Australian Government
Australian Pesticides and
Veterinary Medicines Authority

# ATRAZINE

## FINAL REVIEW REPORT AND REGULATORY DECISION

The reconsideration of the active constituent, registration of products containing Atrazine and approvals of their associated labels.

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# FOREWORD

The Australian Pesticides & 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 can reconsider the approval of an active constituent, the registration of a chemical product or the approval of a label for a container for a chemical product at any time. This is outlined in Part 2, Division 4 of the Agvet Codes.

The basis for the current reconsideration was whether the APVMA was satisfied that continued use of the active constituent atrazine and products containing atrazine in accordance with the instructions for their use:

- would not be an undue hazard to the safety of people exposed to atrazine during handling; and
- would not be likely to have an effect that is harmful to human beings; and
- would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment; and
- would not unduly prejudice trade or commerce between Australia and places outside Australia.

The APVMA also considered:

- whether the use of products containing atrazine in accordance with the instructions for use that the APVMA has approved would be effective according to the criteria set by the APVMA for the products; and

- whether product labels carry adequate instructions and warning statements.

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 reconsideration process includes a call for information from a variety of sources, a review of that information and, following public consultation, a decision about the future use of the chemical or product. The information and technical data required by the APVMA to review the safety of both new and existing chemical products must be derived according to accepted scientific principles, as must the methods of assessment undertaken.

In undertaking reconsiderations (hereafter referred to as reviews), the APVMA works in close cooperation with advisory agencies including the Office of Chemical Safety within the Department of Health and Ageing, the Department of the Environment, Water, Heritage and the Arts (DEWHA) and state departments of agriculture, as well as other expert advisers as appropriate.

The APVMA has a policy of encouraging openness and transparency in its activities and community involvement in decision-making. The publication of review reports is a part of that process.

The APVMA also makes these reports available to the regulatory agencies of other countries as part of bilateral agreements. The APVMA recommends that countries receiving these

reports not utilise them for registration purposes unless they are also provided with the raw data from the relevant applicant.

This document is the *Atrazine final review report and regulatory decision: The reconsideration of the active constituent, registrations of products containing atrazine and approvals of their associated labels, summary report (volume 1 of 2)* and relates to all products containing atrazine. Volume 2 contains the review's technical report. The review's findings and regulatory decision are based on information collected from a variety of sources. Both volumes are on the APVMA website at: http://www.apvma.gov.au/chemrev/chemrev.html.

# ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| ACPH | Advisory Committee on Pesticides and Health (superseded by the Advisory Group on Chemical Safety) |
| ADI | Acceptable daily intake |
| ANZECC | Australian and New Zealand Environment and Conservation Council |
| ARfD | Acute reference dose |
| ARMCANZ | Agriculture and Resource Management Council of Australia and New Zealand |
| bw | Body weight |
| DEWHA | Department of the Environment, Water, Heritage and the Arts |
| DoHA | Department of Health and Ageing |
| FAO | Food and Agriculture Organization of the United Nations |
| IARC | International Agency for Research on Cancer |
| JMPR | Joint FAO/WHO Meeting on Pesticide Residues |
| LOEL | Lowest observable effect level |
| µg | Microgram |
| mg | Milligram |
| MOA | Mode of action |
| MRL | Maximum residue limit |
| NHMRC | National Health and Medical Research Council |
| NOAEL | No observable adverse effect level |
| NOEL | No observable effect level |
| NWQMS | National Water Quality Management Strategy |
| OCS | Office of Chemical Safety |
| ppb | Parts per billion |
| ppm | Parts per million |
| SD rats | Sprague-Dawley rats |
| TT | Triazine tolerant |
| US EPA | United States Environmental Protection Agency |
| WHO | World Health Organization |

# CONTENTS

# OVERVIEW

The Australian Pesticides & Veterinary Medicines Authority (APVMA) has completed its review of the active constituent atrazine and all products containing atrazine, although its review of some labels for atrazine products will continue, pending provision of additional data.

Atrazine is a selective systemic herbicide developed in the 1950s. It is used in Australia as a pre- and post-emergence herbicide for grass and broadleaf weeds on summer crops such as sorghum, maize and sugarcane. Atrazine is also used in the establishment of pine and eucalypt plantations and is applied to triazine tolerant (TT) canola, including raised bed crops in higher rainfall areas in Australia.

The APVMA decided to review atrazine because of concerns over human and animal carcinogenicity, environmental impacts including the potential for atrazine to contaminate ground and surface water, and residue and efficacy uncertainties. The review began in December 1995 and a report was published in November 1997.

Regulatory actions undertaken in 1997 included cancellation of industrial and non-agricultural uses of atrazine (home garden uses and all commercial turf uses), deletion of use patterns and maximum residue limits (MRLs) for label claims for which there were no current use patterns (citrus, grapes and pineapples) and the introduction of a range of label instructions to reduce the risk of atrazine entering waterways. In addition, registrants were required to provide additional residue and monitoring data.

Further reports were published in 2002 and 2004, taking into account additional data and argument, but no more regulatory actions were implemented.

New and emerging research continues into the biological and biochemical effects of atrazine. Therefore, in addition to finalising the main aspects of the atrazine review, the APVMA has initiated a project to re-examine the possibility that the triazines (atrazine and related chemicals with a similar mode of action (MOA)) may have previously unreported biological effects, taking into account ongoing research. This project will take into account international reports, such as the work of the Joint Meeting on Pesticide Residues (JMPR). The APVMA will consider initiating a new review if further data provide credible evidence of a previously uncharacterised risk.

Most of the regulatory actions detailed in this report were proposed in the 2004 report. These include amended label instructions intended to further reduce the risk of atrazine entering waterways, updated information on withholding periods and additional information on weed resistance reporting.

The APVMA also proposes to determine that the risk of atrazine entering waterways at harmful levels when used post-emergence on TT canola, when grown on raised beds, may be unacceptable. However, because this proposed finding is based on limited information which became available after 2004, the APVMA has determined that it is appropriate to require that additional data be generated so that it can further evaluate this concern. Registrants who have a product whose label specifies a claim for weed control on TT canola will be required to either generate additional data or include an additional label restraint that specifies that atrazine must not be used post-emergence on TT canola grown on raised beds.

With these changes, the APVMA is satisfied that the continued use of products containing atrazine meets the criteria for continued registration and label approval as prescribed by the Agvet Codes, pending provision of additional data in relation to TT canola.

# EXECUTIVE SUMMARY

Atrazine is a selective systemic herbicide that can be used both pre- and post-emergence for the control of grass and broadleaf weeds. It is mainly absorbed through the roots of plants and then carried to the actively growing tips and leaves, although some foliar absorption occurs. Atrazine kills the plant by inhibiting photosynthesis.

In Australia, atrazine is used to control weeds in summer crops such as sorghum, maize and sugarcane, and it is also widely used in Western Australia to control weeds in lupins. Other uses include control of weeds in lucerne, grass seed, pasture and potatoes. Atrazine is important in the establishment of pine and eucalypt plantations and for control of parthenium weed in Queensland, the Northern Territory and northern parts of New South Wales. Atrazine is also applied to triazine tolerant (TT) canola, including raised bed cropping in higher rainfall areas in Australia.

As of February 2008 there were 48 registered products and seven active constituent approvals (refer to Appendices A & B).

The review of atrazine was announced in December 1995 as part of the APVMA's first cycle of chemical reviews. The active constituent atrazine, products containing atrazine, and their product labels were placed under review due to concerns over:

- human and animal carcinogenicity claims;
- moderate potential chronic toxicity risk;
- potential to contaminate ground and surface water;
- absence of maximum residue limits (MRLs) for major commodities; and
- reported breakdown in efficacy.

While these were the major reasons why a high priority was given to the review of atrazine, the scope of the review covered all considerations relevant to the continued registration and approval of atrazine.

There was a high level of public interest in the APVMA's review, with over 150 submissions received in response to the initial review announcement and call for information. The APVMA released a report in November 1997 and took regulatory action following public consultation to address the report findings, which were based on the assessment of all information available.

The 1997 report concluded that there were no major toxicological concerns relating to the use of atrazine and moreover, that atrazine posed no undue hazard to most users. As well, new conditions for use of atrazine were implemented in order to reduce chemical handling by workers, and reduce drift and runoff into waterways. However, additional environmental monitoring data and residue data were required to address remaining concerns related to the potential risk atrazine's use posed to the environment and the validity of a number of maximum residue limits (MRLs). An MRL is the maximum concentration of a chemical residue that is permitted in or on a food or food commodity.

Registrants were given up to three years to generate the required environmental monitoring data and residue data. Assessment of these data led to the development of a draft final report, which was released for public comment in April 2002. A second draft final report was published in October 2004. These reports included amended findings and proposed regulatory approach, based on the assessment of new information, including the required residue and environmental data and new published studies.

New overseas studies were published after 2004, or foreshadowed in 2004, that raised additional concerns that atrazine might cause adverse developmental and reproductive effects, particularly in frogs. Because of emerging information, the APVMA delayed finalisation of the review and revisited the toxicological and environmental risks of using atrazine.

Some of the research work now becoming available has been contradictory and controversial. In the expectation that resolution of the scientific debate would occur, the APVMA reserved judgement to allow time for a clearer scientific consensus to develop.

Although it is clear further studies will be forthcoming, the APVMA has now decided to finalise its review of atrazine and undertake regulatory action based on the available information at this time.

Most of the regulatory outcomes detailed in this report were proposed in the 2004 report. The APVMA also proposes to determine that the risk of atrazine entering waterways at harmful levels when used post-emergence on TT canola, when grown on raised beds, may be unacceptable. However, because this proposed finding is based on limited information which became available after 2004, the APVMA has determined that it is appropriate to require that additional data be generated so that it can further evaluate this concern.

Registrants who have a product whose label specifies a claim for weed control on TT canola will be required to either generate additional data or include an additional label restraint that specifies that atrazine must not be used post-emergence on TT canola grown on raised beds.

## REVIEW FINDINGS

### *Active constituent assessment*

The toxicological database for atrazine and four of its metabolites is extensive. The chemistry aspects (manufacturing process, quality control procedures, batch analysis results and analytical methods) of the active constituent atrazine meet current standards. There have been no revised findings in relation to the toxicology of the active constituent.

### *Toxicological assessment*

One of the concerns that led to the review of atrazine was that atrazine may be a human and animal carcinogen. The APVMA requested the Department of Health and Ageing (DoHA) to undertake a toxicological assessment to examine this concern as part of the review. The primary toxicology assessment, contained in the 1997 report, concluded that atrazine is not a carcinogen. This finding was not revisited in the April 2002 draft final report. However, in 2004 an additional assessment considered whether epidemiological and environmental reports on the carcinogenic, amphibian development and endocrine-disruption potential of atrazine would change the human health assessment and recommendations of the 1997 report.

The 1997 report identified that atrazine caused neuroendocrine disruption in Sprague-Dawley

(SD) rats, but that it did not bind to the oestrogen receptor or have any oestrogenic activity. In 2004 the OCS (the Office of Chemical Safety within DoHA) advised the APVMA that atrazine is unlikely to be an endocrine disruptor in humans, based on the known MOA in SD rats.

In addition, the OCS concluded that the epidemiological data provided no support for any carcinogenic potential of atrazine.

No changes to the existing health standards for atrazine are recommended by the OCS.

