased incidence of lateral prostatitis was noted in adult male offspring that had been exposed neonatally to atrazine via lactation during postnatal days 1–4. The uncertainty factor was 100 (10× for interspecies extrapolation and 10× for intraspecies variability). An additional safety factor of 3× was applied to account for the neuroendocrine modulating potential of atrazine. The ARfD was calculated to be 0.04 mg/kg bw (12.5 ÷ 300 = 0.04). This is considered protective of infants and children who may be exposed through breast milk.

Hydroxyatrazine
A toxicological endpoint attributable to one-day exposures to hydroxyatrazine in the diet could not be identified. Therefore, a risk assessment for acute exposure to hydroxyatrazine was not conducted.

3.4.2 Acceptable daily intake

Atrazine and its chlorinated metabolites
The chronic (lifetime) dietary reference dose or ADI selected for all populations was 0.006 mg/kg bw/day. This was based on the study NOAEL for the most sensitive endpoint, which was attenuation of LH surge from a 6-month study in female SD rats. This endpoint is considered relevant to all populations as it is a biomarker indicative of atrazine's mode of action (disruption of the hypothalamic-pituitary axis). An uncertainty factor of 100 was applied to the NOAEL of 1.8 mg/kg bw/day (10× for interspecies extrapolation and 10× for intraspecies variability), with an additional 3× safety factor to account for the neuroendocrine modulating potential of atrazine (1.8 ÷ 300 = 0.006).

Hydroxyatrazine
The chronic (lifetime) dietary reference dose or ADI selected for all populations was 0.01 mg/kg bw/day. This was based on the study NOAEL of 1 mg/kg bw/day from a combined chronic/carcinogenicity study in rats, based on gross and histological effects at a LOAEL of 7.7 mg/kg bw/day. An uncertainty factor of 100 was applied to the NOAEL (10× for interspecies extrapolation × 10× for intraspecies variability).

3.4.3 Dietary exposure

Acute and chronic dietary exposure and risk estimates were generated using the Dietary Exposure Evaluation Model (DEEM®) software and updated consumption data from the Food and Drug Administration's (FDA) Continuing Survey of Food Intakes by Individuals, CSFII (1994–1998).

Uses of atrazine in the U.S. (i.e., formulation types, application rates and use sites) encompass Canadian registered uses. Anticipated residues for both atrazine and its chlorinated metabolites, and hydroxyatrazine, derived by the USEPA, were considered relevant to the Canadian scenario.

For both atrazine and its chlorinated metabolites, and hydroxyatrazine assessments, dietary exposure of atrazine contributed to less than 1% of either the acute or chronic reference doses. These chronic and acute dietary risk assessments demonstrated that there are no health concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. Furthermore, there are no health concerns for nursing or pregnant females or based on gender in general.

3.4.4 Exposure from drinking water

Drinking water exposure was addressed by calculating, for each population subgroup, drinking water levels of comparison (DWLOCs) for acute and chronic exposure to atrazine and its chlorinated metabolites. The DWLOC expresses the difference between the reference dose and the non-drinking water exposure. The acute and chronic DWLOCs for the most sensitive population subgroup were 1300.5 and 41.9 µg/L, respectively. These values were compared to the maximum and average estimated environmental concentration (EEC) of atrazine in water (see section 4.1).

The EECs of atrazine in water, based on modelling and a review of water monitoring data available to the PMRA, do not exceed the acute and chronic DWLOC for the most sensitive subpopulations. Therefore, residues of atrazine in drinking water, when considered along with dietary exposure, is unlikely to be of concern.

3.5 Aggregate exposure assessment

As all residential uses of atrazine are being discontinued, the aggregate risk assessment for atrazine is comprised of food and water exposure only, which are addressed in the preceding section (**3.4.4)**.

4.0 Environmental assessment

The PMRA has not completed the environmental assessment portion of atrazine re-evaluation. Only the assessment of drinking water has been completed and is included in the PACR. The PMRA is working closely with registrants to develop an atrazine water monitoring protocol.

4.1 Concentration of atrazine in drinking water

Residues of atrazine in potential drinking water sources were estimated through the use of models and available monitoring data. The LEACHM and PRZM/EXAMS models were used to estimate the concentrations of atrazine in groundwater and surface water (reservoirs and dugouts), respectively. In both cases, scenarios were used which closely approximated the conditions of use.

