



**National
Registration
Authority**

for Agricultural and
Veterinary Chemicals

REPORT OF ADVERSE EXPERIENCES 2000

JULY 2001



**National Registration Authority for Agricultural and
Veterinary Chemicals
Adverse Experience Reporting Program**

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2000**

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EXECUTIVE SUMMARY

During the year 2000 the National Registration Authority's (NRA) Adverse Experience Reporting Program (AERP) was actively promoted within the veterinary profession. Quarterly articles were published in the Australian Veterinary Journal in an effort to increase the level of reporting from veterinarians, which appeared to have a favourable impact.

This annual report presents a descriptive overview of all the post-market adverse experience reports submitted voluntarily by members of the public, veterinarians, manufacturers or registrants of veterinary chemical products throughout the calendar year 2000. The introductory section in last year's report discussed in detail the outcomes of the AERP since it began in 1995. Section one of this report focuses on the practical implications of these outcomes and specifically what they mean for the veterinarian in private practice.

A total of one hundred and seventy nine voluntary adverse experience reports were submitted to the NRA throughout 2000. This is the largest number of voluntary reports submitted for any calendar year since inception of the AERP. It represents an increase of approximately sixty-two percent over the previous year. This trend is continuing into 2001.

Veterinarians submitted approximately twenty five percent of the voluntary reports (a total of forty four reports). Of the remaining one hundred and thirty five reports, one hundred and nine were reported by the manufacturers or registrants of the chemical products involved, seventeen were reported by animal owners and nine were sent in by others associated with the veterinary industry (eg veterinary officers with the State Departments of Agriculture).

No reports involving environmental damage were received involving veterinary chemical products in 2000.

Figure 1 – The total number of adverse experience reports received by animal species

Production animals	No. reports for 2000	Companion animals	No reports for 2000	Human reports	No reports for 2000
Cattle	58	Birds	2	Humans	20
Pigs	2	Cats	20		
Sheep	13	Dogs	35		
Goats	2	Horses	18		
		Rabbits	2		
Total	75	Total	77	Total	20

Again dogs and cattle featured highly. This reflects the animal husbandry practices in Australia, as they are the most commonly kept domestic animals both privately and commercially.

Twenty adverse experience reports to veterinary chemicals in humans were received. Over half of them involved accidental exposure to the product whilst treating animals such as needle-stick injuries.

1 INTRODUCTION

1.1 Program Outline

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is the Australian agency responsible for regulating agricultural and veterinary chemicals up to and including the point of retail sale. Under the National Registration Scheme, the NRA evaluates and registers agricultural and veterinary chemicals and manages quality assurance programs that monitor ongoing safety and performance of registered products.

The NRA's Adverse Experience Reporting Program (AERP) is a quality assurance program. It was established in January 1995 to provide a national mechanism for reporting, recording and analysing adverse experiences with veterinary chemical products. The intention of the program is to develop better use practices, prevent avoidable side effects and aid continuous improvement to manufacturing practices.

An adverse experience is defined as 'an unintended or unexpected effect on animals, human beings or the environment, including injury, toxicity, sensitivity reactions or lack of efficacy associated with the clinical use of a veterinary chemical product'. In general, adverse experiences refer to abnormalities that occur when a veterinary chemical product is administered at an appropriate dose rate for the purpose intended. However, often in veterinary medicine, veterinary chemical products may be used that are primarily intended for use in humans or species not listed on the product labels. Limited or no information may be available on appropriate dose rates and adverse reactions in such species. For this reason the NRA also considers reports of such adverse experiences.

It is important to note that for all adverse experience reports no causality is assumed between the use of the product and the observation of an adverse experience until the report has been assessed and classified. This is because the NRA encourages veterinarians and members of the public to report all suspected adverse experiences to assist the NRA in identifying potentially previously unrecognised problems with veterinary chemical products.

