Report of Adverse Experiences for Agricultural Chemicals

Calendar Year 2005

Adverse Experience Reporting Program
for agricultural chemicals

Report of Adverse Experiences for Agricultural Chemicals

Calendar year 2005

June 2006

ISSN 1443-1343

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The Adverse Experience Reporting Program for agricultural chemicals (AERP Ag) and the AERP for veterinary medicines (AERP *Vet*) comprise the Australian post-registration quality assurance programs that facilitate the responsible management of veterinary medicines and agricultural chemicals throughout their lifecycle, from registration to end-product user. They also provide clear guidance for registrants in complying with their legislated obligations.

This report contains information on adverse experience reports for agricultural chemicals. Further details of adverse experience reports for veterinary medicines can be found on the APVMA Website.

The purpose of the AERP Ag is to provide the APVMA with feedback about the performance of agricultural chemical products in the field to:

- ensure that registration decisions being made by the APVMA are appropriate and effective, and
- promote and maintain public confidence in the APVMA and the National Registration Scheme.

The AERP *Ag* assessed, evaluated and classified 196 adverse experience reports during 2005, being 36 lack of effect reports, 30 human reports, 4 environmental reports and 126 crop reports.

This Annual Report contains a summary of all adverse experience reports assessed, evaluated and classified as 'Probable' or 'Possible' (see Section 1.7) by the APVMA during the 2005 Calendar Year under the AERP *Ag*.

As the AERP *Ag* is a relatively new program, a number of activities were undertaken in 2005 to promote the program within the wider community and these include:

- meetings with the New South Wales Department of Environment and Conservation, South Australian Department of Primary Industries and Resources, Western Australian Department of Health, Australian Ground Sprayers Association and the ChemCert National Conference,
- contributing to the National ChemCert Training Manual,
- communication with 670 local councils,
- communicating with Australian Local Government Association, Australian Medical Association and various other medical and community groups, and
- a submission to the South Australian Parliamentary Enquiry on Multiple Chemical Sensitivity.

Some registrants are in the process of undertaking voluntary (i.e. not at the APVMA's request) label changes as a result of information that they have received as part of their adverse experience reporting programs.

1. INTRODUCTION

1.1 Program Outline

The APVMA is the independent Australian Government Statutory Authority responsible for the assessment and registration (marketing authorisation) of pesticides and veterinary medicines prior to sale, and their regulation up to and including the point of retail sale. *Pesticides* include agricultural and many household chemicals such as insecticides, herbicides and fungicides; water treatment products including swimming pool and spa products; products for treating algae and mould; products for preventing rot and infestation in marine structures and other similar products. *Veterinary medicines* include all veterinary chemical products such as vaccines, antibiotics, worming treatments, flea and tick washes and other parasiticides for both domestic and production animals. Under the National Registration Scheme, the APVMA evaluates and registers agricultural and veterinary chemicals and manages quality assurance programs that monitor the safety and performance of registered products.

The Adverse Experience Reporting Program for agricultural chemicals (AERP Ag) is a post-registration quality assurance program established by the APVMA to facilitate responsible management of agricultural chemicals throughout their lifecycle. The program provides a means for identifying corrective actions necessary to assure the continued safety, quality and effectiveness of registered agricultural chemicals. Recording and investigating reports of adverse experiences is an important step in detecting unusual or rare conditions that were not evident in clinical or field trials and as a result, could not be assessed during the product registration process. The AERP Ag helps to ensure that products on the market:

- remain safe, effective and of acceptable quality,
- are used in the best possible way, and
- that instructions and warnings on the label are appropriate.

1.2 What is an adverse experience?

> *"An adverse experience is an unintended or unexpected effect (deleterious) on plants, plant products, animals, human beings or the environment, including injury, sensitivity reactions or lack of efficacy associated with the use of an agricultural chemical product when used according to label directions."*

The following definitions outline what constitutes "serious", "minor" and "urgent" adverse experiences.