However, on the basis of recent advice from the OCS the APVMA has initiated a project to re-examine the possibility that the triazines (atrazine and related chemicals with a similar MOA) may have unintended harmful effects on humans, taking into account ongoing research into a newly hypothesised endocrine MOA. This project will take into account international reports, such as the work of the Joint Meeting on Pesticide Residues (JMPR).

The APVMA will consider initiating a new review if further data provide credible evidence of a previously uncharacterised risk.

### *Occupational health and safety assessment*

The APVMA sought advice in relation to any possible occupational health and safety risk associated with the use of atrazine. The then National Occupational Health and Safety Commission (succeeded by the Australian Safety and Compensation Council in 2005) undertook the occupational health and safety assessment. The commission's advice is contained in the 1997 report. This advice has not been revisited in subsequent assessments.

### *Residues assessment*

The 1997 report stated that the animal transfer studies evaluated at that time indicated that measurable atrazine residues were unlikely to occur in animal commodities. However, in 1997, no Table 4 entries for atrazine existed in the MRL Standard. Consequently, information on group residues, including forage and fodder residue data consistent with Australian use patterns, were required in order to determine withholding periods for grazing on sorghum, pastures and lucerne, and to confirm primary animal feed commodity MRLs. These parameters were required to assess residue levels on treated crops and therefore subsequent residues in animal commodities through use of crops for animal feed. This in turn allowed an estimate of potential risks to human health through consumption of such commodities, and of potential risks to trade.

Residue data for forage sorghum, grain sorghum and maize were assessed, as was reported in section 10 of the 2004 report, allowing the confirmation of MRLs to cover residues in primary animal feed and animal commodities. In addition, a 28-day grazing withholding period now applies for approved crop uses (except canola). Grazing and harvesting withholding periods for canola remain unchanged at 15 weeks when applied pre-emergence and six weeks post-emergence.

The residue assessment concludes that when atrazine is used according to the revised label directions, residues are unlikely to pose an unacceptable risk to human health.

### *Environmental assessment*

One of the concerns that led to the review of atrazine was the potential for unintended impacts on the environment, including contamination of ground and surface water. The environmental assessment undertaken by the Department of Water, Heritage and the Arts (DEWHA) examined these concerns. In 1997 the APVMA required certain measures to reduce the overall load of atrazine in the environment, and also required that water monitoring be conducted to determine the effect of these measures. Before the 2004 report, the DEWHA reviewed data from forestry industry studies on contamination of groundwater and surface water, and monitoring activities in annual cropping areas. The DEWHA also evaluated the environmental significance of atrazine residues in water.

The potential effects of atrazine on amphibian development and sexual differentiation were assessed, based on data submitted or available in the literature before 2004. The DEWHA has also considered a range of studies and additional information made available after 2004 and has concluded that these data do not alter the findings reported in 2004 with the exception of use of atrazine on raised bed crops (TT canola).

There are reported developmental effects on amphibians after constant exposure to atrazine at concentrations in excess of the freshwater quality guideline. However, data on impacts on amphibians at very low levels of atrazine are equivocal and it is for this reason that the US EPA has required substantial further testing to reduce any uncertainty regarding the potential risk of atrazine to amphibians. Currently, it appears that healthy amphibian populations occur at sites where atrazine is present. In considering the weight of evidence the DEWHA has concluded that current data indicate that it is unlikely that atrazine is impacting adversely on Australian amphibian populations at current levels of exposure. However, the issue of atrazine and amphibians may be revisited should the outcome of the testing requested by the US EPA indicate adverse effects at concentrations in the same order of magnitude as the Australian freshwater moderately reliable trigger value of 13 μg/L[1].

**Use of atrazine on TT canola**

As a result of feedback and further information provided in response to the 2004 report, there has been a change to the proposed risk assessment finding in relation to the use of atrazine on raised beds, particularly in relation to post-emergent use on TT canola.

The issue of waterway contamination as a result of treatment of drainage lines was discussed in the 2004 report, where it was reported that:

*the pattern of atrazine contamination in Australian surface waters indicates that safety margins continue to be narrow in some areas [of] annual cropping. The key factor that determines the likelihood of aquatic contamination appears to be the vulnerability of the soil to surface runoff… A major risk factor in…annual cropping areas appears to be the treatment of ephemeral drainage lines. Ephemeral drainage lines should not be treated with atrazine, particularly if runoff events are likely to follow (pg 69).*

The use of atrazine on TT canola grown on raised beds was specifically highlighted, when it was reported that:

[1] The freshwater moderate reliability trigger value is set in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality (2000), part of Australia's National Water Quality Management Strategy (NWQMS). 'Moderate reliability' trigger values apply to ecosystems classified as slightly to moderately disturbed.

*there are potential future environmental concerns associated with use of atrazine on TT canola, particularly associated with raised bed cropping practices. Raised bed cropping is often employed in areas where soil tends to become waterlogged, thereby killing crops…Use on TT canola has substantially increased the amount of atrazine used in Australia, particularly in very wet areas. Because the primary problem with atrazine is its potential to run off and contaminate waterways, there are implications for greater ecosystem load of atrazine in these wet regions.*

*If TT canola were to become the dominant land use in such regions, then there is a risk of greater or more persistent atrazine burdens in catchments, particularly in wet years. As yet, however, there is no evidence that this is occurring. Therefore, at this stage, there are no specific concerns to recommend changes to use patterns (pg 19).*

In response to ongoing concerns outlined in public submissions following the 2004 report, the DEWHA assessed potential risks associated with the use of atrazine post-emergence on TT canola on raised beds. In addition, the APVMA became aware of relevant work and contacted Southern Farming Systems, a Victorian-based grower group, seeking more information. Limited evidence, including Australian and overseas information provided to the APVMA at that time, suggested that waterlogging mitigation measures such as raised beds can result in increased runoff of both water and atrazine into waterways. On the basis that there was insufficient evidence to conclude that Australian raised bed cropping practices do not have an unintended harmful effect on the environment, in 2006 the DEWHA proposed to conclude that the practice of surface application of atrazine post-emergence on raised beds is not supportable without effective buffer dams, or a method of application that ensures pesticide is applied to the tops of raised beds only. This assessment alters the proposed finding reported in 2004.

In late 2007 and early 2008 the APVMA and DEWHA discussed the revised finding with affected registrants, state officials and TT canola grower groups. No consensus was reached on the issue.

In early 2008 Southern Farming Systems provided further information, but no additional data. The DEWHA considered the further information, and its conclusion in response to that specific scenario is detailed in Volume 2 of this report. The DEWHA found that it remains unable to recommend that the APVMA can be satisfied that use of atrazine on raised beds would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

At this stage the APVMA cannot conclude that the use of atrazine on TT canola, when applied post-emergence to raised beds, would not be likely to have an unintended harmful effect on the environment. However, evidence to date on this issue is very limited. Therefore the APVMA has determined that affected registrants will be provided with an opportunity to demonstrate that this potential problem is either non-existent or can be mitigated with enforceable amended label instructions. It is anticipated that it will require a further two cropping seasons for additional data to be generated and 12 months after that for the results to be evaluated and a regulatory position adopted.

In the interim the APVMA has concluded that the review of atrazine should not be delayed while any further investigation of alternative methods of use and/or containment controls is undertaken. The APVMA will therefore apply the label amendments detailed in the 2004 report. In addition, any registrant who does not elect to provide a commitment to generate the

required data will be required to amend their label to exclude the post-emergent use of atrazine on TT canola grown on raised beds.

### *Public submissions*

Responses to the 2004 report included concerns that the proposed regulatory approach did not go far enough to reduce health and environmental risks arising from the use of atrazine. In particular, community representatives expressed concerns that atrazine at very low levels could affect hormonal development in male frogs and that this raised concerns for human health if atrazine were to make its way into drinking water.

On 22 June 2007 the APVMA met with community representatives to allow them the opportunity to update concerns with the use of atrazine in Australia. A range of drinking water and environmental experts, as well as Australian regulators and health professionals, attended the forum.

After carefully considering the information presented and taking advice from the OCS and the DEWHA, the APVMA has concluded that at the present time there is no scientific consensus on the issues raised by community representatives.

The APVMA has not seen any direct evidence that current uses of atrazine pose a risk to human health. Indeed, extensive studies in laboratory animals show that there are no effects on health or reproduction in mammals maintained on drinking water containing atrazine and related compounds at low levels. Even at concentrations up to 100 times the levels that can sometimes be found in groundwater in the USA, laboratory test results indicate there were no toxic effects on the animals, their progeny or their ability to reproduce.

Furthermore, frog populations do not appear to be affected from season to season by exposure to atrazine, indicating that low level exposure in the environment is not likely to be having any long-term effects on amphibians.

## REVIEW OUTCOMES

The APVMA has initiated a project to re-examine the possibility that the triazines (atrazine and related chemicals with a similar MOA) may have unintended harmful effects on humans, taking into account ongoing research into a newly hypothesised endocrine MOA. This project will take into account international reports, such as the work of the Joint Meeting on Pesticide Residues (JMPR).

Registrants who have a product whose label specifies a claim for weed control on TT canola will be required to either generate additional data or include an additional label restraint that specifies that atrazine must not be used post-emergence on TT canola grown on raised beds.

After consideration the additional assessments completed after 1997 the APVMA accepts the recommendations of the OCS and the 2004 recommendations of the DEWHA, and the following regulatory actions have been applied:

1. Active constituent approvals have been affirmed.
2. Existing label instructions have been deemed to be inadequate and the most recently approved labels have been amended as follows:
    a) Labels have been amended to specify additional restraints to further reduce the risk of

contamination of waterways[2].

b) Withholding period instructions have been amended.

c) Herbicide resistance reporting details have been added to labels.

These variations to label instructions satisfy the requirements for continued registration of products; and so

3. Product registrations have been affirmed.

4. To ensure that all labels are in line with the recommendations of the 2008 report any previously approved labels that do not contain the amended instructions have been cancelled.

As an associated outcome of the review, changes will be made to the MRL Standard to align entries in the standard with existing approved use patterns.

[2] Where the amended label includes a claim for use on TT canola, and does not specifically exclude use of the product post-emergence on TT canola grown on raised beds, the amended label will be subject to the condition that additional data must be generated within two growing seasons and provided to the APVMA to enable an additional assessment to be undertaken in relation to the risk to the environment associated with this use.

# 1 INTRODUCTION

The APVMA has reviewed the approval of the active constituent atrazine, registered products containing atrazine and the associated label approvals for products containing atrazine. This document summarises the final data considered before finalisation of the review report and regulatory decision.

## 1.1 REGULATORY STATUS OF ATRAZINE IN AUSTRALIA

Atrazine is a triazine herbicide used for the control of grass and broadleaf weeds in crops such as sorghum, maize, sugarcane, and triazine tolerant (TT) canola. In addition, atrazine is widely used on lupins in Western Australia. Minor uses include control of weeds in lucerne, grass seed, pasture and potato crops. Atrazine is also important in the establishment of pine and eucalypt plantations, and for control of parthenium weed in Queensland, the Northern Territory and northern parts of New South Wales.

Since the review began in December 1995, product labels have been amended to include use of atrazine to control weeds in TT canola and chickpeas. These uses have been added to a number of atrazine products. In addition, uses have been extended to include the control of parthenium weed in New South Wales and the Northern Territory.

Atrazine is one of the main herbicides used in Australia. As of February 2008 there were seven active constituent approvals for atrazine (see Appendix A), 48 registered products containing atrazine and 23 atrazine product registrants (see Appendix B).

Available formulations are dry flowable, liquid, liquid concentrate, granular, wettable powder, water dispersible granule, and suspension concentrate products.