1.2 Reporting and Evaluation Procedures

Procedures for dealing with adverse experience reports are as follows:

- The NRA receives adverse experience reports from veterinarians, farmers, and other users of veterinary chemical products. In the first instance, each report is referred to the product registrant (or manufacturer) for investigation and comment.
- Registrants are required to report their investigation findings and comments directly back to the AERP Coordinator.
- In considering the submitted reports, the AERP Coordinator also:
 - a. researches the available scientific literature (eg. worldwide veterinary, medical and toxicological databases); and

- b. examines published information from pharmacovigilance agencies in other countries (eg. the Food and Drug Administration website).
- A decision on whether the adverse experience is product-related or not (see below) is made by an in-house panel of veterinary clinicians and pharmacologists.
- Possible actions stemming from this decision may include:
 - a. recommendations made to the registrant regarding certain aspects of the product (such as a label change);
 - b. review of the chemical under the NRA's Chemical Review Program;
 - c. education of the veterinary profession, farming community or wider public on issues relating to use of products.

1.3 Classification of Adverse Experiences

On the basis of available information the NRA classifies each report as one of the following:

- **Product related:** where the NRA is satisfied that the adverse reaction, whether expected or unexpected, is related to the use of the product. Included in this group are those reactions where it is probable or almost certain that the adverse experience is related to the use of the product.
- **Possibly product related:** where the NRA is not satisfied that the product was responsible for the reaction but the possibility that the product was implicated cannot be excluded.
- **Not product related:** where the NRA is satisfied that the reaction is definitely not related to the use of the product, or there was not enough information to allow classification.
- **Caused by not using the product according to label directions:** where there is clear evidence of incorrect dosing or incorrect route of administration and other such causes. This category includes reactions reported after off-label use of products by veterinarians exercising their professional right to prescribe an appropriate treatment.

It is important to note that not all reports can be classified. Some reports that involve the use of products that are not regarded as veterinary chemicals under the legislation are not classified. This report only discusses reports that the NRA has classified as product-related and possibly product-related. However, some reports that were classified as not product-related or caused by not using the product according to label directions may have resulted in regulatory action. These actions are discussed in Section 1.

1.4 Report Structure

The report is arranged into the following sections:

- | | |
|-----------|--|
| Section 1 | In this section the practical implications for veterinarians and other chemical users are discussed in detail. |
|-----------|--|

- Section 2 The second section contains nine tables arranged alphabetically by species. Each table shows the number of voluntary reports received during 2000 (that have been classified) for each class of product; the number of animals involved in the reports and the final classification given to the reports by the NRA. A brief discussion of the adverse experiences, by product categories, follows each species table.
- Section 3 The third section contains a table and discussion of adverse experience reports received during 2000 regarding human reactions.
- Section 4 The fourth section contains a summary table with details of all individual reports of adverse animal reactions and their final classification since publication of the 1999 report. The table lists each animal species in alphabetical order and is divided into sections that show for each of the products identified by active constituent, the number of animals involved, a brief description of each adverse reaction and the NRA classification of the incident.
- Section 5 The fifth section provides a summary table of all reports of alleged lack of efficacy received during the 2000 reporting period.

1.5 For further information

For information about the Adverse Experience Reporting Program please contact:

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2 SECTION 1

2.1 Summary of outcomes of AERP throughout 2000 and practical implications for private practitioners

2.1.1 Importance of veterinary profession reporting

As in previous years it is emphasised that responsible and accurate reporting of adverse experiences by the veterinary profession is important to the success of the AERP. The attending veterinarian should obtain an accurate history from the animal owner to determine which product or products might have been involved and what other factors might be important (such as the general condition of the animal, including disease status, at the time of treatment and access to toxic plants etc). The veterinarian should also investigate the incident as carefully as possible by examining any affected animals, taking blood samples when necessary and sending samples for pathology if possible. The veterinarian should then contact the manufacturer directly and discuss the incident and ask them to provide advice on investigating the matter further if necessary. Manufacturers have a mandatory requirement to notify the NRA of any adverse experience reports that they receive. The collection of this information will assist the NRA in assessing and classifying each incident.