The 90th percentile of averaged concentrations over 20 years is provided from the LEACHM model. This is considered appropriate at this level since residues in groundwater do not fluctuate as widely over time as they do in surface water and closely follows the process outlined by the USEPA. LEACHM predicted that 132 and 164 µg/L of atrazine will reach groundwater following application to corn in Ontario and Quebec.

Results from PRZM/EXAMS predicted that the acute (yearly peak) and chronic (yearly average) concentrations of atrazine at the 90th percentile in reservoirs resulting from runoff would be 31.5 and 11.7 µg/L for corn in Ontario and 30.6 and 10.7 µg/L for corn in Quebec, respectively. Concentrations in dugouts were calculated for pre- and post-emergence application on corn in Manitoba. For pre-emergence application to corn, the acute and chronic concentrations in dugouts were determined to be 45.5 and 32.8 µg/L, whereas for post-emergence application, the values were 50.8 and 33.9 µg/L.

In addition to the modelling, a search for atrazine water monitoring data in Canada was conducted. Atrazine was detected in two Canadian groundwater monitoring studies with a maximum detection frequency $\leq$44% and a maximum concentration of 1.2 µg/L. Given the lack of monitoring data for atrazine in groundwater available to the PMRA, the Agency chose to consider data present in the United States Geological Survey National Water Quality Assessment program (NAWQA) database. Based on the monitoring data from the NAWQA database, which reflects the higher use rates and the wider use of atrazine in the U.S., the maximum detected concentration of atrazine and the transformation products desethylatrazine (DEA) and desisopropylatrazine (DIA) in groundwater was 5.01 µg/L.

Available monitoring data from Canadian studies, generated after the reduction in atrazine application rates (1993 to present), were used to determine acute and chronic exposure estimates for surface water and for water from drinking water facilities. The acute exposure value was estimated by determining the 95th percentile of the maximum concentration detected in the individual monitoring studies. The chronic exposure value was estimated by determining the 95th percentile of the arithmetic means of all samples at each site (detects and non-detects) from the monitoring studies for which samples were from potential drinking water sources.

The monitoring data for surface waters currently reviewed by the PMRA are insufficient to fully characterize exposure potential. The acute and chronic concentrations of atrazine (not including DEA and DIA) detected in surface water from Canadian monitoring studies were 22.8 µg/L and 3.8 µg/L, respectively. The acute and chronic concentrations determined for DEA were 3.1 and 0.5 µg/L, respectively and the acute and chronic concentrations determined for DIA were 1.1 and 0.2 µg/L, respectively. It was determined that the acute and chronic concentrations of atrazine (not including DEA and DIA) in drinking water facilities were 12.4 and 3.3 µg/L, respectively.

4.1.1 Drinking water monitoring program

The EECs of atrazine in surface water, based on modelling and monitoring data available to the PMRA, do not exceed the acute and chronic DWLOC for the most sensitive subpopulations. However, the monitoring data reviewed by the PMRA are limited and are insufficient to fully characterize exposure potential. As a result, additional monitoring data are required by the PMRA to confirm that acceptable levels are not exceeded.

Registrants are requested to compile and submit to the PMRA existing monitoring data[3] for atrazine in drinking water. In addition, the registrants are requested and have agreed to generate confirmatory drinking water data for atrazine residues in selected community water systems which, following a review of existing available data, are identified to have a higher risk of drinking water contamination. Registrants are required to develop and submit to the PMRA for approval a protocol for a water monitoring program to be implemented for the 2004 use season. The protocol should include sampling of raw and finished water at treatment plants supplied by either surface or ground water sources. These monitoring data will be reviewed by the PMRA and appropriate measures will be taken, if necessary, to mitigate any concerns.

5.0 Value

The following information is based on the currently registered uses of Atrazine.

Atrazine is a photosynthetic electron transport inhibitor at the photosystem II receptor site. Corn tolerance is attributed to rapid detoxification by glutathione transferases. It is a selective systemic herbicide, absorbed principally through the roots, but also through the foliage, with translocation acropetally in the xylem and accumulation in the apical meristems and leaves. Atrazine belongs to the herbicide group 5 according to the Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

[3] Some additional monitoring data from Ontario water treatment plants have been provided by the registrant and will be reviewed by the PMRA.