Definition of a serious adverse experience:

"A serious adverse experience is one that involves:

- *widespread and significant crop and plant damage (e.g. crop death, severe stunting or significant yield loss),*
- *life-threatening or other significant effects in a human, including death,*
- *farm, domestic and native animal deaths, or*
- *significant environmental damage, including fish kills and water quality issues.*

Definition of a minor adverse experience:

"A minor adverse experience is one that involves:

- *crop and plant damage that is not widespread or significant (eg minor wilting or yellowing of crops, minor yield loss),*
- *human health effects that require medical attention, but are not life-threatening,*
- *injury to domestic and native animals that require veterinary attention, or*
- *minor environmental damage."*

A number of agricultural chemicals have known side effects when used as directed and it is useful to maintain a record of this so that the true incidence of these side effects can be assessed. Therefore it is important that all adverse experiences are reported.

1.3 Who can report an adverse experience?

Anyone — voluntary reporting is encouraged from members of the public, farmers and other chemical users, agronomists, bystanders, health workers (including doctors, nurses, alternative medicine specialists etc), and state and territory authorities.

Section 161 of the *Agvet Codes* requires registrants to provide the APVMA with any 'new information' that they become aware of. This 'new information' includes adverse experience information relating to human health issues, harm to animals, damage to plants, property or the environment and lack of efficacy when the products are used according to label directions.

The 'registrant' component of the AERP Ag is one method that product registrants can meet certain legislative obligations of section 161 of the *Agvet Codes.*

1.4 Reporting an adverse experience

Adverse experiences with agricultural chemicals may be reported using the Adverse Experience Reporting Form for agricultural chemicals available from the APVMA or on the APVMA website at http://www.apvma.gov.au/qa/aerp_ag.shtml

1.5 Benefits of the AERP Ag

The AERP Ag provide numerous benefits to a wide range of stakeholders:

Benefits to the community

- Ensures the safety and efficacy of registered products in the marketplace.
- Provides confidence in the regulatory system.

Benefits to states

- Provide and integrated approach between national and state programs.
- Provides a format for communication of issues that cross over jurisdictional boundaries.

Benefits to farmers

- Provides up-to-date safety information on registered products.
- Ensures that the latest safety information is available on product labels.
- Provides information on modifications needed to work practices to ensure safe use of chemicals.
- Identifies and acts on emerging issues quickly.

1.6 Evaluation of adverse experience reports

Reports received by the APVMA are assessed to determine whether the adverse experience is related to the use of, or exposure to, the product or not. The APVMA may rely on advice from other commonwealth government agencies (such as the Department of Health and Ageing), and relevant state or territory agencies (such as the relevant Department of Agriculture) when assessing adverse experience reports. The APVMA will also take into account any published material available from similar reports as well as any relevant scientific literature published worldwide.

The conclusions drawn by the APVMA during investigation and evaluation of each adverse experience report will be provided to the reporting person. This will include an explanation of whether the APVMA considers that the observed adverse effects (including health symptoms) were related to the use of or exposure to the product. The APVMA will explain what these conclusions are and what corrective action, if any, will be taken in response to the information.

1.7 Classification of adverse experience reports

Once the relationship between the use of the product and the reported effect has been assessed after investigation of the incident it is expressed in terms of:

Probable

For inclusion in the category 'probable' all of the following minimum criteria should be met:

- there should be a reasonable association between the use of the product and onset and duration of the reported adverse experience,
- the description of the effect should be consistent with or at least plausible given the known mode of action, toxicology and metabolism of the product, and
- there should be no other equally plausible explanation (or contributing factors) for the clinical signs.

When any of the above criteria cannot be satisfied (due to lack of sufficient information or conflicting data) then the association cannot be assessed as 'probable'.

Probable/Off-label

As per the classification of 'probable' and where there is obvious evidence of off-label use (including use in crops/plants/situations not listed on the product label, excessive rates etc).

Possible

For inclusion in the category 'possible' association of the adverse experience with use of the product is one of other possible and equally plausible explanations (or contributing factors) for the described adverse experience.

Possible/Off-label

As per the classification 'possible' and where there is obvious evidence of off-label use (including use in crops/plants/situations not listed on the product label, excessive rates etc).

Unlikely

Where sufficient information exists to establish that the described adverse experience was not likely to have been associated with use of the product(s), or other more plausible explanations exist, the assessment should be categorised as 'unlikely'.

Unknown

All adverse experiences where reliable data is either unavailable or is insufficient to make an assessment should be categorised as 'unknown'.