2.1.2 Product label information

The NRA continues to monitor all reports of adverse experiences to veterinary chemical products and make this information available in both the product label information and in the scientific literature. For example, many of the adverse experience reports received during 2000 were classified as hypersensitivity or anaphylactic reactions. In some cases label changes were made in an attempt to make both the prescribing veterinarian and the animal owner or product user aware that such reactions had been previously reported when using the product and to take caution when using it. It is therefore important for all veterinarians to carefully read the current full product label including any leaflets or flyers to be aware of any such changes and information.

2.1.3 Prescribing veterinary medicines

It also highlights the need for the prescribing veterinarian to provide the full label, including any leaflets or flyers to the product user at the time of sale and to make the product user aware of any such relevant information. The product leaflet is part of the approved label and therefore a copy should be included when the product is dispensed. Veterinarians should exercise caution when prescribing veterinary chemical products and it is their responsibility to make product users aware of all side effects and possible adverse reactions that might occur when using the products on their animals.

2.1.4 Other available information

Prescribing veterinarians should also be aware of any information available in the scientific literature pertaining to the use of veterinary chemical products especially when deciding to prescribe off-label uses for such products. In some cases published information is available that indicates that caution should be taken when using a product in a particular animal

species. This should be duly noted when using the product in that species. Please see articles published by the NRA in the Australian Veterinary Journal throughout 2000 and previous annual reports available on the NRA Website for further details on such information.

2.1.4 Constructive comments from veterinarians welcome

When submitting adverse experience reports to the NRA it would be of value if the attending veterinarian could make constructive comments regarding any action they feel is necessary. This may include suggestions on product label wording such as additional warning statements, or advice on what the animal owner should do if an adverse experience occurs. This type of feedback will assist the NRA in improving the quality of information available to both veterinarians and the general public on the safe use of veterinary chemical products.

2.2 Adverse experiences reported for cats during 2000

Table 1 – Cats

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
External parasiticides	7	8	7	1	0	3	0	4
Vaccines	3	19	6	1	2	0	1	0
Internal parasiticides	2	11	11	0	2	0	0	0
Anaesthetics	1	2	2	1	1	0	0	0
Anti-anxiety therapies	1	1	1	0	1	0	0	0
Anti-inflammatory therapies*	1	1	1	1	NA	NA	NA	NA
Anti-microbial therapies	2	2	2	0	1	0	1	0
Other**	1	NA	1	0	NC	NC	NC	NC
Total	18	44	31	4	7	3	2	4

* This report is still under investigation.

** The NRA did not classify these reports.

2.2.1 Summary

A total of eighteen adverse experience reports were received throughout 2000 involving the use of veterinary chemical products in cats. Most of the reports that were classified as product-related involved previously reported reactions that are known to occur with the particular product (such as hypersensitivity reactions, anaphylactic reactions and known side effects). These reactions include hypersensitivity reactions to vaccines, sterile injection site lesions, gastrointestinal reactions to worming medications and sedation reactions are use of anti-anxiety products. For each adverse experience report that is submitted the product label is examined to ensure that adequate information is available about possible side effects and advice on what the animal owner should do if an adverse experience occurs

2.2.2 External parasiticides

Seven reports were submitted to the NRA that involved the use of external parasiticides in cats. Of these three were classified as possibly product-related and four as caused by not using the product according to label directions.

2.2.2.1 Fipronil

A total of four cats were treated with products containing fipronil in the three reports that were classified as possibly product-related. In these reports there was a temporal relationship established between the use of the products and the observed clinical signs in the cats. In one report the cat began scratching and became agitated soon after the product was applied. This might have been as a result of a hypersensitivity to the product. In another report a cat became anorexic over the four days following treatment. The cat stopped grooming itself and the coat then became quite greasy. In a third report a cat that had been treated with this product for the previous six months without incident appeared to become distressed and began salivating and hyperventilating within twelve hours of treatment. The cat died twenty-four hours post-treatment and although it was not possible to link the use of the product with the death of the cat the possibility could not be completely ruled out.

2.2.3 Vaccines

Three reports of adverse experiences in cats involving the use of vaccines were received throughout 2000. Of these two reports were classified as product-related and the third as not product-related.