## 1.2 PROPERTIES AND MODE OF ACTION (MOA)

Atrazine is mainly absorbed through the roots of plants and then carried to the actively growing tips and leaves, although some foliar absorption occurs. In susceptible plant species, atrazine inhibits photosynthesis, whereas it is metabolised in tolerant plants.

Atrazine is slightly hydrophilic, with a water solubility of about 30 mg/L. It is moderately to highly mobile in soils with low clay or organic matter content. Because it does not adsorb strongly to soil particles and has a half-life ranging from 60 to greater than 100 days, atrazine has a high potential for water contamination, despite its moderate solubility in water.

Atrazine is persistent in soil, and can exist for longer than a year under dry or cold conditions. The primary breakdown route of atrazine is via chemical hydrolysis, followed by degradation by soil micro-organisms. Atrazine can also be residually active in soil, which has the potential to cause toxicity to rotational crops if planted at an incorrect interval. Soybeans, vegetable crops, cereal grains, peanuts and potatoes are very sensitive to atrazine.

Atrazine is practically non-toxic to birds, slightly toxic to fish and some aquatic invertebrates, and moderately toxic to marine copepods and shrimp. It is highly toxic to some algae and aquatic vascular plants (e.g. duckweed). Atrazine is readily absorbed through the gastrointestinal tract and also through the lungs or the skin. The World Health Organization (WHO) classifies it as a mild skin irritant and a severe eye irritant (WHO 1996). Overall, it is considered slightly to moderately toxic to humans and other mammals. At high doses,

atrazine can cause neuro-muscular effects in laboratory animals, such as motor incoordination, limb paralysis, respiratory distress and hypothermia. A full toxicological assessment was published in the 1997 report (see http://www.apvma.gov.au/chemrev/downloads/atrazine_tox.pdf). An additional toxicological assessment was published in the 2004 report, (see http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf). A third toxicological assessment, undertaken ahead of a community forum on atrazine held in June 2007, is in Volume 2 of this report.

## 1.3 REASONS FOR ATRAZINE REVIEW

The review of the chemical atrazine was announced in December 1995 as part of the APVMA's first cycle of chemical reviews. The active constituent atrazine, products containing atrazine, and their product labels, were placed under review due to concerns over:

- human and animal carcinogenicity claims;
- moderate potential chronic toxicity risk;
- potential to contaminate ground and surface water;
- absence of MRLs for major commodities; and
- reported breakdown in efficacy.

The scope of the review covered these specific issues as well as all aspects affecting continued registration and approval of atrazine.

## 1.4 SCOPE OF THE REVIEW

The scope of the review was to determine whether the APVMA could be satisfied that the continued use of products containing atrazine in accordance with the instructions for their use would be unlikely to adversely affect human health, the environment, or trade and would be effective for the purpose claimed.

## 1.5 REGULATORY OPTIONS

The basis for a reconsideration of the registrations and approvals for a chemical is whether the APVMA is satisfied that the requirements for continued registration and approval are being met, as specified by the Agvet Codes. There can be three possible outcomes to the reconsideration of the registration of products containing atrazine and their labels. Based on the information reviewed, the APVMA may be:

- satisfied that the products and their labels continue to meet the prescribed requirements for registration and approval and therefore affirms the registrations and approvals
- satisfied that the conditions to which the registration or approval is currently subject can be varied in such a way that the requirements for continued registration and approval will be complied with and therefore varies the conditions of registration or approval
- not satisfied that the requirements for continued registration and approval continue to be met and suspends or cancels registration and/or approval.

# 2 SUMMARY OF 1997 ATRAZINE REPORT OUTCOMES

The APVMA published a report on its findings to date in November 1997. The conclusions were as follows:

- Non-agricultural/home garden uses were to be cancelled as they posed an undue risk to the environment.
- Product labels were to be modified to include suitable warnings to protect the environment by reducing water contamination.
- Product labels were to be modified to include suitable warnings to protect worker safety, including modifications to recommended personal protective equipment to increase user protection.
- Approval of extensions of some uses then under permit, such as TT canola and parthenium weed, was recommended.
- MRLs for which there were no associated registered uses were to be deleted.

The 1997 report also identified that additional studies and information were required to alleviate remaining environmental and human health concerns, as follows:

- Residue data were required to confirm animal feed commodity MRLs.
- Registrants were to provide the APVMA with information on annual sales.
- Registrants were to report incidents of herbicide resistance to the APVMA.
- Additional water monitoring studies were to be conducted by registrants and user groups to determine whether the levels of atrazine in the environment were above or below the level that would impact on the environment.

These dot points are elaborated upon below.

### *Cancellation of home garden/non-agricultural use patterns*

The potential for atrazine to contaminate ground and surface water was one of the key reasons for its review. When the review commenced, atrazine products could be applied to lawns, golf courses, irrigation channels, drains, roadsides, industrial premises and other non-agricultural areas. It was concluded that these uses contributed significantly to the total environmental load of atrazine and thus such uses could not be continued (excluding the control of parthenium weed on roadsides). As an outcome of the 1997 report, all home garden/non-agricultural use patterns were cancelled in December 1998.

### *Label changes*

The 1997 report made recommendations intended to reduce the overall load of atrazine in the environment, especially its presence in water. Changes to label statements for this purpose included limitations on the quantities that could be used, buffer zones, and restraint statements relating to spray drift, weather conditions, and application to waterlogged soil.

The 1997 report also recommended changes to safety directions in order to protect workers. The changes included additional requirements for personal protective equipment and

restrictions on application methods.

### *Label cancellations*

In March 2001 the APVMA cancelled the approvals of all labels approved before November 1997, to ensure that all labels were in line with the recommendations of the 1997 report.

### *Maximum residue limits*

As an associated outcome of the 1997 report, MRLs for citrus fruits, grapes and pineapples were deleted because there were no use patterns on labels and new MRLs were established for primary animal feed commodities, edible offal and milks.

Additional forage and fodder residue data for sorghum, pasture and lucerne were required to confirm residue levels for primary animal feed commodity MRLs and those of animal commodities. These data were assessed in section 10 of the 2004 report, available at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf.

### *Reporting on annual sales and herbicide resistance*

Registrants were required to report to the APVMA the amounts of atrazine products sold over one year. A total of 2,100 tonnes of active ingredient were sold in the financial year 1997–98.

Registrants were also required to report to the APVMA any incidents of herbicide resistance to atrazine and any follow-up investigations they conducted. Registrants advised that they received no reports of herbicide resistance. However, the APVMA noted that current labels did not give users an address or contact to enable users to report resistance incidents to registrants. The report recommended modifying labels to address this shortcoming (see section 6 of the 2004 report).

### *Additional water monitoring requirements*

The 1997 report required certain measures to reduce the overall load of atrazine on the environment, and recommended that water monitoring be conducted to determine the effect of these measures. Monitoring would also provide information on trends in atrazine contamination in both ground and surface water.

For cropping situations, initial investigations found that a number of water monitoring programs were already established in various areas of Australia and that these programs included atrazine monitoring. The principal registrant, Syngenta Crop Protection Pty Ltd, collated information from many of these programs. As sufficient information was available from these surveys, no additional studies were required.

In 1994, the APVMA issued a provisional label for use of atrazine in forestry. This label was issued on the understanding that the forestry industry would undertake a nationwide series of trials to evaluate the effects of atrazine, applied at the nominated rates, on water quality in forestry use situations.

The Forest Herbicide Research Management Group was formed to establish research proposals for design, assessment and management of field trials. The group's report was presented to the APVMA in May 2000. Together with information collected from around Australia, this report forms the basis for the environmental assessment in sections 11 and 12

of the 2004 report (see http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf).

### *Water quality guidelines*

#### Drinking water

The 1997 report concluded that exposure of people to atrazine in food was very unlikely, although concerns were raised over the potential for exposure from drinking water. Because atrazine is both mobile in soil and reasonably stable in the environment, exposure of the human population would most likely occur from contamination of drinking water. It was therefore recommended that consideration be given to updating the Australian Drinking Water Guidelines (2004) for atrazine, and to including the atrazine specific metabolites, desethylatrazine and hydroxyatrazine, with atrazine in the definition for the guideline value.

The National Health and Medical Research Council (NHMRC) in collaboration with the National Resource Management Ministerial Council (NRMMC) finalised the drinking water guidelines for atrazine in 2004. See http://www.nhmrc.gov.au/publications/synopses/eh19syn.htm.

The guidelines state that although atrazine should not be present at detectable levels in drinking water, if present atrazine would not be a health concern unless concentrations exceeded 0.04 mg/L. If atrazine is detected, then remedial action should be taken to stop contamination. The practical limit of determination of atrazine is 0.0001 mg/L.

#### Aquatic ecosystems

In 1997, Australia had yet to establish a water quality guideline for protection of aquatic ecosystems. A guideline value for atrazine of 2 µg/L was employed overseas and had been proposed for local application.

Australian and New Zealand Guidelines for Fresh and Marine Water Quality were published in October 2000. The water quality guidelines are estimates of concentrations at which individual chemicals should not cause direct toxic effects in the environment. If the guideline value for a chemical is exceeded, there is a potential risk of an environmental impact. The freshwater moderate reliability trigger value for atrazine was set at 13 µg/L. The values apply to the overall or surrounding quality of water; they do not apply to a point of discharge or mixing zone.[3]

[3] APVMA note: It is not clear where a point source, mixing zone or point of discharge ends and a waterway begins.

# 3 SUMMARY OF DATA ASSESSMENTS POST 2004

## 3.1 TOXICOLOGY

The primary toxicology assessment for atrazine was published in the 1997 report (see http://www.apvma.gov.au/chemrev/downloads/atrazine_tox.pdf). This report summarises the findings of over 300 studies (see section 3 of the report at http://www.apvma.gov.au/chemrev/downloads/atrazine_prs.pdf). A further toxicology assessment completed in 2004 is in sections 3 and 13 of the 2004 report at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf.

The OCS did more work after the 2004 report to consider whether reports published since 2004 on carcinogenicity, amphibian development and the endocrine-disruptor potential of atrazine would change the recommendations of its 1996 assessment (published in the APVMA's 2007 atrazine report). OCS also considered the current level of exposure to mixtures of triazine compounds via food and drinking water and whether a cumulative risk assessment was warranted.

The post-2004 reports were epidemiological studies, which considered a possible link between atrazine exposure and human cancer, and environmental studies, which investigated possible effects on frog development. These environmental studies were included because of possible links to atrazine's endocrine-disrupting potential. The new epidemiological data provided no support for any carcinogenicity potential for atrazine. The OCS came to the conclusion that the environmental studies were unlikely to have direct relevance to human health.

The 1997 report identified that atrazine caused neuroendocrine disruption in Sprague-Dawley (SD) rats, but did not bind to the oestrogen receptor or have any oestrogenic activity. Therefore it is unlikely to be an endocrine disruptor in humans based on the known MOA in SD rats. The current level of exposure to mixtures of triazine compounds via food and drinking water is not of concern, although cumulative risk assessment would be a consideration if the level of exposure were significant.

For these reasons, the OCS does not recommend any changes to the existing health standards for atrazine.

### *APVMA conclusions*

The APVMA has not seen any direct evidence that atrazine is a risk to human health for current uses. Indeed, extensive studies in laboratory animals show that there are no effects on health or reproduction in mammals maintained on drinking water containing atrazine and related compounds at low levels. Even at concentrations up to 100 times the levels that can sometimes be found in groundwater in the USA, laboratory test results indicate there were no toxic effects on the animals, their progeny or their ability to reproduce.

