




Australian Government

**Australian Pesticides and
Veterinary Medicines Authority**

ADVERSE EXPERIENCE REPORTING PROGRAM FOR AGRICULTURAL CHEMICALS

GUIDELINES FOR REGISTRANTS

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ADVERSE EXPERIENCE REPORTING PROGRAM FOR AGRICULTURAL CHEMICALS

GUIDELINES FOR REGISTRANTS

The APVMA's Adverse Experience Reporting Program for agricultural chemicals (AERP Ag) is a quality assurance program established by the APVMA to facilitate responsible management of agricultural chemicals (pesticides) throughout their lifecycle. The aim of the AERP Ag is to ensure that products on the market remain safe, effective, are of acceptable quality and are used in the best possible way, and that instructions and warnings on labels are appropriate.

Introduction

The APVMA is the independent Australian government 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 products; products for treating algae and mould; products for preventing rot and infestation in marine structures and other similar products.

As a Commonwealth Statutory Authority, the APVMA operates in accordance with its governing legislation. The principal responsibilities of the APVMA are described in the *Agricultural Chemicals (Administration) Act 1992* and the *Agricultural and Veterinary Chemicals Code Act 1994*.

In accordance with these 'Agvet Codes' the APVMA is required to ensure that pesticide products and veterinary medicines sold in Australia:

- are of a high quality,
- do not pose a threat to people, domestic or native animals, crops, plants, things or the environment,
- will not pose any unacceptable risk to trade with other nations, and
- continue to work effectively.

It is essential that risk management systems (such as the regulatory system operated by the APVMA) have strong feedback loops to ensure that decisions being made are appropriate and effective¹.

¹ The Australian Agricultural and Veterinary Chemicals Management System, A Report to Government by the APVMA on recent reviews of the system, June 2003.

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* (**Attachment 1**). The APVMA acknowledges that many product registrants already have in place programs for receiving, recording, investigating, evaluating and classifying adverse experience reports that they receive. The APVMA does not wish to cause duplication of such programs and agrees that processes and procedures consistent with the guidelines of the AERP Ag would be acceptable evidence to the APVMA that these registrants are meeting their obligations under section 161 with respect to adverse experience reports. Any inquiries regarding the level of equivalence of individual programs can be directed to the APVMA.

It is important to note that if product registrants do not wish to participate in the AERP Ag then the onus is on them to demonstrate compliance with the mandatory requirements of section 161.

Objectives of the AERP Ag

Specifically objectives of the AERP Ag are to:

- facilitate product registrant compliance with the requirements of section 161 of the *Agvet Codes*,
- 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.

Information received regarding suspected adverse reactions, or “adverse experiences” (see below) may identify a need for corrective actions with respect to the product label (eg additional instructions, warning statements or precautions), manufacturing process, formulation, batch recall or review of registration, or education of the agricultural industry and the general public (via mechanisms such as articles in appropriate journals and publications) in better use or safety practices.

Scope of the AERP Ag

The Scope of the AERP Ag covers adverse experience reports involving:

- human health issues, where people are exposed to pesticides either by using them or as bystanders,
- animal health issues, including both domestic and native birds and animals,
- crop and plant damage,
- trade and residue issues,
- environmental damage, and
- lack of efficacy.

The scope does not include:

- registered veterinary medicines (these are dealt with as part of the AERP *Vet*),
- trade issues as these do not fall within the definition of an ‘adverse experience’ (see below),
- household or home garden product issues (such as damaged packaging of home-use pesticides not caused by the product itself, minor efficacy issues), which are dealt with under other arrangements such as consumer protection, trade practices legislation etc,
- packaging design faults, which also do not fall within the definition of an ‘adverse experience’,
- illegal off-label uses (ie contrary to label that include instances where products are used on resistant or suspect resistant pest populations if the label specifically warns against such use), or
- products not registered by the APVMA.

It is also noted that submission of other forms of information such as trial data would fall within the scope of section 161, but would not be part of AERP Ag. The APVMA is considering clarifying other information reporting requirements under section 161.

Definition of an adverse experience

The following definition of an “adverse experience” captures the elements of section 161 of the *Agvet Codes* and is to be used by product registrants when determining what information should be submitted to the APVMA. The definition is “descriptive” rather than “prescriptive” because it is almost impossible to provide a complete list of what constitutes an adverse experience. This will leave the definitions open to some interpretation, however the APVMA considers that what should be included in these definitions is fairly straightforward.