2.2.3.1 Combined feline leukaemia, panleucopenia, rhinotracheitis and calicivirus vaccines

In one report a cat was re-presented to the veterinary clinic twenty-four hours post-vaccination. The owner reported that the cat had become agitated, anorexic and appeared uncomfortable when handled. The attending veterinarian reported that the cat was pyrexia and had a mild swelling at the site of vaccination. The localised reaction at the site of the vaccination was determined to be a Type I Hypersensitivity and the systemic signs were either a Type I or Type III Hypersensitivity.

2.2.3.2 Feline panleucopenia, rhinotracheitis and calicivirus vaccine

In another report four of seventeen cats vaccinated became depressed, lethargic and listless within hours of treatment. All the cats recovered and again this was considered to have been a Type I Hypersensitivity reaction.

2.2.4 Internal parasiticides

2.2.4.1 Levamisole

Two reports of adverse experiences with internal parasiticides containing levamisole were submitted to the NRA in 2000. Both were classified as product-related as the clinical signs observed in the cats (vomiting) were consistent with previously reported clinical signs for this product. The active constituent levamisole is known to be quite unpalatable and this is the most likely cause of the nausea and vomiting. The product label contains a specific warning that gastrointestinal upset may occur after the use of this product.

2.2.5 Anaesthetics

2.2.5.1 Alphaxalone and alphadolone acetate

Only one report of a suspected problem with an anaesthetic containing alphaxalone and alphadolone acetate was reported in 2000. Two cats were involved in the incident. One cat was found dead in its cage shortly after it had been anaesthetised. The second cat developed fluid in its chest and the veterinarian commented that on auscultation the lung sounds were increased. It also became cyanotic, but recovered with appropriate treatment.

All general anaesthetics are associated with a certain level of risk. A polyoxyethylated castor oil is the vehicle or carrier substance for the active constituents in this product. This may liberate mast cell histamine in the cat and induce arterial hypotension (1). Allergic reactions such as hyperaemia of ears and peripheral oedema are commonly seen in cats and an anaphylactic reaction may have been responsible for the reactions seen in this report.

Again it is important to carefully monitor and record any suspected reactions reported about anaesthetic agents by programs such as the AERP to ensure that any increase in incidence for a particular batch or lot is identified early and appropriate action is taken.

2.2.6 Anti-anxiety therapies

2.2.6.1 Clomipramine

A single report was received that involved the use of a newly registered anti-anxiety therapy containing clomipramine for dogs and cats. The treated cat became sedated and lethargic for a short time post treatment. It was noted that the cat received quite a large dose of the product. The cat recovered fully within twenty-four hours. This is a known side effect for this product and a label warning on the product states that clinical signs such as these may occur.

2.2.7 Anti-microbial therapies

2.2.7.1 Enrofloxacin

Only two reports involving the use of anti-microbial therapies in cats were received in 2000. In one report the owner noticed that lumps had formed at the sites of injection of this product. The masses were excised and a pathology report recorded that they were due to traumatic folliculitis consistent with an injection site. Such sterile injection site lesions can occur with any injectable product.

2.3 Adverse experiences reported for cattle during 2000

Table 2 – Cattle

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
External parasiticides	27	8100+	7285	0	16	1	1	9
Anti-microbial therapies (Intra-mammary)	16	1500+	300+	NR	NC*	NC*	NC*	NC*
Internal parasiticides**	8	457	104	39	2	0	1	1
Anti-bloat therapies	2	15	2	2	0	2	0	0
Anti-microbial therapies (Injectable)	2	7	4	1	1	1	0	0
Other (ie not veterinary chemical products)	2	160+	110+	133	NC*	NC*	NC*	NC*
Total	57	10239+	7800+	175	19	5	2	10

* The NRA did not classify these reports.

** Some reports are still under investigation.

2.3.1 External Parasiticides

Of the twenty-seven reports received involving the use of external parasiticides in cattle, sixteen were classified as product-related, one possibly product-related, one not product-related and nine as caused by not using the product according to label directions.

2.3.1.1 Synthetic pyrethroids (zeta-cypermethrin, deltamethrin)

Twenty-three of the reports involved the use of products containing synthetic pyrethroids. Clinical signs of generalised irritation such as tail swishing, licking at the back and restlessness were most commonly observed. This does not normally cause a significant problem, however the cattle can become restless when being milked.