1.8 Corrective action determination

There are many factors that need to be considered when determining whether corrective action is required and if so, what corrective action is needed to mitigate the issue.

For each registered agricultural chemical, and more broadly for each active constituent, the APVMA conducts a trend analysis of all adverse experience reports received. All reports that have been classified as 'probable' or 'possible' are compared to the total number of units sold within the relevant financial year and a 'reporting incidence' is calculated (ie the number of adverse experience reports per number of units sold). A control limit or "warning line" for reporting incidence figures, which indicate that further action may be required is one or more per 10,000 units sold. If the reporting incidence is greater than one per 10,000 in two out of three consecutive years or an exceptional incidence of three or more per 10,000 occurs on any one occasion, or a consistent rising trend is seen over five years (irrespective of the reporting incidence) then action may be required.

The APVMA considers the scientific literature and information relating to trend analysis and risk assessment when determining whether corrective action is required. The APVMA also takes into account the severity of observed effects (ie more severe signs may trigger corrective action at a lower reporting incidence) and whether the observed effects are listed in warning statements on the product label, in which case a slightly higher reporting incidence may be acceptable.

1.9 Outcomes of the program

Based on the assessment of adverse experience reports certain risk mitigation strategies or corrective actions may be requested. These may include, but are not restricted to, the following:

- registration amendments, such as label changes, changes to the method of manufacture or product's physical or chemical design, changes to container design, changes to production line processes, or suspension and/or cancellation of registration and approval
- referral for action, such as compliance action, including product and batch recalls, referral to state authorities for action, or nomination of products or active constituents for formal chemical review by the APVMA, (note that once the recommendation for review has been made by the AERP the review program will conduct consultation and scoping prior to determining whether a review is necessary or not); and
- education and publicity, such as providing scientific papers or articles on issues identified for relevant journals, magazines or newspapers.

The conclusions drawn by the APVMA during investigation and evaluation of each adverse experience report will be provided to the reporting person. This will include an explanation of whether the APVMA considers that the observed adverse effects (including health symptoms) were related to the use of or exposure to the product. The APVMA will explain what these conclusions are and what corrective action, if any, will be taken in response to the information.

The information contained in this Annual Report is only a general reference to the type of adverse experience that farmers, health professionals, bystanders, and others have reported either to the APVMA or to product registrants. This information should NOT be used for:

- associating adverse effects with a particular product or active constituent,
- assessing the safety and efficacy of a product or active constituent,
- establishing acceptable frequency of occurrence of an adverse experience, or
- comparing one product or active constituent with another product or active constituent.

1.10 Report Structure

This report is arranged into the following sections:

- **Section 1** — a summary of adverse experience reports other than human health (including crop damage, environmental damage and lack of efficacy) listed by active constituent, and
- **Section 2** — a summary of adverse experience reports involving human health.

1.11 For further information

This report is report is presented by active constituent and not by individual products. The written consent of the product registrant is required for the release of further information on adverse experiences to specific products.

For information about the Adverse Experience Reporting Program please contact:

Dr Bruce Johnson
Phone: (02) 6210 4803
Fax: (02) 6210 4813
E-mail: bruce.johnson@apvma.gov.au

2. SECTION 1

2.1 A summary of adverse experience reports involving crop damage, domestic animal harm, environmental damage or lack of efficacy listed by active constituent

The following information is contained in this section:

The active constituent name

- Each active constituent is listed alphabetically, with a summary of the adverse experience reports.
- It is important to note that the number of adverse experience reports and the presenting signs observed may be listed under more than one active constituent if they refer to a product that contains multiple active constituents.

The number of reports

- Only adverse experience reports that were classified by the APVMA as being either 'probable' or 'possible' have been included in these lists. The summary table indicates how many reports were classified as 'probable' and how many were classified as 'possible'.

The presenting signs

- All observed effects for reports that were classified as 'probable' and 'possible' are listed in order of frequency.
- It is important to note that multiple adverse effects have been noted in some individual reports. Therefore the list of observed effects does not relate directly to the total number of reports received.

Summary of corrective action

- A short narrative is provided on any corrective action taken as a result of assessment of the adverse experience information for each active constituent.