For most corn growers, the actual application timing is pre-emergence or early post-emergence. Almost all (over 99%) of treated corn fields in Canada receive only one application per year because of resistance concerns. The typical application rate is 0.8–1.0 kg a.i./ha. Applications to corn are most often pre-emergence (mid-April through mid-May in the major corn growing areas). Post-emergence applications are most likely to occur up to the end of June, until corn reaches 30 cm in height. There is some variability in timing based on geographical regions.

Ontario has the largest area planted to corn in Canada being 61% of the total national area. Quebec has 32% followed by Manitoba which accounts for 5% of the corn grown in Canada. The sum of corn production of all the other provinces accounts for only about 2% of the total area. The usage of atrazine has decreased significantly in recent years because of the Label Improvement Program implemented by the PMRA in the early 1990s, as a result of which application rates were reduced and some use patterns were deleted. For example, atrazine usage in field corn in Ontario declined from 999 410 kg a.i. in 1988 to 585 208 kg a.i. in 1993, and 573 721 kg a.i. in 1998. The percent crop treated is currently 40–45% of total corn fields for Ontario and 20% for Quebec and Manitoba.

Alternative products to atrazine are available to Canadian corn growers. Most of these alternative products are more expensive than atrazine herbicides. They have different modes of action and most of the modern products control a narrower spectrum of weeds than atrazine. In Canada, atrazine is often used with other herbicides, either in pre-mix formulations or tank mixtures, to reduce cost, decrease potential for weed resistance development and broaden the spectrum of weeds controlled. Therefore, atrazine is useful for product sustainability. Approximately 56 herbicides use atrazine as a tank mixture partner.

For comparison, in the U.S., based on the “Interim Reregistration Eligibility Decision for Atrazine (Case No. 0062)” published by the USEPA, atrazine is used on a number of food and non-food crops including corn (field and sweet), guavas, macadamia nuts, sorghum, sugarcane, range grasses, pasture, conifer forests, Christmas tree farms, sod farms, summer fallow, golf courses and residential lawns. Estimates for total annual use of atrazine in the U.S. are approximately 34.73 million kilograms of active ingredient. Corn accounts for the greatest use which is about 83% of total atrazine usage. The weighted average percent crop treated is 75% for corn. The maximum application rate is 2.2 kg a.i./ha if a single application is made either pre-emergence or post-emergence. A maximum of two applications is allowed per year, however, the total allowable seasonal application rate for corn is 2.8 kg a.i./ha per year.

6.0 Other assessment consideration

The assessment of atrazine with regards to the Toxic Substances Management Policy (TSMP) and PMRA Regulatory Directive DIR99-03 (*The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*), has not yet been completed. This will be considered during the completion of the environmental assessment for atrazine.

7.0 Proposed regulatory action

The PMRA has determined that the risks to human health for atrazine are acceptable provided that the mitigation measures proposed below are adopted. The acceptable uses for atrazine products, together with proposed mitigation measures and use limitation are presented in Appendix IV.

7.1 Proposed mitigation measures and label changes

The proposed measures to mitigate the risks arising from the use of atrazine are presented in Appendix IV.

In light of the fact that the technical registrants are not supporting the continued registration of atrazine use in lowbush blueberries, atrazine-tolerant canola, and industrial and residential uses, the PMRA is proposing a phase-out of these use patterns.

Registrants will be requested to amend the labels of atrazine products to reflect these measures. The PMRA proposes that product sold by registrants after January 1, 2004 contain the revised labelling.