2.3.1.2 Amitraz

A herd of twelve cattle were treated with a product containing amitraz to control ticks. All of the cattle developed clinical signs of depression and decreased appetite. Some of the more severely affected cattle were treated with an antidote agent. All cattle recovered however their growth rate was impaired for some time. This incident was classified as product-related however it is noted that the owner may not have mixed the concentrated product adequately when diluting it before use.

2.3.2 Internal parasiticides

Of the eight reports involving internal parasiticides in cattle four are still under investigation and have not yet been classified. Two of the four reports that have been assessed were classified as product-related, one as not product-related and one related to off-label use of the product.

2.3.2.1 Levamisole

In one report 6-8 cattle were back lined with a product containing levamisole and within one hour of treatment two of the cattle began hypersalivating and one died. This incident was classified as product-related as there was a temporal relationship between the use of the product and the development of clinical signs and hypersalivation is recorded in the toxicological data available for levamisole.

2.3.2.2 Abamectin

In another report eighty calves were treated with a product containing abamectin and the following day approximately thirty calves were showing signs of ataxia and had become dull. Two animals had died overnight. This report was classified as product-related however it is noted that some of the cattle may have received an overdose.

2.3.3 Anti-bloat therapies

2.3.3.1 Monensin

Anti bloat treatments containing monensin were the subject of two reports in 2000. Both reports were classified as possibly product-related. One animal died in each case and when the capsules were recovered from the rumen at post mortem they were found to have fully paid out. The product should continue to pay out for at least 100 days. The reason for the increased rate of pay out of this product is unknown. Incidents similar to this have been published in previous NRA publications however the incidence of these types of reports is very low.

2.3.4 Anti-microbial therapies (injectable)

2.3.4.1 Oxytetracycline

One of the two adverse experience reports involving the use of anti-microbial therapies was classified as product-related and most probably a type 1 hypersensitivity reaction.

2.3.4.2 Tylosin

In the second report an odorous orange-coloured vaginal discharge was noticed in three of six cattle treated with a product containing tylosin. This report was classified as possibly product-related and similar reactions have been reported previously in a very small number of cases both in Australia and overseas with this and other antibiotics. It does not however appear to cause any significant problems.

2.4 Adverse experiences reported for dogs during 2000

Table 3 – Dogs

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
External parasiticides	8	9	9	2	1	4	2	1
Vaccines*	7	15+	10+	3+	4	2	0	0
Internal parasiticides	5	8	7	1	3	0	0	2
Anti-microbial therapies	4	5	5	0	2	2	0	0
Anti-inflammatory	2	2	2	2	0	1	0	1
Anaesthetics	1	1	1	0	0	0	1	0
Anti-emetics	1	1	1	1	0	0	1	0
Other**	2	2	2	0	NC	NC	NC	NC
Total	30	43+	37+	9+	11	8	4	4

* One report involving the use of vaccines was not classifiable, however the information gained from this report has been used to provide advice to the veterinary profession when administering vaccines. This advice is also outlined in Section 1 of this report.

** The NRA did not classify these reports.

2.4.1 External Parasiticides

Eight reports of suspected adverse reactions to external parasiticides were received in 2000. Of these reports one was classified as product-related, four possibly product-related two not product-related and one as caused by not using the product according to label directions.

2.4.1.1 Fipronil

Three of the reports involved the use of products containing fipronil. In one of these reports a dog developed diarrhoea approximately one week after being treated with the product. The dog also began vomiting and became slightly ataxic some time later. This report was classified as possibly product-related, however the causality association was considered to be unlikely. In a second report a dog became lethargic and off its food within days of treatment. It then became pyrexemic and developed papules and erythema over the dorsal skin of the neck and shoulders. This report was classified as possibly product-related and may have been the result of a hypersensitivity reaction. Hypersensitivity reactions to these products have been reported to the NRA previously and as a result the label now warns against using the product if the user or animal has a known hypersensitivity to alcohol or insecticides.