However, on the basis of recent advice from OCS, the APVMA has initiated a project to re-examine the possibility that the triazines (atrazine and related chemicals with a similar MOA) may have unintended harmful effects on humans, taking into account ongoing research into a newly hypothesised endocrine MOA. This project will take into account international reports, such as the work of the Joint Meeting on Pesticide Residues (JMPR).

The APVMA will consider a new review if further data provide credible evidence of a previously uncharacterised risk.

## 3.2 ENVIRONMENT

The primary environmental assessment for atrazine completed in 1997 is summarised in section 6 of the 2007 atrazine report at http://www.apvma.gov.au/chemrev/downloads/atrazine_prs.pdf. Further environmental assessments were published in the 2002 report (see section 3 of the report at http://www.apvma.gov.au/chemrev/downloads/atrazine_final.pdf) and in the 2004 report (see sections 3, 11 and 12 at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf).

The DEWHA's 1997 environmental assessment considered the potential for atrazine to contaminate waterways. It reviewed data from forestry industry studies on contamination of groundwater and surface water, and monitoring activities in annual cropping areas, and evaluated the environmental significance of atrazine residues in water.

The potential effects of atrazine on amphibian development and sexual differentiation were assessed, based on data submitted or available in the literature before 2004. DEWHA also considered studies and additional information made available after 2004 and has concluded that these data do not alter the findings reported in 2004, with the exception of use of atrazine on raised bed crops post-emergence (TT canola).

### *Use of atrazine on TT canola*

As a result of feedback and further information provided in response to publication of the 2004 report, the DEWHA has changed the proposed risk assessment finding in relation to the use of atrazine on raised beds, particularly in relation to TT canola.

The issue of waterway contamination as a result of treatment of drainage lines was discussed in the 2004 report, where it was reported that:

*the pattern of atrazine contamination in Australian surface waters indicates that safety margins continue to be narrow in some areas [of] annual cropping. The key factor that determines the likelihood of aquatic contamination appears to be the vulnerability of the soil to surface runoff…A major risk factor in…annual cropping areas appears to be the treatment of ephemeral drainage lines. Ephemeral drainage lines should not be treated with atrazine, particularly if runoff events are likely to follow (pg 69).*

The use of atrazine on TT canola grown on raised beds was specifically highlighted, when it was reported that:

*there are potential future environmental concerns associated with use of atrazine on TT canola, particularly associated with raised bed cropping practices. Raised bed cropping is often employed in areas where soil tends to become waterlogged, thereby killing crops…Use on TT canola has substantially increased the amount of atrazine used in Australia, particularly in very wet areas. Because the primary problem with atrazine is its potential to run off and contaminate waterways, there are implications for greater ecosystem load of atrazine in these wet regions.*

*If TT canola were to become the dominant land use in such regions, then there is a risk of*

*greater or more persistent atrazine burdens in catchments, particularly in wet years. As yet, however, there is no evidence that this is occurring. Therefore, at this stage, there are no specific concerns to recommend changes to use patterns (pg 19).*

In response to ongoing concerns outlined in public submissions following the 2004 report, the DEWHA assessed potential risks associated with the use of atrazine post-emergence on TT canola on raised beds. In addition, the APVMA became aware of relevant work and contacted Southern Farming Systems, a Victorian-based grower group, seeking more information. Limited evidence from Australia and overseas, including information provided to the APVMA at that time, suggested that waterlogging mitigation measures such as raised beds can result in increased runoff of both water and atrazine into waterways. On the basis that there is insufficient evidence to conclude that Australian raised bed cropping practices do not have an unintended harmful effect on the environment, in 2006 the DEWHA proposed to conclude that the practice of surface application of atrazine post-emergence on raised beds is not supportable without effective buffer dams, or a method of application that ensures pesticide is applied to the tops of raised beds only. This assessment alters the proposed finding reported in 2004.

In late 2007 and early 2008 the APVMA and DEWHA discussed the revised finding with affected registrants, state officials and TT canola grower groups. No consensus was reached on the issue.

In early 2008 Southern Farming Systems provided further information, but no additional data, in response to this concern. The DEWHA considered the submission put forward by Southern Farming Systems, and its conclusion in response to that specific scenario is detailed in Volume 2 of this report. The DEWHA found that it remains unable to recommend that the APVMA can be satisfied that use of atrazine on raised beds would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

At this stage the APVMA cannot conclude that the use of atrazine on TT canola, when applied post-emergence to raised beds, would not be likely to have an unintended harmful effect on the environment. However, evidence to date on this issue is very limited. Therefore the APVMA has determined that affected registrants will be provided with an opportunity to demonstrate that this potential problem is either non-existent or can be mitigated with enforceable amended label instructions. It is anticipated that it will require a further two cropping seasons for additional data to be generated and another 12 months after that for the results to be evaluated and a regulatory position adopted.

In the interim the APVMA has concluded that the review of atrazine should not be further delayed while more investigation of alternative methods and/or containment controls is undertaken. The APVMA will therefore apply the label amendments detailed in the2004 report. In addition, any registrant who does not elect to provide a commitment to generate the required data will be required to amend their label(s) to exclude the post-emergent use of atrazine on TT canola grown on raised beds.

### *Atrazine and amphibians*

There are reported developmental effects on amphibians after constant exposure to atrazine at concentrations in excess of the freshwater quality guideline. However, data on impacts on amphibians at very low levels of atrazine are equivocal and it is for this reason that the US EPA has required substantial further testing to reduce any uncertainty regarding the

potential risk of atrazine to amphibians. Currently, it appears that healthy amphibian populations occur at sites where atrazine is present. In considering the weight of evidence the DEWHA concluded that current data indicate that it is unlikely that atrazine is impacting adversely on populations of Australian amphibians at current levels of exposure. However, the issue of atrazine and amphibians may be revisited should the outcome of the testing required by the US EPA indicate adverse effects at concentrations in the same order of magnitude as the Australian freshwater moderately reliable trigger value of 13 µg/L[4].

Continued registration of atrazine products depends not only on whether unintended effects are likely to occur, but also on whether these unintended effects will have adverse consequences for amphibian populations. Atrazine is considered slightly toxic to tadpoles and the no observable effect level (NOEL) in laboratory tests is generally in the order of 2.6 mg/L. Mesocosm[5] studies have established adverse effects on size and weight after exposure to concentrations of 200 µg/L atrazine over several weeks. Following concerns regarding the potential for endocrine disruption in amphibians, the main unintended effect of atrazine considered in this report is disruption of sexual differentiation. Some studies have reported such effects at low exposure levels typical of those that may occur in the Australian environment. However, it has not been possible to independently reproduce these effects at the same low exposure levels, although some of the effects have been replicated in the laboratory at higher exposures (25 µg/L).

One study identified delayed metamorphosis and reduced metamorphic size as potential unintended adverse effects of exposure to atrazine at concentrations of 40 and 320 µg/L, under laboratory conditions. Reduced immune function has also been reported in laboratory amphibians exposed to 3 µg/L and 30 µg/L atrazine. However, similar reduced function has been reported in the field where there was no evidence of atrazine exposure.

DEWHA has considered the likelihood of harmful effects on amphibian populations from exposure to atrazine at concentrations below the freshwater guideline value. The evidence for persistent harmful effects at levels below the guideline value is equivocal, with inconsistencies between studies and results. Indeed, in the absence of a clear dose-response relationship, the US EPA has sought additional data to reduce any uncertainty regarding the potential risk of atrazine to amphibians. Based on the weight of evidence to date, the likelihood that atrazine is adversely impacting on immune function or sexual differentiation in Australian amphibian populations at the reported levels of exposure is considered low.

If the additional data required by the US EPA, which have been designed to eliminate uncertainty regarding the test conditions, demonstrate that adverse effects occur at concentrations in the same order of magnitude as the trigger value of 13 µg/L, then the APVMA may revisit the issue of atrazine and amphibians.

## 3.3 RESIDUES

The animal transfer studies evaluated for the 1997 report indicated that measurable residues of atrazine were unlikely to occur in animal commodities (see http://www.apvma.gov.au/chemrev/downloads/atrazine_tox.pdf). However, in 1997, no Table

[4] The freshwater moderate reliability trigger value is set in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality, part of Australia's National Water Quality Management Strategy (NWQMS). 'Moderate reliability' trigger values apply to ecosystems classified as slightly to moderately disturbed.
[5] Mesocosms are field model ecosystems. For more information see previous reports, and in particular section 12 of the2004 report at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf.

4 entries for atrazine existed in the MRL Standard. Consequently, information on group residues, including forage and fodder residue data for sorghum, pastures and lucerne, were necessary to set animal feed commodity MRLs. These data were also needed to confirm or change withholding periods for grazing such crops. The residues assessment completed in 2002 is in section 2 of the 2002 report at http://www.apvma.gov.au/chemrev/downloads/atrazine_final.pdf.

A further residue assessment was completed in 2004 (see section 10 of the 2004 report at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf).

As described in the 2002 report, the new residue data for forage sorghum, grain sorghum and maize enabled confirmation of MRLs to cover residues in primary animal feed and animal commodities. A new 28-day grazing withholding period applies for approved crop uses, except canola. Grazing and harvesting withholding periods for canola remain unchanged at 15 weeks when applied pre-emergence and six weeks post-emergence.

The APVMA concludes that, when atrazine is used according to label directions, residues are unlikely to pose an unacceptable risk to human health.

## 3.4 OVERSEAS REGULATORY STATUS

### *United States of America*

Information on the US EPA regulatory position on atrazine is compiled in the Decision Documents for Atrazine at http://www.epa.gov/oppsrrd1/REDs/atrazine_combined_docs.pdf, comprising:

- Atrazine IRED [Interim Reregistration Eligibility Decision] (January 2003);
- Revised Atrazine IRED (31 October 2003); and
- Finalisation of Atrazine IRED, and Completion of Tolerance Reassessment and Reregistration Eligibility Process (6 April 2006).

The US EPA Drinking Water Level of Comparison is comparable to Australia's drinking water Health Value. The US Drinking Water Level of Comparison for atrazine is 68 parts per billion (ppb), whereas the Australian value is 40 ppb.

The US EPA also noted the inconsistency and lack of reproducibility across studies and an absence of a dose-response relationship, and sought additional data to reduce uncertainty about the potential risk of atrazine to amphibians. The EPA evaluated the latest amphibian developmental studies for consideration at a meeting of its Science Advisory Panel (9–12 October 2007); the EPA's white paper[6] concluded that, based on a review of 36 open literature and registrant-submitted studies related to the potential effects of atrazine on gonadal development in amphibians, the weight-of-evidence does not show that atrazine produces consistent, reproducible effects across the range of exposure concentrations and amphibian species tested.

[6] US EPA (2007) US, Environmental Protection Agency, Washington D.C. Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, Environmental Fate and Effects Division Washington, D.C. *White Paper on the Potential for Atrazine to Affect Amphibian Gonadal Development*, submitted to the FIFRA Scientific Advisory Panel for Review and Comment October 9-12, 2007.

As in Australia, in 2003 the US required the implementation of certain risk mitigation strategies in watersheds and ecological monitoring to address concerns about aquatic ecosystems. In the US atrazine can continue to be used to control weeds in crops such as sugarcane, corn, guava, wheat stubble, commercial lawns, Bermuda grass, forest plantings, golf courses and lawns. However, there are ongoing calls in the US for further limits on atrazine and for more health assessments to be done.