“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 product² when used according to label directions³.”

² The term ‘agricultural chemical product’ includes all pesticides and household insecticides and pesticides.

³ Or “when a product is believed to have been used in accordance with the label”.

The following definitions outline what constitutes “serious” and “urgent” adverse experiences that are expected to be reported quickly to the APVMA by the product registrant.

Definition of a serious adverse experience

“A serious adverse experience is one that involves:

- *widespread and significant crop and plant damage (eg 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,*
- *significant environmental damage, including fish kills and water quality issues.*

Definition of urgent matters

“Urgent matters include serious adverse experiences that involve acute effects.”

The APVMA has developed the following timeframes that product registrants should use when providing this information to the APVMA.

Reporting timeframes

The APVMA has developed the following timeframes that product registrants should use when providing this information to the APVMA.

Definitions of reporting timeframes

*“The product registrant is responsible for providing the APVMA with initial notification that they have received a serious **and** urgent adverse experience report within ten working days of receipt⁴. This should be followed up with a progress report within a further twenty-eight working days and then a final investigation report including conclusions should be submitted as soon as practically possible.*

For all serious and non-urgent adverse experiences these should be investigated and evaluated as soon as possible and the findings reported to the APVMA as soon as practically possible.

All non-serious adverse experience reports should be recorded, investigated and assessed by the registrant and reported to the APVMA in accordance with the Adverse Experience Reporting Program Registrant’s Summary of Reported Adverse Experiences Form at the end of each financial year (this information does not need to be provided in this format, but all the information listed in this form should be provided) – Attachment 2.”

⁴ The interim report should set out an investigation plan and likely timeframe for the final report after the first ten days. For serious and urgent reports the final report should be available within three months.

Voluntary Reports

Where a reporting person submits a Voluntary Report directly to the APVMA and indicates via the privacy statement that he or she agrees to the APVMA seeking advice and information from the product registrant on the matter, the APVMA will request the registrant to:

- investigate the matter and provide an initial investigation report to the APVMA within twenty-eight working days of receipt.
- provide the APVMA with the concluding investigation report within three months of receipt of the original adverse experience report.

The APVMA acknowledges that there is no specific legislative requirement for registrants to investigate such matters, but we believe that this approach ensures that registrants are involved in the investigation and evaluation process for their products in the name of good product stewardship. In addition, the investigation of these matters can assist the APVMA to continue to be satisfied that the product meets all the requirements of the essential criteria specified under the Agvet Code. Should the APVMA not be satisfied that the product meets all requirements of the essential criteria the registrant may be asked to justify why the product should continue to be registered.

Information Required

All adverse experiences reported to registrants of agricultural chemical products should be recorded, investigated and assessed by the registrant and reported to the APVMA in accordance with the *Adverse Experience Reporting Program Registrant's Summary of Reported Adverse Experiences Form (KP82F5 – see Attachment 2)* (this information does not need to be provided in this format, but all the information listed in this form should be provided). The APVMA only requests a line listing of adverse experience reports classified as 'probable' or 'possible', with an indication of whether there was off-label use involved or not (see Classification below).

The registrant should ensure:

- any adverse experience reports sent directly to any and all manufacturers of their products are recorded, investigated and assessed by an appropriately qualified representative;
- all the information required by these guidelines is submitted to the APVMA within the required timeframes; and
- the appropriate Form is:
 - signed by the Registrant or their legally responsible person/representative;
 - submitted with a covering letter containing a brief overview of all the adverse experience reports included in the summary (eg the number of products involved, the number of reports for each product, the types of reports – lack of efficacy, crop safety, human safety, animal safety and environmental damage) and comments on any reports that should be highlighted; and
 - accompanied by a copy of the actual label text of the respective agricultural chemical products involved.

All adverse experience reports for each product should be grouped together and specific comments made at the end of the listing for the product as per the *Adverse Experience Reporting Program Registrant's Summary of Reported Adverse Experiences Form (KP82F5 – see Attachment 2)*.

Figure 1: Reporting timeframes

Investigation

The APVMA will request registrants to investigate all adverse experience reports that they receive for the purposes of determining whether the adverse experience is related to the use of or exposure to the product or not. Only reports that fit within the scope of the AERP Ag should be investigated for possible submission to the APVMA.