2.4.1.2 Fenthion

Another two reports involved the use of a product containing fenthion to control fleas. In the first report the dog developed generalised urticaria and oedema of the lips and ears. This was considered to be a hypersensitivity reaction and classified as possibly product-related.

2.4.1.3 Permethrin

The remaining two reports involved a product containing permethrin used also to control fleas. One dog became lethargic and dull within twenty-four hours of treatment. This was considered to be product-related due to the temporal and clinical relationship between the use of the product and the clinical signs observed. In the other report the dog began scratching at the site of application of the product and developed a localised lesion. This was considered to be product-related.

2.4.2 Vaccines

Again vaccines featured highly in the total number of reports of adverse experiences in dogs, however considering the large number of doses of vaccines sold each year it represents a relatively small proportion. Reported reactions included site reactions (lumps), vomiting, collapse, cyanosis, facial swelling and very rarely death.

2.4.3 Internal parasiticides

Of the five reports involving the use of internal parasiticides three were classified as product-related and two as off-label use.

2.4.3.1 Melarsomine dihydrochloride

In one report a dog was being treated for sub-clinical heartworm disease with a product containing melarsomine dihydrochloride and three days later it developed dyspnoea and bloody diarrhoea. The dog died later that day. This incident was considered to have been related to the use of the product as an immune reaction to the death of adult heartworms present in the right atrium of the heart was the most probable cause of death of the dog.

2.4.3.2 Ivermectin and pyrantel embonate

Another dog was treated with a product containing ivermectin and pyrantel embonate for heartworm and intestinal worm prevention. Within twelve hours of treatment the dog became very weak in the hind legs. This occurred on three occasions after treatment with this product. Therefore this incident was classified as product-related. This type of report is very rare and does not appear to pose a serious risk to animal health.

2.4.3.3 Levamisole

Vomiting was also observed in a number of dogs treated with intestinal worming tablets containing levamisole. The active constituent levamisole is known to be quite unpalatable and this is the most likely cause of the nausea and vomiting. The product label contains a specific warning that gastrointestinal upset may occur after the use of these products.

2.4.4 Anti-microbial therapies

Only four reports involving the use of antimicrobial therapies were submitted throughout 2000. Most involved development of skin eruptions or localised lesions to injection sites. Two were classified as product-related and two as possibly product-related. Warning statements are current on these types of products that indicate that such reactions may occur and that cessation of treatment will result in resolution of clinical signs.

2.4.5 Anti-inflammatory agents

The NRA received two reports involving anti-inflammatory agents in 2000. One was classified as possibly product-related and the other was associated with a dose rate frequency greater than the label recommendations.

2.5 Adverse experiences reported for horses during 2000

Table 4 - Horses

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
Anti-microbial therapies	8	8	8	4	8	0	0	0
Internal parasiticides	3	43	4	2	0	0	1	2
Sedatives	2	2	2	0	2	0	0	0
Anti-inflammatories	1	1	1	0	1	0	0	0
External parasiticides	1	4	1	0	1	0	0	0
Smooth muscle relaxants	1	5	3	0	1	0	0	0
Vitamin supplement	1	2	1	1	1	0	0	0
Other*	1	10	11	0	0	1	0	0
Total	18	66	31	7	14	1	1	2

* This report involved the use of a product for trial purposes.

2.5.1 Antimicrobials

2.5.1.1 Procaine penicillin, benzathine penicillin, penethamate hydriodide, trimethoprim, sulfadiazine

Antimicrobial agents again featured highly in the total numbers of reports involving use of veterinary chemical products in horses. All eight reports were classified as product-related and were determined to have been caused by anaphylactic reactions. The common clinical signs observed included excitation immediately after being treated, convulsions, incoordination, collapse and thrashing.

This information highlights the need for attending veterinarians to be vigilant for signs of anaphylaxis and be prepared to take the appropriate action necessary when required.

2.5.2 Sedatives

Both reports involving the use of sedative agents were classified as product-related.

2.5.2.1 Xylazine hydrochloride

In one report the attending veterinarian injected a small amount of a product containing xylazine hydrochloride into the right metacarpal vein with a fine needle. A swelling developed shortly after the injection was given and oedema of the leg from the mid cannon region to the hoof was present within a few hours. This was most likely caused by haematoma development.