2,4-D

Crop

Number of reports	Probable	Possible
51	19	32

Presenting Signs	Number of reports
Crop damage	51

These reports have been forwarded to the APVMA's Chemical Review Prgram for information, as part of the formal reconsideration of 2,4-dichlorophenoxyacetic acid active constituent approval and product registrations.

2,4-D-B PRESENT AS THE DIMETHYLAMINE SALT

Crop

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Crop damage	1
Lack of effect	1

BENTAZONE AS THE SODIUM SALT

Crop

Number of reports	Probable	Possible
13	13	0

Presenting Signs	Number of reports
Lack of effect	13

CLOPYRALID PRESENT AS THE TRIISOPROPANOLAMINE SALT

Crop

Number of reports	Probable	Possible
2	0	2

Presenting Signs	Number of reports
Crop damage	2

FIPRONIL

Crop

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Quality control	1

These reports have been forwarded to the APVMA's Chemical Review Prgram for information, as part of the formal reconsideration of fipronil active constituent approval and product registrations.

GLYPHOSATE PRESENT AS THE POTASSIUM SALT

Crop

Number of reports	Probable	Possible
5	2	3

Presenting Signs	Number of reports
Lack of effect	5

IMAZAPIC

Crop

Number of reports	Probable	Possible
2	0	2

Presenting Signs	Number of reports
Lack of effect	2

IMAZAPYR

Crop

Number of reports	Probable	Possible
2	0	2

Presenting Signs	Number of reports
Lack of effect	2

MCPA PRESENT AS THE POTASSIUM SALT

Crop

Number of reports	Probable	Possible
13	13	0

Presenting Signs	Number of reports
Lack of effect	13

METHAM PRESENT AS SODIUM SALT

Crop

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Lack of effect	1

SODIUM FLUOROACETATE (1080)

Canine

Number of reports	Probable	Possible
3	3	0

Presenting Signs	Number of reports
Death	3
Seizure	3
Vomiting	3

These reports have been forwarded to the APVMA's Chemical Review Prgram for information, as part of the formal reconsideration of sodium monofluoroacetate active constituent approval and product registrations.

TRALKOXYDIM

Crop

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Lack of effect	1

TRI-ALLATE

Crop

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Lack of effect	1

3. SECTION 2

3.1 A summary of adverse experience reports in humans listed by active constituent

The following information is contained in this section:

The active constituent name

Each active constituent is listed alphabetically, with a summary of the adverse experience reports.

It is important to note that the number of adverse experience reports and the presenting signs observed may be listed under more than one active constituent if they refer to a product that contains multiple active constituents.

The number of reports

Only adverse experience reports that were classified by the APVMA as being either 'probable' or 'possible' have been included in these lists. The summary table indicates how many reports were classified as 'probable' and how many were classified as 'possible'.

The presenting signs

All observed clinical signs for reports that were classified as 'probable' and 'possible' are listed in order of frequency.

It is important to note that multiple adverse effects have been noted in some individual reports. Therefore the list of observed effects does not relate directly to the total number of reports received.

Summary of corrective action

A short narrative is provided on any corrective action taken as a result of assessment of the adverse experience information for each active constituent.

ALPHA-CYPERMETHRIN

Human

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Burning sensation	1

BETACYFLUTHRIN

Human

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Illness	1

CHLOROTHALONIL

Human

Number of reports	Probable	Possible
1	0	1

Presenting Signs	Number of reports
Burning sensation	1

CHLORPYRIFOS

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Headache	1
Nausea	1
Odour	1

DI-N-PROPYL ISOCINCHOMERONATE

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Rash	1

DIETHYLTOLUAMIDE

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Rash	1

GLYPHOSATE

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Conjunctivitis	1
Coughing	1
Ocular damage	1
Rash	1

METHAM PRESENT AS SODIUM SALT

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Lacrimation	1
Nasal discharge	1
Respiratory problems	1

N-OCTYL BICYCLOHEPTENE DICARBOXIMIDE

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Rash	1

PERMETHRIN (40:60::CIS:TRANS)

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Headache	1
Malaise	1
Nausea	1

TRICLOSAN

Human

Number of reports	Probable	Possible
1	1	0

Presenting Signs	Number of reports
Rash	1