7.2 Residue of Concern (ROC) definition

Currently, there is no formal definition of the residue of concern (ROC) for atrazine. In accordance with the USEPA, it is recommended that the PMRA establish two separate ROC; the first for atrazine and its chlorinated metabolites, and the second for the hydroxylated metabolites of atrazine. As such, the definition of the ROC for atrazine and its chlorinated metabolites would be the sum of atrazine (2-chloro-4-ethylamino-6-isopropylamino-s-traiazine), deethylatrazine (2-amino-4-chloro-6-isopropylamino-s-traiazine), deisopropylatrazine (2-amino-4-chloro-6-ethylamino-s-traiazine), and diaminochlorotriazine (2-chloro-4,6-diamino-s-traizine). The definition of the ROC for the hydroxylated metabolites of atrazine would be the sum of hydroxyatrazine (2-hydroxy-4-ethylamino-6-isopropylamino-s-triazine), deethylhydroxyatrazine (2-amino-4-hydroxy-6-isopropylamino-s-triazine), deisopropylhydroxyatrazine (2-amino-4-hydroxy-6-ethylamino-s-traizine), and diaminohydroxyatrazine (2,4,-diamino-6-hydroxy-s-triazine).

7.3 Maximum residue limits (MRLs) of atrazine in food

In general, when the re-evaluation of an agricultural pesticide has been completed, the PMRA intends to protect the food supply from continued use of the pesticide by recommending new residue limits at the limit of quantification (LOQ) for any agricultural commodities not approved for continued treatment in Canada, unless sufficient data are provided to support specific MRLs for import purposes. The implementation date of lowered MRLs will take into consideration the last date of legal use of products in Canada and the expected time for treated commodities to clear the channels of trade, usually one year. In future, proposed amendments to the Food and Drug Regulations reflecting these MRLs will be published in the *Canada Gazette*. The USEPA undertakes similar action in such circumstances.

Currently, atrazine residues on all agricultural commodities must not exceed 0.1 ppm, a default value specified by the Food and Drug Regulations subsection B.15.002(1). It is recommended that the PMRA adopt the following MRLs:

Corn (fresh and grain):

- 0.2 ppm for atrazine and its chlorinated metabolites (based on the sum of the LOQ (0.05 ppm) for each component of the ROC).
- 0.08 ppm for the hydroxylated metabolites of atrazine (based on the sum of the LOQ (0.02 ppm) for each component of the ROC).

Meat, meat by-products, fat of cattle, milk of cattle, goat and sheep:

- 0.1 ppm for atrazine and its chlorinated metabolites (based on the maximum theoretical dietary burden (MTDB) from treated corn).

All other agricultural commodities:

- MRL at the LOQ of any component of the ROCs (i.e., 0.05 ppm for parent and chloro-metabolites; 0.02 ppm for hydroxy-metabolites).

Parties interested in supporting an MRL to allow imports of other commodities treated with atrazine should contact the PMRA during the consultation period to discuss the submission of appropriate data.

8.0 Data requirements

8.1 Occupational

Exposure data on the mixing, loading and application of atrazine with fertilizers, both commercially and on-farm, would help to refine risk estimates for these exposure scenarios and clarify uncertainties.

8.2 Dietary

Data or the USEPA data evaluation report (DER) is requested from a storage stability study depicting the stability of atrazine and its chlorinated metabolites, frozen in representative commodities (e.g., corn raw agricultural commodities (RACs) and processed fractions) for up to 40 months. The PMRA also requests either the limited rotational crop study submitted to the USEPA (OPPTS 860.1900), or the USEPA DER of this study.

8.3 Drinking water

Drinking water monitoring data are required as described in Section 4.1.1. The technical registrants have agreed to generate these monitoring data in selected community water systems which, following a review of available data from community water systems, are identified as having a higher risk of drinking water contamination. The registrants have recently submitted additional data from Ontario water treatment plants to the PMRA, but they have not yet been reviewed.

8.4 Product Chemistry

For technical atrazine Registration number 18438 (Syngenta) the guarantee is expressed as a nominal value but the guarantees of Registration number 20583 (I. Pi. Ci.) and Registration number 24722 (Makhteshim-Agan) are expressed as a minimum. For Registration number 20583 and Registration number 24722 the following data are required to convert the guarantee to nominal:

(a) A copy of revised Statement of Product Specification Form (SPSF) which includes the nominal concentration (NC), lower limits (LL) and upper limits (UL) for the active ingredient, the NC and UL for all impurities if present in the product at level >0.1% and impurities of toxicological concern present at any level. The NC, LL and UL should be provided for atrazine and for the guaranteed related triazines.

(b) Analytical data from 5 batches of the technical product to below 0.1% and for impurities of toxicological concern to limit of detection to support the data on the revised SPSF.