### *Canada*

The Canadian re-evaluation of atrazine was released for public comment in November 2003 and the Re-evaluation Decision Document in May 2004 (PMRA 2003; 2004). The documents conclude that atrazine is of low to slight acute toxicity and that its primary MOA is via impairment of hypothalamic-pituitary function in the rat. The acute reference dose (ARfD) was set at 0.04 mg/kg bw, based on a four-day rat study. The no observable adverse effect level (NOAEL) was 12.5 mg/kg bw/d, with an uncertainty factor of 10 x 10 x 3).

Atrazine was used in Canada for control of weeds in corn, blueberries and TT canola. Registrants did not wish to generate the data to support the latter two uses, which are therefore being phased out. However, uses in corn have been retained, with restrictions on application rates and no aerial application allowed. Canada has also required additional water monitoring data.

The Pest Management Regulatory Agency published the Proposed Acceptability for Continuing Registrations Document covering the environmental assessment for the continued use of atrazine on corn on 22 May 2007 (see http://www.pmra-arla.gc.ca/english/pdf/rvd/rvd2007-05-e.pdf). The completed environmental risk assessment for atrazine use on corn continues to support existing uses, subject to specific mitigation measures.

### *European Union*

In March 2004, the Commission of the European Communities decided that authorisation for the use of atrazine in the EU was to be withdrawn by September 2004[7]. It did not do this because of any specific toxicological reasons but because it was concerned that residues in groundwater might exceed its nominal limit of 0.1 ppb, which it has set for all chemicals for which specific values have not been established. However, 'essential' uses (on maize and in forestry in Ireland and the UK and on maize in Spain, Portugal, Hungary and Poland) were still permitted in EU countries until December 2007.

### *International Agency for Research on Cancer (IARC)*

Dosing with atrazine can lead to an earlier onset of tumours in one strain of female rats. The IARC concluded in 1999 that atrazine's MOA is species specific and thus not relevant to humans and downgraded the classification of atrazine from Group 2B 'possible human carcinogen' to Group 3 'not classifiable' (see http://www.inchem.org/documents/iarc/vol73/73-03.html).

[7] *Commission Decision of 10 March 2004 concerning the non-inclusion of atrazine in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance (notified under document number C(2004) 731) (2004/248/EC).* Official Journal of the European Union L 78/53.

### *Joint FAO/WHO Meeting on Pesticide Residues*

The Joint Meeting on Pesticide Residues (JMPR), a joint committee of the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), published its reassessment of atrazine in September 2007 (see http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/JMPRreports.htm). The report concludes on page 47 that in relation to atrazine:

*A range of epidemiological studies (including cohort studies, case-control studies, and ecological or correlational studies) assessed possible relationships between atrazine or other triazine herbicides and cancer in humans. For some cancer types, such as prostate or ovarian cancer and non-Hodgkin lymphoma, the increased risks reported in single studies could either be explained by the methodology used or had not been confirmed in more reliable studies. Thus, the weight-of-evidence from the epidemiological studies did not support a causal association between exposure to atrazine and the occurrence of cancer in humans. The Meeting concluded that the existing database on atrazine is adequate to characterize the potential hazards to foetuses, infants and children.*

The JMPR established an acceptable daily intake (ADI) for humans of 0.02 mg/kg bw/d, which is higher than Australia's ADI of 0.005 mg/kg bw/d.

The JMPR ADI is based on an overall no observable adverse effect level (NOAEL) from a wide range of toxicity studies of 1.8 mg/kg bw/d, which is higher than Australia's no observable effect level (NOEL) of 0.5 mg/kg bw/d.

## 3.5 SUMMARY OF PUBLIC SUBMISSIONS IN RESPONSE TO THE 2004 REPORT

Submissions to the APVMA before October 2004 are summarised in section 4 of the 2004 report at http://www.apvma.gov.au/chemrev/downloads/atrazine_draftfinal2.pdf.

Responses to the 2004 report included concerns from stakeholders that the proposed regulatory approach did not go far enough to reduce health and environmental risks arising from the use of atrazine. In particular, community representatives expressed concerns that atrazine at very low levels could affect hormonal development in male frogs and that this raised concerns for human health if atrazine were to make its way into drinking water.

Eleven submissions included comments on the environmental assessment. These were provided to the DEWHA. Of these, six submissions which included comments on human health were forwarded to the OCS. These submissions raised a variety of concerns, ranging from claims that the proposed label instructions were too restrictive, to claims that atrazine should be banned because it has not been proven to be safe.

### *Advice from OCS on public submissions related to human health*

A summary of concerns raised and the OCS response to the six submissions sent to the OCS is below. Further information and additional recommendations from the DEWHA are in the environmental assessment (section 3, Volume 2 of this report).

1. The Pesticides Advisory Committee (PAC) in Western Australia examined the 2004 report and noted the relevance of toxicological data generated from long-term studies with Sprague-Dawley (SD) rats in relation to effects in humans. The PAC recommended that the

APVMA strengthen this part of the report to include the most up-to-date information on the MOA of atrazine in SD rats, suggesting that the toxicological effects seen in SD rats are not relevant to humans. The PAC was of the view that this additional information would strengthen the review and provide a direct answer to those who still wished to follow the line that atrazine is an endocrine disruptor or carcinogen. A recent article[8] was cited. The PAC also noted that the ADI was based on mammary tumour incidence from a two-year SD rat study. In light of the MOA producing mammary tumour being specific to SD rats, the PAC suggested that a different NOEL that has relevance to human toxicity should be used to set the ADI.

***OCS response:*** In relation to mammary tumours associated with atrazine exposure in female SD rats, Meek *et al.* (2003) postulated that atrazine suppresses the release of luteinizing hormone (LH) from the pituitary gland such that there is an insufficient level of LH to trigger ovulation. When ovulation fails, follicles within the ovum continue to produce oestrogen. Repetitive failure of ovulation leads to prolonged exposure to endogenous oestrogen and/or prolactin creating a state of persistent oestrus. Over a sufficiently long period of time, this would translate into a hastened ageing process and the development of mammary fibroadenoma/carcinoma. Thus, in SD female rats, reproductive ageing is characterised by persistent hyperestrogenemia and hyperprolactinemia with low levels of LH and follicle-stimulating hormone (FSH). In contrast, reproductive ageing in women is characterised by exhaustion of ovarian follicles resulting in low levels of oestrogen and prolactin. LH and FSH levels in postmenopausal women remain high. Meek *et al.* concluded that on the basis of differences in reproductive physiology, it would appear that the atrazine response in SD rats is not relevant to humans.

In the 1997 report, the OCS stated that 'In female SD rats, no increase in the overall incidence of pituitary or mammary tumours was seen but there was a somewhat earlier onset of mammary fibroadenoma/carcinoma at 20 mg/kg bw/d atrazine. An increased number of days in oestrus or under oestrogen dominance were observed, which suggested that the earlier onset of mammary tumours could relate to an accelerated ageing of the neuroendocrine system. In humans, menopausal women develop episodes of declining oestrogen secretion and longer periods of low oestrogen levels, in contrast to the situation in ageing SD rats. Therefore, it would appear that the atrazine response in SD rats is not an appropriate surrogate for the assessment of human risk for mammary tumour development'. The OCS considers that the MOA discussed in the 1997 report is essentially similar to that postulated by Meek *et al.* (2003). Therefore, no changes to the OCS recommendations are necessary.

A NOEL of 0.5 mg/kg bw/d (10 ppm) was selected in a two-year SD rat study, with a LOEL of 70 ppm (2.8–4.5 mg/kg bw/d) based on a statistically significant increase in mammary tumour incidence at this dose. Whilst the incidence of mammary tumours was not considered to be relevant to human health, the response was considered to reflect a neuroendocrine effect and thus was an appropriately conservative endpoint for establishing the ADI.

After having considered these suggestions, the OCS has concluded no changes to the recommendations in the 1997 report are necessary. The Meek (2003) study has been included in the revised toxicology assessment (sections 1 and 2, Volume 2 of this report).

[8] Meek ME, Bucher JR, Cohen SM, Dellarco V, Hill RN, Lehman-McKeeman LD, Longfellow DG, Pastoor T, Seed J & Patton DE (2003) A framework for human relevance analysis of information on carcinogenic modes of action. Critical Reviews in Toxicology 33:591–653.

2. Dr John Pollak (University of Sydney) commented that 'it is essential that the APVMA changes its present attitude of ignoring the concentration additive toxic effects of mixtures of triazine herbicides that are reported and permitted to be used in Australia'.

Dr Pollak said that in establishing whether a cumulative risk assessment is warranted for a group of similarly acting compounds, the OCS should be satisfied that exposure is likely to occur. It was noted in the1997 report that atrazine was used in high volumes, predominantly as a herbicide in preparation for plantings for coarse grains and sugarcane, with minor uses in forestry and legumes.

***OCS response:*** The 1992 Australian Market Basket Survey (National Food Authority, AGPS)[9] conducted assays for atrazine and simazine in meat and cereal foods. Because of their use pattern (just before or after crop emergence) it was considered unlikely that residues would be present in food. In addition, no residues of either herbicide were detected. This finding was in agreement with US data; in over 30 years of use, atrazine had not been detected in edible portions of plants or livestock nor had it been detected in market basket surveys. The OCS concluded that exposure of the population to atrazine in food is very unlikely.

However, the fact that atrazine is both mobile in the soil and reasonably stable in the environment indicates that non-occupational exposure to atrazine, if it occurs, is likely to occur through contamination of drinking water. Indeed the 1997 report noted that consideration should be given to amending the Australian drinking water guidelines to include the four metabolites with parent atrazine in the definition of atrazine; this action would have the equivalent effect of lowering the guideline value[10] (0.0005 mg/L) for atrazine alone since, in water samples in which atrazine is detected, one or more metabolites are commonly detected, but were disregarded in the current Standard. This issue was also referred by the OCS to the Advisory Committee on Pesticides and Health (ACPH). Recognising the need to take into account toxicologically significant metabolites from an exposure risk assessment perspective, the ACPH supported modification of the atrazine guideline value in the 1996 Australian Drinking Water Guidelines. The ACPH proposed that, rather than including all four metabolites (desethylatrazine, desisopropylatrazine, diaminochlorotriazine and hydroxyatrazine) as outlined above, only the atrazine-specific metabolites desethylatrazine and hydroxyatrazine be included with atrazine in the definition for the guideline value.

ACPH therefore recommended that it was appropriate that the issue of drinking water guidelines for atrazine be referred to the NMHRC and ARMCANZ[11] for consideration by the joint committee responsible for updating the Australian Drinking Water Guidelines. A health based guideline of 0.04 mg/L was established by the NHMRC. However it was noted that if atrazine is detected in the drinking water, then remedial action should be taken to stop the contamination; the practical limit of determination is 0.0001 mg/L (0.1 ppb). It was also recognised by ACPH that the metabolites of atrazine (desethylatrazine, desisopropylatrazine, diaminochlorotriazine and hydroxyatrazine) may constitute approximately 50 per cent of the total atrazine-derived triazine compounds in some ground and surface water samples, and this was accounted for by the addition of an extra two-fold safety factor. Similarly, for simazine, a

[9] National Food Authority (1992) *The 1992 Australian Market Basket Survey*, NFA, Canberra.
[10] APVMA note: The level at or above which action should take place to identify the source and prevent further contamination.
[11] APVMA note: The 2004 *Australian Drinking Water Guidelines* (ADWG) have been developed by the National Health and Medical Research Council (NHMRC) in collaboration with the Natural Resource Management Ministerial Council (NRMMC). See http://www.nhmrc.gov.au/publications/synopses/eh19syn.htm.

health based guideline value of 0.05 mg/L was established, with a guideline value of 0.0005 mg/L, above which remedial action should be taken to remove the source of contamination.[12]

It may be further noted that atrazine has rarely been found in Australian reticulated water supplies. In groundwater it has been reported at concentrations of up to 0.002 mg/L in an area where atrazine was used to suppress weed growth in irrigation channels for 10 years (NHMRC 1996). It was furthermore concluded that all uses that contributed to the total environmental load of atrazine – such as atrazine products applied to lawns, golf courses, irrigation channels, drains, roadsides, industrial premises and non-agricultural areas – could not be maintained.