The second report also involved the use of a product containing xylazine hydrochloride. Approximately 30 seconds following intravenous administration of the product, the horse began to toss its head in the air, followed by rearing up and throwing itself over backwards, violently thrashing all four legs and throwing head. Within two minutes it staggered to its feet. The clinical signs observed in this horse were considered to be directly related to the administration of the product. It is possible that the reaction was related to intra-carotid injection, however we recognise that these types of reactions have occurred after intravenous injection of xylazine products in a very rare number of incidents.

2.5.3 Anti-inflammatory agents

2.5.3.1 Flunixin meglumine

Approximately one minute after the horse was injected with this product, it staggered and flipped over backwards. It became recumbent and remained so for 20 minutes. This was classified as product-related and considered to have been as the result of an anaphylactoid reaction.

2.5.4 External parasiticides

2.5.4.1 Permethrin

A large superficial corneal ulcer developed on the eye of a horse treated with a pour-on product containing permethrin. As a result of this a change was made to the label of this product to emphasise the need to take care when applying the product on the head.

2.5.5 Smooth muscle relaxants

2.5.5.1 Propantheline bromide

Three out of five mares treated with propantheline bromide to assist in rectal examinations developed colic within hours. This is a recognised side effect of this product and a warning is present on the product label. This incident was therefore classified as product-related.

2.6 Adverse experiences reported for sheep during 2000

Table 5 – Sheep

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
External parasiticides*	5	5359	1322	278	2	2	0	0
Internal parasiticides	4	1528	15	14	1	1	0	2
Vaccines*	1	1000	15	15	0	0	0	0
Total	10	7887	1352	307	3	3	0	2

* Some reports are still under investigation.

2.6.1 External parasiticides

Of the five adverse experience reports involving the use of external parasiticide products in sheep, two were classified as product-related and two as possibly product-related. One other report is still under investigation.

2.6.1.1 Diflubenzuron

In one report 488 sheep were treated with a product containing diflubenzuron to control lice and blowflies. The farmer noticed that the applicator gun was not working properly and that the product did not spray out over the backs of the sheep as expected. Some of the sheep were noticed to have lesions along their back lines at the site of application approximately one month post-treatment. Although this was classified as product-related it highlights the need to ensure all equipment used when treating animals in such situations is working properly and effectively.

Another two reports also involved the use of this product and a very small proportion of the treated lambs developed lumpiness and scabs in the wool on the back line. These reports were classified as possibly product-related as other factors may have been involved in causing this (such as skin infections unrelated to the use of the product).

2.6.1.1 Diazinon

Based on this report and other similar reported adverse experiences the label directions for ovine ectoparasiticides will be re-evaluated. The findings of this will be used to improve the label directions for use of these products.

2.6.2 Internal parasiticides

Assessment of these four reports revealed that one report was classified as product-related, one a possibly product-related and two as caused by not using the products according to label directions.

2.6.2.1 Levamisole

In two reports involving the use of levamisole, a very small number of sheep treated developed signs of toxicity (head shaking, lip licking, salivation, frothing at the mouth, muscle tremors, agitation) and died soon after treatment. Many environmental factors may have contributed to these problems such as extreme temperatures and stress factors involved with mustering and handling. These reports were classified as product-related and possibly product-related.

2.7 Adverse experiences reported for goats during 2000

Table 6 – Goats

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
Internal parasiticides	1	200	30	4	0	0	0	1
Anti-microbial therapies (Intra-mammary)	1	5	5	0	0	0	0	1
Total	2	205	35	4	0	0	0	2

Both reports involving the use of veterinary chemicals in goats were classified as caused by not using the product according to label directions.

2.8 Adverse experiences reported for pigs during 2000

Table 7 – Pigs

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
Vaccines*	1	NR	15%	15%	0	0	0	0
Other**	1	NR	134	134	NA**	NA**	NA**	NA**
Total	2	NR	134+	134+	0	0	0	0

* The one report involving the use of a vaccine in pigs is yet to be assessed and classified.