Evaluation

The APVMA will request that registrants evaluate the investigation findings for all adverse experience reports that they receive for their products for the purposes of classification. The use of an algorithm (Attachment 3) was established as a scientifically valid and rigorous method for assessing causality of adverse experience reports after consideration of methods used by international agencies dealing with adverse experience reports. The algorithm will be provided in the registrant guidelines for the AERP Ag, and registrants will be requested to use the algorithm for assessing causality.

Classification

Registrants will be requested to provide the APVMA with their classifications of all adverse experience reports that they receive. The APVMA will then conduct validation of the registrant classifications by conducting our own causality assessment of all Voluntary Reports that have been referred to the registrant for investigation, all serious and high and medium risk reports and a random sample of all non-serious and low risk reports.

Trend analysis

Registrants will be requested to conduct trend analysis of the cumulative reports for all products they are responsible for. Included in this analysis registrants will be requested to provide the APVMA with the following information:

- a calculation of the relationship between the number of adverse experience reports classified as probably product-related or possibly product-related against the total amount of product sold for the reporting period, and
- a brief statement assessing the safety and/or efficacy of the pesticide with reference to published scientific articles/papers, where applicable.

For all products in which high or medium priority issues are current, the APVMA will validate the trend analysis of the registrants and will conduct validation of a random sample of all others.

Corrective action

Registrants will be requested to provide the APVMA with a short narrative on what corrective action is necessary in light of the evaluation/classification and trend analysis of the adverse experience information, or provide justification for why no action is required.

The APVMA will then consider the adverse experience information for all products with similar formulations, the respective registrant comments and determine recommendations for corrective action required.

The APVMA will write to each affected registrant and include a summary of the details of all other adverse experiences for the products involved and provide a recommendation on corrective action proposed. All registrants will have the opportunity to provide the APVMA with comments on the proposed recommendations and provide a submission as to why they do not consider that the recommended corrective action is required if they so believe.

After taking into account all submissions and comments the APVMA will provide all affected registrants with their final conclusions and recommendations. Registrants will also be given a timeframe in which the corrective action is to be completed.

The AERP Ag Advisory Committee

The AERP Ag Advisory Committee, will consist of the following members:

- the AERP Coordinator,
- an AERP Ag Reviewer,
- the Pesticide Division Principal Scientist (supported by appropriate members of the relevant Pesticide Division Teams and Review Team as required),
- a representative from the Department of Health and Ageing,
- a representative from the Department of Environment and Heritage,
- an industry member (for assisting with strategic planning),
- one external member with appropriate agricultural scientific experience, and
- one medical expert with experience in treating pesticide-related illness.

Meetings of the AERP Ag Advisory Committee will be held on an as-needs basis depending on the numbers and types of adverse experience reports received. The meetings will be structured so that not all members will be required to attend all meetings. For example one meeting may be called to discuss reports only involving plant or crop damage, therefore the medical experts may not be required to attend.

Feedback

The conclusions drawn by the APVMA during investigation and evaluation of each adverse experience report will be reported back 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 (see also Classification above). The APVMA will explain what these conclusions are and what corrective action recommendations, if any, will be taken in response to the information.

It should be noted that in some instances if a causal link is not established between the use of or exposure to the product, or if there is not enough information to make a definite conclusion then regulatory action may not be taken.

Reporting

Based on the assessment and evaluation of the adverse experience reports received each year, the APVMA will publish “Annual Reports of Adverse Experiences”. The information in these reports will be arranged according to the active constituent of the products, therefore individual products are not identified. A summary of regulatory actions taken by the APVMA will also be included in these reports.

It is also proposed that information on “situations” will be included in these Annual Reports. For example information on situations where road-side spraying by councils are causing health concerns for communities can be identified and located geographically using post code information. Also information pertaining to the types of chemicals or products that are causing concerns for some communities can be similarly located (eg cotton growing areas). Targeted regulatory action can then be taken based on this geographic information. This information could be summarised in the Annual Reports in map form.

The APVMA will also publish interim reports if appropriate.