Therefore, while acknowledging there is a basis for consideration of a risk assessment of atrazine as part of a group of triazine pesticides based on a common MOA, the OCS considers that current exposure to atrazine and simazine in food is very unlikely, while available data suggest that exposure to atrazine, simazine and propazine in reticulated drinking water is likely to be negligible. Considering the negligible exposure to the major triazine compounds available in Australia, a cumulative risk assessment of these compounds on public health grounds is not warranted at present. Nevertheless, the utility of both aggregate and cumulative risk assessment methodology for the assessment of risks posed by agricultural and veterinary chemicals to public health is under consideration by the OCS. See section 2.7, Volume 2.

3. The St Helens Marine Farmers provided the results of water tests for atrazine performed in 1993 by the Government Analyst Laboratory, Tasmania. The laboratory tested water samples from streams in the catchment area that supplied water to St Helens in Tasmania. In 1994 the Chemistry Department of the University of Tasmania determined the combined level of atrazine and simazine in drinking water sampled from several localities in the Break O'Day Municipality, Tasmania. It is not clear whether this water was collected from streams in the catchment area or from tap water.

The results showed that atrazine level was below the detection limit (0.001 mg/L) in the water samples from St Helens. The highest combined level of atrazine and simazine in water sampled from the Break O'Day Municipality was less than 0.001 mg/L (0.0009 mg/L simazine and 0.00009 mg/L atrazine), although the detection limit was not stated.

***OCS response:*** In the 1997 report, the OCS proposed the Australian Drinking Water Guideline value and the health value for atrazine as follows:

$$\textbf{\textit{Health Value}} = \frac{0.005 \text{ mg/kg bw/d} \times 70 \text{ kg} \times 0.1}{2 \text{ L/d}} = 0.02 \text{ mg/L}$$

where:
- 0.005 mg/kg bw is the ADI, calculated from the NOEL using a safety factor of 100
- 70 kg is taken as the average body weight of an adult
- 0.1 is based on 10% of the ADI
- 2 L/d is the estimated (maximum) amount of water consumed by an adult

***Guideline Value*** = 0.0005 mg/L (10% of the ADI); if atrazine is detected at or above this value, the source should be identified and action taken to prevent further contamination.

[12] APVMA note: The NHMRC published drinking water health based guideline value for simazine is 0.02 mg/L with a guideline value of 0.0005 mg/L. See http://www.nhmrc.gov.au/publications/synopses/_files/adwg_11_06.pdf.

In 2001, the OCS referred this matter to the NHMRC for consideration and participated in an update of the Australian Drinking Water Guidelines for atrazine. The current (updated September 2001) NHMRC Australian Drinking Water Guideline value for atrazine is 0.0001 mg/L, and the health value is 0.04 mg/L. The guideline value was lowered in 2001 from 0.0005 mg/L and the health value was increased from 0.02 mg/L. This decrease[13] in the guideline value was due to better detection methods. The higher health value was due to an increase in the proportionality factor of the ADI and is based on the assumption that at least 50 per cent of the ADI will arise from the consumption of drinking water[14]. Atrazine has rarely been found in the Australian food supply.

The atrazine level detected in 1994 in water from Break O'Day Municipality is more than 400-fold lower than the current health value and just below the Australian Drinking Water Guidelines value for atrazine. The simazine level was 55-fold lower than the current health value (0.05 mg/L) and slightly above the Australian Drinking Water Guidelines value for simazine (0.0005 mg/L). Thus, whilst there is no basis for concern about human health effects at the 1994 levels, ongoing monitoring strategies would be worthwhile.

4. The National Toxics Network Inc. disagreed with the three conclusions reached by the OCS following the review of the toxicological and epidemiological data for atrazine.

4.1 Conclusion 1: 'Published epidemiological data provide support for the absence of carcinogenicity potential for atrazine.'[15]

The National Toxics Network Inc. claimed that 'there was an association between atrazine exposure and increased incidence of various cancers'. This assertion was based on four published studies [16,17,18,19].

***OCS response:*** In general, these studies did not support a causal link between atrazine and cancer due to the lack of exposure data. The International Agency for Research on Cancer (IARC) and the US EPA have assessed the epidemiology data and concluded that the human epidemiology database did not provide sufficient evidence to associate atrazine with cancer of any human tissue. Consequently, the IARC downgraded the classification from *possibly* causing cancer in humans (Group 2B) to *unlikely* to cause cancer in humans (Group 3) in 1999. The APVMA review of all available atrazine data published in the 1997 report and updated in 2002 and 2004, and the US EPA review in 2003, independently arrived at the same

[13] APVMA note: From 0.0005 mg/L to 0.0001 mg/L.
[14] APVMA note: Fifty per cent was used rather than the standard assumption that exposure from drinking water will constitute 10 per cent of total dietary intake. It also took into account the fact that atrazine metabolite could make up around half of the total atrazine derived compounds in an environmental water sample.
[15] APVMA note: This was the proposed finding of the OCS in 2004. Note that the conclusion has now been reworded to state 'The published epidemiological data provided no support for any carcinogenicity potential for atrazine' (see sections 1 and 2, Volume 2 of this report).
[16] Mill PK (1998) Correlation analysis of pesticide use data and cancer incidence rates in California counties. Arch. Environ. Health 53:410–413.
[17] Van Leeuwen JA *et al.* (1999) Associations between stomach cancer incidence and drinking water contamination with atrazine and nitrate in Ontario (Canada), agroecosystems 1987–1991. Internat. Epidemiol. Assoc. 28:836–840.
[18] Scammell M (2005) Briefing paper St Helens, human health observations for the Tasmanian AMA. See also http://www.oztoxics.org/cmwg/library/casestudies/cm%20tasmania.pdf.
[19] US EPA (2003) Review of additional data on potential atrazine exposure and review comments submitted by Syngenta and NRDC on atrazine and cancer epidemiology study: 'Follow-up study of cancer incidence among workers in triazine-related operations at the Norvatis St Gabriel plant' DP Barcode D287278, MRID#455184-01, Chemical#080803.

conclusion as the IARC's 1999 classification.

In relation to the alleged increase in cancer of reproductive organs in St Helens in Tasmania, the OCS has already addressed this issue separately.

4.2 Conclusion 2: 'Effects on frog development should be considered as equivocal until such time as validated test methods can reliably reproduce recent findings. While these findings may impact on the environmental assessment of atrazine, any findings are unlikely to have a direct relevance to human health.'

The National Toxics Network Inc. stated in their submission that 'The Office of Chemical Safety dismissal of the relevance to human health of endocrine disruption is premature when there has been no investigation into health incidences in areas of atrazine use in Australia.'

***OCS response:*** The OCS addressed this issue in 2004. The final assessment is section 1, Volume 2 of this report.

4.3 Conclusion 3: 'Atrazine causes neuroendocrine disruption in SD rats, but does not bind to the oestrogen receptor or have any oestrogenic activity. It is unlikely that atrazine is an endocrine disruptor in humans based on the known mechanism of action in SD rats.'

The National Toxics Network Inc. argued that 'atrazine has been linked to endocrine disruption in humans, even if these impacts are not oestrogen-mediated but rather explained by their ability to induce aromatase *in vitro*'. Two *in vitro* studies which showed that atrazine induces aromatase activity (the enzyme that converts androgen to oestrogen) were cited.

***OCS response:*** *In vivo* and *in vitro* experimental data (uterine weight, receptor binding) evaluated in the 1997 report demonstrated that atrazine has no intrinsic oestrogenic activity. The relevance of induced aromatase activity in *in vitro* systems to altered oestrogenic signalling *in vivo* is at present unclear. On the weight of evidence from the *in vitro* and *in vivo* studies, atrazine is unlikely to be an oestrogenic compound.

5. A member of the APVMA's Community Consultative Committee alleged that *'atrazine has been linked to an increase in prostate cancer among atrazine factory workers, higher risk of breast cancer in women who drank water containing atrazine, low sperm count in men and causes deformities in frogs'*.

***OCS response:*** For a response on prostate and breast cancer, refer to 4.1 above[20]. For deformities in frogs, refer to 4.2 above.

*'Atrazine has been linked to low sperm counts in men'*

[20] APVMA note: The JMPR report published in September 2007 concludes on page 47 that in relation to atrazine *'A range of epidemiological studies (including cohort studies, case-control studies, and ecological or correlational studies) assessed possible relationships between atrazine or other triazine herbicides and cancer in humans. For some cancer types, such as prostate or ovarian cancer and non-Hodgkin lymphoma, the increased risks reported in single studies could either be explained by the methodology used or had not been confirmed in more reliable studies. Thus, the weight-of-evidence from the epidemiological studies did not support a causal association between exposure to atrazine and the occurrence of cancer in humans. The Meeting concluded that the existing database on atrazine is adequate to characterize the potential hazards to foetuses, infants and children.'*

***OCS response:*** Mixed results have been observed in animal studies. No testicular toxicity, as assessed by sperm morphology, sperm counts and testicular weights, was seen in mice treated daily for five days with atrazine intraperitoneally at doses of 38–600 mg/kg bw/d[21] (this study was included in the 1997 report). In contrast, decreases in sperm numbers and motility were observed in Fischer rats treated with atrazine intraperitoneally at doses of 30–120 mg/kg bw twice a week over 60 days[22]. However, given that the likely human exposure to atrazine would be via the oral and dermal routes, no occupational or public exposure will ever be likely to achieve these high doses. It should also be noted that atrazine, when administered orally to both male and female rats at 30 mg/kg bw/d, did not cause any impairment in reproductive performance. Therefore, the animal data suggest that effects of atrazine on sperm counts in men exposed to atrazine at environmental levels typical of those seen in human populations are unlikely.

6. The Allergy, Sensitivity & Environmental Health Association Qld Inc. raised some concerns about atrazine and human health. Below is the OCS response to each issue.

'*Atrazine has endocrine-disruption potential*'

The OCS addressed this issue in 2004. The final assessment is section 1, Volume 2 of this report.

'*Atrazine has been associated with birth defects and other reproductive problems*'

This issue is addressed in sections 1 and 2, Volume 2 of this report.

'*Atrazine is listed as a skin sensitiser (NIOSH)…. is a human allergen*'

As discussed in the 1997 report, 'although conflicting results were obtained in animal studies, atrazine does not appear to be a dermal sensitiser in humans'. A human study, using a 0.5 per cent weight per volume suspension of an 80W[23] formulation in water, showed that atrazine is not a skin sensitiser. Additionally, patch tests conducted on 50 human volunteers did not reveal any evidence of contact sensitivity with atrazine. Correspondence from medical officers at Ciba-Geigy's St Gabriel and McIntosh manufacturing plants in the United States certified that no cases of skin irritation or other atrazine-related illness have been seen at the plants.