(c) Label revised at the printing time to reflect the new nominal guarantee if approved.

TSMP Track-1 microcontamination

As described in Regulatory Directive DIR99-03, the PMRA's strategy for implementing the Toxic Substances Management Policy (TSMP), the PMRA will work with registrants to reduce/eliminate microcontaminants of concern in line with the best available technology from a manufacturing perspective and encourage the development of new technology. One manufacturer has reported measurable levels of hexachlorobenzene (HCB) in technical atrazine and has proposed a plan to reduce this microcontaminant to the lowest levels achievable.

9.0 Proposed re-evaluation decision

The Pest Management Regulatory Agency has carried out an assessment of available information and has concluded that the use of atrazine and associated end-use products does not entail an unacceptable risk of harm to human health provided that the proposed mitigation measures are implemented. Further measures may be proposed at a future date pending completion of the environmental risk assessment.

The PMRA will accept written comments up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

Further measures may be necessary/proposed at a future date pending completion of the environmental risk assessment and the outcome of the cumulative risk assessment for all triazines which share a common mechanism of toxicity.[4]

[4] The PMRA has determined, based on products registered in Canada, that atrazine and simazine, and their common chlorinated degradater, share a common mechanism of toxicity as has the US EPA.

List of abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
bw	body weight
C	commercial
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
CSFII	Continuing Survey of Food Intakes by Individuals
d	day(s)
DEA	desethylatrazine
DEEM®	Dietary Exposure Evaluation Model
DER	data evaluation report
DIA	desisopropylatrazine
DWLOC	drinking water level of concern
EAD	Environmental Assessment Division
EC	emulsifiable concentrate
EEC	estimated environment concentration
EP	end-use product
FDA	*Food and Drugs Act*
GnRH	gonadotropin-releasing hormone
GR	granular
h	hour(s)
ha	hectare(s)
HED	Health Evaluation Division
HCB	hexachlorobenzene
IMAC	interim maximum acceptable concentration
IPM	integrated pest management
kg	kilogram(s)
LC_{50}	mean lethal concentration
LD_{50}	mean lethal dose
LEACHM	Leaching Estimation And CHemistry Model
LH	luteinizing hormone
LIP	Label Improvement Program
LL	lower limit
LOEL	lowest observed adverse effect level
LOQ	limit of quantification
m	metre(s)
mg	milligram(s)
M/L/A	mixing, loading and applying
MOE	margin of exposure
MRL	maximum residue limit
MTDB	maximum theoretical dietary burden
NAWQA	National Water Quality Assessment
NC	nominal concentration

NOAEL	no observed adverse effect level
PACR	Proposed Acceptability for Continued Registration
PCP	Pest Control Products
PHED	Pesticide Handlers' Exposure Database
PMRA	Pest Management Regulatory Agency
PP	pre-plant
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PPI	pre-plant incorporated
PRZM/EXAMS	Pesticide Root Zone Model/Exposure Analysis Modelling System
RAC	raw agricultural commodity
ROC	residue of concern
SD	Sprague-Dawley (rat)
SF	safety factor
SPSF	Statement of Product Specification Form
SU	suspension
T	technical
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
UL	upper limit
U.S.	United States
USC	use-site category
USEPA	United States Environmental Protection Agency
WG	wettable granule
WP	wettable powder

Appendix I Atrazine products registered for use in corn

Products containing atrazine alone				
Registrant code	**Registration number**	**Product name**	**Market class**	**Formulation type**
SYZ	18438	Atrazine Technical	T	N/A
IPI	20583	Atrazine Technical	T	N/A
MKC	24722	Atranex Technical	T	N/A
MKC	14096	Atrazine 80W Wettable Powder Agricultural Herbicide	C	WP
MKC	14616	Atrazine 90W Agricultural Herbicide	C	WP
SYZ	14842	Aatrex Nine-O Agricultural Herbicide	C	WG
SYZ	18450	Aatrex Liquid 480 Agricultural Herbicide	C	SU
DRX	18805	Drexel Atrazine 500 Flowable Herbicide (Agricultural)	C	SU
DRX	18812	Drexel Atrazine 600 Flowable Agricultural Herbicide	C	SU
UAG	20997	Clean Crop Atrazine 480 Herbicide	C	SU
UAG	23583	Atrazine 90WG Herbicide	C	WG
AET	26277	Converge 480 Herbicide Agricultural	C	SU