Further Information

For further information about the AERP Ag contact:

AERP Coordinator
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604
Telephone (02) 6210 4806
Facsimile (02) 6210 4813
E-mail AERPCoordinator@apvma.gov.au

The three complementary components of the AERP Ag:

1. The '*voluntary*' component that encourages the general public (including farmers and other chemical users, agronomists and bystanders), and health workers (including doctors, nurses, alternative medicine specialists etc) to report any adverse experiences to both the APVMA and the product registrant.
2. The '*state*' component through which state agencies are encouraged to report to the APVMA any adverse experience reports that they receive that are within APVMA jurisdiction. It also provides a mechanism for the APVMA to inform the relevant state authority of any information that it becomes aware of that falls within state jurisdiction (such as state control of use issues etc).
3. The '*registrant*' component that provides a mechanism for registrants of pesticides to report to the APVMA any adverse experiences that they become aware of for their products.

**ADVERSE EXPERIENCE REPORTING PROGRAM FOR AGRICULTURAL CHEMICALS
REGISTRANT'S SUMMARY OF REPORTED ADVERSE EXPERIENCES FORM**

REGISTRANT NAME

PERIOD OF REPORT ____ / ____ / ____ to ____ / ____ / ____

PRODUCT NAME	NCRIS NUMBER (if known)

Registrant's Ref no.	Product Batch number	Crop treated or situation	Date of treatment/exposure	Date of effect	Use not according to label directions (Y/N)	Registered name of all products involved in the adverse experience	Details of incident/nature of problem	Registrant's investigation findings	Registrant's causality assessment

Safety and efficacy citations (a brief statement assessing the safety and/or efficacy of the agricultural chemical product with reference to published scientific articles/papers). **[WHEN NECESSARY/RELEVANT]**

Reporting incidence (a calculation of the relationship between the number of adverse experience reports classified as probably product-related or possibly product-related against the total amount of product sold for the reporting period).

Actions taken for safety reasons (a short narrative on what corrective action is necessary in light of the adverse experience information, or provide justification for why no action is required).

Narrative review (a concise critical analysis and opinion on the risk/benefit profile of the agricultural chemical product including evidence of previously unidentified toxicity or safety concerns, increased frequency of known toxicity or expected adverse experiences, chemical interactions, overdose and its treatment, human adverse experiences associated with the use of the agricultural chemical product, and should indicate whether the safety data remain in line with the cumulative experiences to date and the approved label texts and should specify any future action recommended and the reasons why.) **[WHEN NECESSARY/RELEVANT]**

Signature: _____ **Date:** ____/____/____

Please return to:

**Adverse Experience Reporting Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604
Enquiries: (02) 6210-4806**

THE CAUSALITY ASSESSMENT ALGORITHM

Each registrant should conduct a causality assessment for each adverse experience report.

The following algorithm has been adapted from published information and **may be used as a guide** by registrants to conduct causality assessments of adverse experience reports. If registrants wish to conduct causality assessment using another method, then the results of the assessment must be consistent with the APVMA’s requirements.

The APVMA will validate the registrant’s assessments using statistical random sampling techniques.

1. History of product use

Assessment	Score
Effect is generally known to occur in this crop/situation at the rate/method used	+1
Effect is not known to occur in this crop/situation at the rate/method used, but has been previously reported in other crops/situations	0
Product has limited accumulated information	0
Effect previously unreported and product has substantial accumulated information	-1

2. Likely alternative explanations

Assessment	Score
There is no likely alternative that can explain the effect	+2
An alternative exists, but does not explain the effect well	0
The effect commonly occurs in this crop/plant/situation	0
There is a likely alternative explanation for the effect	-1

3. Evidence of excessive rate of application

Assessment	Score
The effect is clearly rate-related and there is evidence that the amount of product used was an overdose for this crop/plant/situation	+1
The effect is not rate-related or there is no evidence of an overdose	0

4. Time between application and effect

Assessment	Score
Timing was consistent and as expected for this type of effect to this product	+1
Do not know what timing to expect	0
Timing was inconsistent for this type of effect to this product	-2

5. Site of application

Assessment	Score
Effect is uniform over the entire area treated	+1
Effect only in areas treated (eg only in paddocks treated)	+1
No pattern to the effect is apparent	0
Effect is not uniform in area treated (eg is in strips or specific areas)	-1

Assessment

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 (algorithm score 3 to 6)

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 (algorithm score 3 to 6)

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 (algorithm score 0 to 2)

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 (algorithm score 0 to 2)

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 (algorithm score -1 to -5)

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'.