'*Atrazine is a possible human carcinogen with links to diseases such as breast cancer, ovarian cancer, uterine cancer, leukaemia, multiple myeloma, non-Hodgkin's lymphoma*'

Refer to the response given at 4.1 above.

'*The risk of health damage may be higher if two atrazine herbicides are present or if there is a mixture of triazine and another chemical*'

Refer to the response to submission 2 above[24].

[21] Osterloh J *et al.* (1983) An assessment of the potential testicular toxicity of 10 pesticides using the mouse-sperm morphology assay. Mutations Res. 116:407–415.
[22] Kniewald J *et al.* (2000) Disorders of male rat reproductive tract under the influence of atrazine. J. Appl. Toxicol. 20:60–68.
[23] The term 80W is a trade name or company code for the formulation tested.
[24] APVMA note: Refer also to section 1, Volume 2 of this report.

'*Unknown impacts of triazine herbicides, singly or in combination with other chemicals, on the foetus and developing child*'

This statement was unreferenced; however, there is no evidence to support the assertion that triazine herbicides cause developmental effects in humans. In animal studies, developmental toxicity was not observed in rat and rabbit studies at doses up to 100 mg/kg bw/d atrazine. Furthermore, as described in the1997 report, animal studies investigating the developmental effects of atrazine in drinking water at doses up to 0.05 mg/L, in combination with other pesticides, revealed no signs of developmental toxicity.

### *APVMA conclusions on public submissions post 2004*

On 22 June 2007 the APVMA met with community representatives to allow them the opportunity to express ongoing and emerging concerns with the use of atrazine in Australia. A range of drinking water and environmental experts, as well as Australian regulators and health professionals, attended the forum.

After carefully considering the information presented and taking advice from the OCS and the DEWHA, the APVMA has concluded that at the present time there is no scientific consensus on the issues raised by community representatives.

The APVMA has not seen any direct evidence that current uses of atrazine pose a risk to human health. Indeed, extensive studies in laboratory animals show that there are no effects on health or reproduction in mammals maintained on drinking water containing atrazine and related compounds at low levels. Even at concentrations up to 100 times the levels that can sometimes be found in groundwater in the US, laboratory test results indicate there were no toxic effects on the animals, their progeny or their ability to reproduce.

The APVMA recognises that atrazine and related triazines continue to be the subject of ongoing research. The APVMA takes a keen interest in the directions in which this research is heading, including possible biochemical MOAs in frogs and in cultured animal and human cells.

The APVMA is seeking further detailed advice from the Australian Government health and environment departments on the implications of recent research in the broader context of what is known about the triazine group of herbicides. In order to implement the 2004 label recommendations this work will be done outside the scope of the current review of atrazine. If the conclusions of these expert advisory agencies suggest new areas of concern, then the APVMA can reconsider appropriate regulatory measures.

# 4 REVIEW OUTCOMES AND REGULATORY DECISION

## 4.1 ASSESSMENT OUTCOMES

The APVMA has initiated a project to re-examine the possibility that the triazines (atrazine and related chemicals with a similar MOA) may have unintended harmful effects on humans, taking into account ongoing research into a newly hypothesised endocrine MOA. This project will take account of international reports, such as the work of the Joint Meeting on Pesticide Residues (JMPR).

Registrants who have a product whose label specifies a claim for weed control on TT canola will be required to either generate additional data or include an additional label restraint that specifies that atrazine must not be used post-emergence on TT canola grown on raised beds.

After consideration of the additional assessments conducted since 2004, the APVMA accepts the recommendations of the OCS and the 2004 recommendations of the DEWHA, and the following regulatory actions have been applied:

1. Active constituent approvals have been affirmed.

2. Existing label instructions are deemed to be inadequate and approved labels have been amended as follows:

    a. Added: *Do NOT apply product to any drainage line. Drainage lines show evidence of the action of periodically flowing water (for example, gravel, pebble, rock or sand bed, scour hole or nick point) and/or an incised channel at least 30 cm deep*[25].

    b. Added: *Do NOT handle, mix, apply or conduct testing operations in areas susceptible to run-off where drainage results in rapid entry into waterways, particularly where no specific and effective action has been taken to prevent run-off into waterways. These areas may include areas mounded perpendicular to the contour, roads, access tracks, snig tracks, and compacted log dumps.*

    c. Removed Protection of Livestock label statement: *'Where treating native pasture, keep stock off for 14 days while Product X takes effect'* (due to inconsistency with the new grazing withholding period).

    d. Added: *Grazing (except canola): Do NOT apply to areas that will or may be grazed or cut for stockfood within 28 days after application*.

[25] Where the amended label includes a claim for use on TT canola, and does not specifically exclude use of the product post-emergence on TT canola grown on raised beds, the amended label will be subject to the condition that additional data must be generated within two growing seasons and provided to the APVMA so that an additional assessment can be made of the risk to the environment associated with this use.

e. In order to ensure that any incidents of resistance following use of atrazine come to the APVMA's attention, the following label statement has been added: *Any incidents of resistance must be reported to [the company name and contact details]*.

3. These variations to label instructions satisfy the requirements for continued registration of products; and so

   a. Product registrations have been affirmed.

   b. To ensure that all labels are in line with the recommendations of the 2008 report any previously approved labels that do not contain the amended instructions have been cancelled.

As an associated outcome of the review, changes are to be made to the MRL Standard to align entries in the standard with existing approved use patterns.

## 4.2 AFFIRM ACTIVE CONSTITUENT

Existing registered active constituents are listed in Appendix A.

## 4.3 AFFIRM EXISTING PRODUCTS

Existing registered products are listed in Appendix B.

## 4.4 LABEL APPROVALS TO BE CANCELLED

Label approvals to be cancelled are listed in Table 1 below.

**Table 1 Label approvals to be cancelled**

| Product Number | Product Name | Registrant | Label Approval Number |
|---|---|---|---|
| 60167¥ | 4FARMERS ATRAZINE 900 WG HERBICIDE | 4 FARMERS PTY LTD | 60167/1005 |
| 62696¥ | OZCROP ATRAZINE 900 WG HERBICIDE | CMS TRADE PTY LTD | 62696/0108 |
| 45774 | ATRADEX WG HERBICIDE | CROP CARE AUSTRALASIA PTY LTD | 45774/01<br>45774/0101<br>45774/0399<br>45774/0898 |

| Product Number | Product Name | Registrant | Label Approval Number |
|---|---|---|---|
| 50243¥ | ATRAGRANZ HERBICIDE | | 50243/0101<br>50243/0301<br>50243/0498 |
| 52584¥ | CROP CARE ATRAZINE FLOWABLE HERBICIDE | | 52584/0100<br>52584/0301<br>52584/1000<br>52584/1101 |
| 60862¥ | CROP CARE ATRAZINE HI-LOAD 600 HERBICIDE | | 60862/0906 |
| 45178 | FARMOZ FARMOZINE 500 FLOWABLE HERBICIDE | FARMOZ PTY LIMITED | 45178/01<br>45178/0801<br>45178/0898 |
| 46810 | FARMOZ FARMOZINE 900 WDG HERBICIDE | | 46810/00<br>46810/0103<br>46810/0501<br>46810/1098<br>46810/0505 |
| 48252 | FARMOZ AA COMBI 500 FLOWABLE HERBICIDE | | 48252/01 |
| 40411 | MACSPRED FOREST MIX GRANULAR HERBICIDE | MACSPRED PTY LTD | Transitional label<br>40411/00<br>40411/0399<br>40411/4321 |
| 51532¥ | MACSPRED FOREST MIX WATER DISPERSIBLE HERBICIDE | | 51532/0799<br>51532/0999 |
| 51538¥ | MACSPRED FOREST MIX SPECIAL BLEND GRANULAR HERBICIDE | | 51538/0599 |
| 46526 | ATRAMET COMBI SC HERBICIDE | MAKHTESHIM-AGAN (AUSTRALIA) PTY LIMITED | 46526/1098 |

| Product Number | Product Name | Registrant | Label Approval Number |
|---|---|---|---|
| 31586 | NUFARM FLOWABLE NU-TRAZINE LIQUID HERBICIDE | NUFARM AUSTRALIA LIMITED | Transitional label<br>31586/0199<br>31586/02<br>31586/0301 |
| 31589 | NUFARM NU-TRAZINE 900 DF HERBICIDE | | Transitional label<br>31589/01<br>31589/0199<br>31589/0200<br>31589/0202<br>31589/4287 |
| 58450¥ | OSPRAY ATRAZINE 900WG HERBICIDE | OSPRAY PTY LTD | 58450/0304 |
| 50164¥ | SIPCAM PACIFIC MAIZINA 500 FLOWABLE HERBICIDE | SIPCAM PACIFIC AUSTRALIA PTY LTD | 50164/0301<br>50164/0998 |
| 50456¥ | SIPCAM PACIFIC MAIZINA 900 WDG HERBICIDE | | 50456/1198 |
| 49547 | SUMMIT ATRAZINE 900DF HERBICIDE | SUMMIT AGRO AUSTRALIA PTY LTD | 49547/01<br>49547/0102<br>495470402<br>49547/0499<br>49547/0206 |
| 51814¥ | SUMMIT COMBO SC HERBICIDE | | 51814/0699 |
| 47615 | FLOWABLE GESAPRIM 500 SC LIQUID HERBICIDE | SYNGENTA CROP PROTECTION PTY LIMITED | 47615/0398<br>47615/0600 |

| Product Number | Product Name | Registrant | Label Approval Number |
|---|---|---|---|
| 47616 | GESAPAX COMBI 500 SC LIQUID HERBICIDE | | 47616/01<br>47616/02 |
| 47928 | GESAPAX COMBI 800 WG HERBICIDE GRANULES | | 47928/01<br>47928/0398<br>47928/0699 |
| 49552 | GESAPRIM GRANULES 900 WG HERBICIDE | | 49552/01<br>49552/0201<br>49552/0398<br>49552/0599<br>49552/0702<br>49552/0802<br>49552/0899<br>49552/1201 |
| 50885¥ | PRIMEXTRA GOLD HERBICIDE | | 50885/0501<br>50885/0599<br>50885/0801 |
| 53892¥ | FLOWABLE GESAPRIM 600 SC LIQUID HERBICIDE | | 53892/0301<br>53892/0302<br>53892/0703<br>53892/0802<br>53892/0404 |
| 58456¥ | UNITED FARMERS ATRAZINE 900 WG HERBICIDE | UNITED FARMERS COOPERATIVE COMPANY LTD | 58456/0204 |

¥ Product registered after commencement of the review but registration conditional on the outcomes of the review.

## 4.5 AMENDMENTS TO THE MRL STANDARD

As an associated outcome of the review, changes are to be made to the MRL Standard (Tables 2 & 3)**.**

**Amendments to the MRL Standard**

**Table 2**

| Compound | | Food | MRL (mg/kg) |
|---|---|---|---|
| **Atrazine** | | | |
| Delete: | MO 0105 | Edible offal (mammalian) | T*0.1 |
| | MM 0095 | Meat [mammalian] | T*0.01 |
| | ML 0106 | Milks | T*0.01 |
| Add: | MO 0105 | Edible offal (mammalian) | *0.1 |
| | MM 0095 | Meat [mammalian] | *0.01 |
| | ML 0106 | Milks | *0.01 |

* Set at or about the limit of analytical quantitation

**Table 3**

| Compound | Animal feed | MRL (mg/kg) |
|---|---|---|
| **Atrazine** | | |
| Delete: | Primary feed commodities | T40 |
| Add: | Forage and fodder derived from cereals, pastures, legumes, sweet corn and sugar cane | 40 |

## 4.6 CONCLUSION

The APVMA is satisfied that the continued use of products containing atrazine meets the criteria for continued registration and label approval as prescribed by the Agvet Codes, pending provision of additional data in relation to TT canola. This decision is based on the outcomes of the initial review (published in the 1997 report), assessment of supplementary information required as a result of that review (published in the 2002 and 2004 reports), and variation to conditions of label approval ensuring the requirements for continued approval or registration are met.