Registrant code	Registration number	Product name	Market class	Formulation type
ZAN	11761	Sutazine + 18:6 Granules Herbicide	C	GR
BAZ	16641	BASF Laddok Liquid Suspension Herbicide	C	SU
ZAN	18223	Sutazine + Selective Herbicide	C	EC
BAZ	19349	Marksman Herbicide (Agricultural)	C	SU
UAG	24608	Shotgun Flowable Herbicide	C	SU
BAZ	25519	Patriot Herbicide	C	SU
SYZ	25730	Primextra II Magnum Herbicide	C	SU
AET	26968	Liberty AT Herbicide	C	SU

AET Aventis Crop Science Canada Co.
BAZ BASF
DRX Drexel Chemical Co.
IPI I.Pi.Ci. Industria Prodotti Ch.
MKC Makhteshim Agan of North America Inc.
SYZ Syngenta Crop Protection Canada Inc.
UAG United Agri Products
ZAN Zeneca Ag Products Inc.

Appendix II Toxicology endpoints for health risk assessment for atrazine*

Exposure Scenario**	Dose (mg/kg bw/day)	Endpoint	Study	UF/SF or MOE[d]
Acute dietary General population	There was no toxicological endpoint attributable to a single exposure for the general population.			
Acute dietary Females 13+	NOAEL = 12.5	Prostatitis in male offspring and inhibition of prolactin release in dams	4-day gavage study in lactating rats	300
	ARfD = 0.04 mg/kg bw			
Chronic dietary	NOAEL = 1.8	Attenuation of LH surge and estrus cycle alterations	26-week dietary study in rats	300
	ADI = 0.006 mg/kg bw/day			
Short-term[a] dermal[b] and inhalation[c]	NOAEL = 5	LH attenuation	28-d gavage study in female rats	300

* Includes atrazine and its chlorinated metabolites

** There is no residential exposure scenario in Canada. Intermediate-term occupational exposure scenarios are not expected under the current registered use patterns in Canada.

a Duration of exposure is 1–30 days

b Since an oral NOAEL was selected, a dermal absorption factor of 6% should be used in route-to-route extrapolation.

c Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

d UF/SF refers to total of uncertainty and(or) safety factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments.

Appendix III Toxicology endpoints for health risk assessment for hydroxyatrazine

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF/SF or MOE[d]
Acute dietary	There was no toxicological endpoint attributable to a single exposure.			
Chronic dietary	NOAEL = 1.0	Kidney effects	2-year rat toxicity	100
	ADI = 0.01 mg/kg bw/day			

Appendix IV Proposed mitigation measures for atrazine

Formulations:
- Wettable powders and wettable granules must be packaged in water soluble bags.

Aerial application:
- Do not use by air

Personal protective equipment:
- Require, at a minimum, coveralls over a long-sleeved shirt and long pants, and chemical-resistant gloves, when applying.
- In addition to the above, face shields must be worn during mixing and loading.

Application rate:
- One application per year at a maximum of 1.2 kg a.i./ha.
- Application to be made either as a pre- or post-emergence only.

Fertilizer:
- Atrazine may only be mixed on the farm with liquid fertilizers as carriers.
- Atrazine may only be mixed with dry flowable fertilizers as carriers under the following conditions:
  - The activity is restricted to commercial facilities (prohibit on-farm impregnation).
  - The facilities must employ a closed mix/load system.
  - Only a maximum of 1500 kg active ingredient can be incorporated per day.
  - This activity must occur for no more than 30 days per year.

Deletion of the following unsupported use patterns:
- Blueberry
- Atrazine-resistant canola
- Industrial use (deleted under LIP)
- Residential use (deleted under LIP)

Buffer zones:
- 30 metre buffer from any body or source of water when mixing or loading
- 10 metre buffer from any body of water when spraying

Pre-harvest interval (PHI):
- 60-day for pre- and post-emergent field corn uses
- 45-day for pre- and post-emergent sweet corn forage uses

Appendix V Use standard for commercial class products containing atrazine

(**NOTE:** The information in this appendix summarizes the acceptable uses, limitations and precautions for commercial class products containing atrazine, but does not identify all label requirements for such products. Registrants are referred to the PMRA Registration Handbook for further guidance on label requirements for pest control products.)