# APPENDIX A ACTIVE CONSTITUENTS INCLUDED IN THE REVIEW

| Approval Number | Active Constituent | Company Name |
|---|---|---|
| 44047 | ATRAZINE | MAKHTESHIM-AGAN (AUSTRALIA) PTY LIMITED |
| 44367 | ATRAZINE | SYNGENTA CROP PROTECTION PTY LIMITED |
| 45076 | ATRAZINE | DOW AGROSCIENCES AUSTRALIA LIMITED |
| 48797 | ATRAZINE | SIPCAM PACIFIC AUSTRALIA PTY LTD |
| 57454 | ATRAZINE | KENSO CORPORATION (M) SDN BHD |
| 57911 | ATRAZINE | AGROGILL CHEMICALS PTY LTD |
| 59410 | ATRAZINE | IMTRADE AUSTRALIA PTY LTD |

# APPENDIX B PRODUCTS INCLUDED IN THE REVIEW

| Product Number | Product Name | Registrant | Label Approval Numbers |
|---|---|---|---|
| 52674¥ | 4FARMERS ATRAZINE 500 SC | 4 FARMERS PTY LTD | 52674/0200$^{\Phi}$ |
| 60167¥ | 4FARMERS ATRAZINE 900 WG HERBICIDE | | 60167/0507$^{\Phi}$<br>60167/1005 |
| 55093¥ | COUNTRY ATRAZINE 900 WG HERBICIDE | A & C RURAL PTY LTD | 55093/0403$^{\Phi}$ |
| 59849¥ | AGROREG ATRAZINE 500 SC HERBICIDE | AGROREG PTY LIMITED | 59849/1005$^{\Phi}$ |
| 59859¥ | AGROREG ATRAZINE 900 WG HERBICIDE | | 59859/1105$^{\Phi}$ |
| 59293¥ | ATRAFLO HERBICIDE | BAYER CROPSCIENCE PTY LTD | 59293/0805$^{\Phi}$ |
| 61303¥ | CMS ATRAZINE 500 SC HERBICIDE | CMS TRADE PTY LTD | 61303/0906$^{\Phi}$ |
| 61305¥ | CMS ATRAZINE 900 WG HERBICIDE | | 61305/0906$^{\Phi}$ |
| 62696¥ | OZCROP ATRAZINE 900 WG HERBICIDE | | 62696/0108 |
| 56276¥ | ATRAQUEST 900 WG HERBICIDE | CONQUEST AGROCHEMICALS PTY LTD | 56276/1002$^{\Phi}$ |
| 45774 | ATRADEX WG HERBICIDE | CROP CARE AUSTRALASIA PTY LTD | 45774/01<br>45774/0101<br>45774/0301$^{\Phi}$<br>45774/0399<br>45774/0898 |
| 50243¥ | ATRAGRANZ HERBICIDE | | 50243/0101<br>50243/0301<br>50243/0498<br>50243/0802$^{\Phi}$ |

| Product Number | Product Name | Registrant | Label Approval Numbers |
|---|---|---|---|
| 52584¥ | CROP CARE ATRAZINE FLOWABLE HERBICIDE | | 52584/0100<br>52584/0301<br>52584/1000<br>52584/1101<br>52584/0405Φ |
| 60862¥ | CROP CARE ATRAZINE HI-LOAD 600 HERBICIDE | | 60862/0906<br>60862/1007Φ |
| 51630¥ | DOW AGROSCIENCES ATRAZINE 500 FLOWABLE HERBICIDE | DOW AGROSCIENCES AUSTRALIA LIMITED | 51630/1299Φ |
| 45178 | FARMOZ FARMOZINE 500 FLOWABLE HERBICIDE | FARMOZ PTY LIMITED | 45178/01<br>45178/0801<br>45178/0898<br>45178/0905Φ |
| 46810 | FARMOZ FARMOZINE 900 WDG HERBICIDE | | 46810/00<br>46810/0103<br>46810/0501<br>46810/1098<br>46810/0505<br>46810/0807Φ |
| 48252 | FARMOZ AA COMBI 500 FLOWABLE HERBICIDE | | 48252/01<br>48252/1298Φ |
| 59764¥ | GENFARM ATRAGEN 900 WG HERBICIDE | GENFARM CROP PROTECTION PTY LTD | 59764/0705Φ |
| 59803¥ | CHEMAG ATRAZINE 900 WG HERBICIDE | IMTRADE AUSTRALIA PTY LTD | 59803/0905Φ |
| 56298¥ | KENSO AGCARE ATRAZINE 500 SC HERBICIDE | KENSO CORPORATION (M) SDN BHD | 56298/1002Φ |
| 58666¥ | KENSO AGCARE ATRAZINE 900 W G HERBICIDE | | 58666/0704Φ |

| Product Number | Product Name | Registrant | Label Approval Numbers |
|---|---|---|---|
| 40411 | MACSPRED FOREST MIX GRANULAR HERBICIDE | MACSPRED PTY LTD | Transitional label<br>40411/00<br>40411/0399<br>40411/0701Φ<br>40411/4321 |
| 51532¥ | MACSPRED FOREST MIX WATER DISPERSIBLE HERBICIDE | | 51532/0104Φ<br>51532/0799<br>51532/0999 |
| 51538¥ | MACSPRED FOREST MIX SPECIAL BLEND GRANULAR HERBICIDE | | 51538/0599<br>51538/1104Φ |
| 46526 | ATRAMET COMBI SC HERBICIDE | MAKHTESHIM-AGAN (AUSTRALIA) PTY LIMITED | 46526/0599Φ<br>46526/1098 |
| 31586 | NUFARM FLOWABLE NU-TRAZINE LIQUID HERBICIDE | NUFARM AUSTRALIA LIMITED | Transitional label<br>31586/0199<br>31586/02<br>31586/0301<br>31586/0902Φ |
| 31589 | NUFARM NU-TRAZINE 900 DF HERBICIDE | | Transitional label<br>31589/01<br>31589/0199<br>31589/0200<br>31589/0202<br>31589/0802Φ<br>31589/4287 |
| 60909¥ | NUFARM NU-TRIAZINE 600 HERBICIDE | | 60909/0906Φ |
| 58450¥ | OSPRAY ATRAZINE 900WG HERBICIDE | OSPRAY PTY LTD | 58450/0106Φ<br>58450/0304 |
| 60810¥ | OSPRAY ATRAZINE 500 SC HERBICIDE | | 60810/0406Φ |

| Product Number | Product Name | Registrant | Label Approval Numbers |
|---|---|---|---|
| 61387¥ | RYGEL ATRAZINE 900DF HERBICIDE | RYGEL AUSTRALIA PTY LTD | 61387/0107Φ |
| 50164¥ | SIPCAM PACIFIC MAIZINA 500 FLOWABLE HERBICIDE | SIPCAM PACIFIC AUSTRALIA PTY LTD | 50164/0301<br>50164/0402Φ<br>50164/0998 |
| 50456¥ | SIPCAM PACIFIC MAIZINA 900 WDG HERBICIDE | | 50456/0301Φ<br>50456/1198 |
| 60471¥ | SIPCAM ATRAZINE 900WG HERBICIDE | | 60471/0106Φ |
| 61065¥ | SIPCAM ATRAZINE 600 FLOWABLE HERBICIDE | | 61065/1007Φ<br>61065/0207 |
| 49547 | SUMMIT ATRAZINE 900DF HERBICIDE | SUMMIT AGRO AUSTRALIA PTY LTD | 49547/01<br>49547/0102<br>495470402<br>49547/0499<br>49547/0206<br>49547/0906Φ |
| 51814¥ | SUMMIT COMBO SC HERBICIDE | | 51814/0699<br>51814/0803Φ |
| 47615 | FLOWABLE GESAPRIM 500 SC LIQUID HERBICIDE | SYNGENTA CROP PROTECTION PTY LIMITED | 47615/0201Φ<br>47615/0398<br>47615/0600 |
| 47616 | GESAPAX COMBI 500 SC LIQUID HERBICIDE | | 47616/01<br>47616/02<br>47616/0398Φ |
| 47928 | GESAPAX COMBI 800 WG HERBICIDE GRANULES | | 47928/01<br>47928/0398<br>47928/0699<br>47928/1199Φ |

| Product Number | Product Name | Registrant | Label Approval Numbers |
|---|---|---|---|
| 49552 | GESAPRIM GRANULES 900 WG HERBICIDE | | 49552/01<br>49552/0201<br>49552/0398<br>49552/0599<br>49552/0702<br>49552/0802<br>49552/0899<br>49552/1201<br>49552/0506Φ |
| 50885¥ | PRIMEXTRA GOLD HERBICIDE | | 50885/0501<br>50885/0599<br>50885/0801<br>50885/0404Φ |
| 53892¥ | FLOWABLE GESAPRIM 600 SC LIQUID HERBICIDE | | 53892/0301<br>53892/0302<br>53892/0703<br>53892/0802<br>53892/0607Φ<br>53892/0404 |
| 61892¥ | GESAPRIM GRANULES HERBICDE | | 61892/0507Φ |
| 62191¥ | TITAN ATRAZINE 900 W G HERBICIDE | TITAN AG PTY LTD | 62191/1007Φ |
| 61143¥ | TRADELANDS ATRAZINE 500 FLOWABLE HERBICIDE | TRADELANDS PTY LTD | 61143/0906Φ |
| 58456¥ | UNITED FARMERS ATRAZINE 900 WG HERBICIDE | UNITED FARMERS COOPERATIVE COMPANY LTD | 58456/0204<br>58456/1104Φ |

¥ Product registered after commencement of the review but registration conditional on the outcomes of the review.

Φ Latest label approval to be varied.

## APPENDIX C STATUS OF PROTECTED INFORMATION/DATA

The APVMA operates a data protection program that provides compensation to those who submit data for a review which meets the criteria specified in the Agvet Codes. The objectives of the program are:

- to provide an incentive for the development of products and data applicable to Australian or local conditions;
- to encourage the availability of overseas products and data; and
- to provide reciprocal protection for Australian products and data under overseas data protection systems.

In general the APVMA designates information as protected registration information for a period of two to seven years, if the information:

- is requested by the APVMA for the purposes of a review; and
- relates to the interaction between the products and the environment of living organisms or naturally occurring populations in ecosystems, including human beings.

If the APVMA proposes to use the same information to determine whether to register or continue registration of another chemical product, the APVMA must not use the information until the parties come to an agreement on terms for compensation, unless the protection period has expired or the APVMA is satisfied that it is in the public interest to use the information.

At the completion of the initial review in November 1997, there were a number of studies submitted for the review which were still within the protection period. As at October 2004, no studies remained protected.

The supplementary environmental and toxicology data submitted for atrazine are not eligible for protection under this program. The residue data (forage and fodder data) are eligible for protection and relevant to the review. However, the protection period has now expired.