GROUND APPLICATION:
To make the information better understood, the specific buffer zones should be more clearly identified in this section. Perhaps the wording of the draft Standardized Label Statements document (Richard Martin) would be appropriate—mainly the same words—just different organization.

COMMON NAME: Atrazine

CHEMICAL NAME: 6-chloro-N2-ethyl-N4-ethyl-N4-isopropyl-1,3,5-triazine-2,4-diamine

FORMULATION TYPE: WP: Wettable powder
EC: Emulsifiable concentrate
WG: Wettable granules
SU: Suspension
GR: Granular

SITE CATEGORIES: USC 13: Terrestrial Feed Crops (Silage, field and seed corn)
USC 14: Terrestrial Food Crops (Sweet corn, popcorn and seed corn)

PERSONAL PROTECTIVE EQUIPMENT (PPE):
See Engineering controls for additional requirements.

During application, wear chemical-resistant gloves, and coveralls over a long-sleeved shirt and long pants. During mixing and loading, wear a face shield in addition to chemical-resistant gloves, and coveralls over a long-sleeved shirt and long pants.

For workers incorporating atrazine into dry bulk fertilizers the following conditions must be met:

- The activity is restricted to commercial facilities (prohibit on-farm impregnation).
- The facilities must employ a closed mix/load system.
- Only a maximum of 1500 kg active ingredient can be incorporated per day.
- This activity must occur for no more than 30 days per year.

Discard clothing and other absorbent materials if accidentally drenched or heavily contaminated with concentrated product. Do not reuse contaminated clothing. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions exist for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

USER SAFETY RECOMMENDATIONS:

User should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash skin thoroughly and put on clean clothing.
- Remove PPE immediately after handling this product. Wash the outside of gloves before removing gloves or clothing.
- Wash skin thoroughly as soon as possible, and change into clean clothing.

ENGINEERING CONTROLS:

Wettable powder (WP), and wettable granule (WG) formulations are permitted only when marketed in water-soluble packages. Water-soluble packets qualify as a closed mixing/loading system when used correctly. Mixers and loaders using water-soluble packets must wear the personal protective equipment required above for mixers/loaders

Mixing of atrazine with dry bulk fertilizers must be restricted to commercial facilities.

SPRAY DRIFT MANAGEMENT FOR GROUND APPLICATIONS:

GENERAL INFORMATION:

Use good pesticide practices and apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and parks is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings used for application.

For the protection of non-target habitats, over-spray or drift to any body of water or other environmentally sensitive habitats must be avoided. The interaction of many equipment and weather-related factors determines the potential for spray drift. The applicator is responsible for considering all these factors when making application decisions.

GROUND APPLICATION:

Avoid over-spray or drift to sensitive aquatic habitats. An appropriate buffer zone is required between the downwind point of direct application and the closest edge of sensitive aquatic habitats including sloughs, coulees, ponds, prairie potholes, lakes, rivers, streams, reservoirs and wetlands that are situated on the periphery of the treated area. Do not apply during periods of dead calm or when winds are gusty.

For ground spray booms, a buffer zone of 30 m is required for protection of aquatic habitats (as indicated above) when mixing or loading and 10 m when spraying.

AERIAL APPLICATION:

Do not apply by air.

SPRAYING:

Protect sprayer operators from drift or mist. Additional information on spray drift management for GROUND APPLICATION is provided in the section "SPRAY DRIFT MANAGEMENT FOR GROUND APPLICATIONS." When low volumes of spray are applied, complete coverage and thorough application are essential for most effective results. Schedule applications in accordance with local conditions. Consult your local agricultural authorities for specific use information.

DIRECTIONS FOR USE:

Apply a maximum of one application of 1.2 kg a.i./ha per year either as a post- or pre-emergent application before corn reaches 30 cm in height. Atrazine may only be tank-mixed with registered tank partners. Refer to the tank partners for further instructions. Do not harvest within 45 days of application on sweet corn (forage uses) and 60 days for field corn.