** This product was not a veterinary chemical product.

2.9 Adverse experiences reported for birds during 2000

Table 8 – Birds

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
Internal parasiticides	1	100	11	9	0	0	0	1
Total	1	100	11	9	0	0	0	1

The one adverse experience report involving birds was classified as caused by not using the product according to label directions.

2.10 Adverse experiences reported for rabbits during 2000

Table 9 – Rabbits

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Caused by not using product according to label directions
External parasiticides	2	2	2	2	0	0	0	2
Total	2	2	2	2	0	0	0	2

Both reports involving the use of veterinary chemicals in rabbits were classified as caused by not using the product according to label directions.

3 SECTION 3

3.1 Table of reports of adverse experiences in humans 2000

The following table and discussion sets out the details of those reports where it has been decided that the adverse experience is product-related or possibly product-related. This summary is intended only to provide general information about the types of reactions that animal owners, veterinarians and others have voluntarily reported to the NRA or the manufacturer after use of the product. The information in the text is not by itself a basis for determining the safety and efficacy of a given product or for comparing one product with another, nor can it be used to predict the frequency of occurrence of a reaction.

3.2 Adverse experiences reported for humans during 2000

Table 10 – Humans

Product Category	No. of Reports Received	No. Treated	No. Affected	No. Died	Product Related	Possibly Product Related	Not Product Related	Accidental injury or exposure
External parasiticides*	10	NA	9	1	2	5	1	1
Vaccines	5	NA	5	0	0	1	0	4
Anti-microbial therapies	2	NA	2	0	0	0	0	2
Anaesthetics	1	NA	1	0	0	0	0	1
Internal parasiticides	1	NA	1	0	0	0	0	1
Prostaglandins	1	NA	1	0	0	0	0	1
Total	20	NA	19	1	2	4	1	1

* One report is under coronial investigation.

Of the reports involving suspected adverse reactions in humans, many were classified as accidental injuries or exposures. Some were classified as possibly product-related and product-related and these involved reactions of the skin or respiratory system after use of external parasiticides.

4 SECTION 4

4.1 Summary of adverse experience reports 2000 – Animal Reaction Category

The following summary sets out the details of those reports where it has been decided that the adverse experience is product-related or possibly product-related.

The table lists the animal species affected; the generic chemical/active constituent; route of administration; number of animals involved; a description of the adverse experience; the classification of the reaction and comments. In evaluating the reports the NRA also takes into consideration climatic conditions at the time of treatment, and health and management of the animal. In situations where a number of products were administered concurrently, the active constituents of all products used are named.

This summary table is intended only to provide general information about the types of reactions that veterinarians, animal owners and others have voluntarily reported to the NRA or the manufacturer after use of the product. The information in the table is not by itself a basis for determining the safety and efficacy of a given product or for comparing one product with another, nor can it be used to predict the frequency of occurrence of a reaction.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATS

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Alphaxalone Alphadolone acetate	Intravenous	2	2	1	One cat was found dead in its cage shortly after it had been anaesthetised. The second cat developed fluid in its chest and the veterinarian commented that on auscultation the lung sounds were increased. It also became cyanotic, but recovered with appropriate treatment.	Product-related All general anaesthetics are associated with a certain level of risk.
Clomipramine	Oral	1	1	Nil	Prior to treatment a full biochemical screen was performed on this cat and all biochemical parameters were within normal limits. The treated cat became sedated and lethargic for a short time post treatment. The cat recovered fully within twenty-four hours. It is noted that the cat received quite a large dose.	Product-related The product label carries a statement that such side effects are possible.
Combined feline parvovirus, rhinotracheitis, calicivirus vaccine	Subcutaneous	17	4	Nil	All affected cats became listless and off its food. One cat vomited. All cats recovered within two days.	Product-related Type I hypersensitivity. Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.
Enrofloxacin	Subcutaneous	1	1	Nil	The owner of the cat noticed two subcutaneous masses in the dorsal shoulder area at the site of injections of this product. These masses were excised. The histopathology report indicated that these lumps were traumatic folliculitis consistent with an injection site.	Product-related Such sterile injection site lesions can occur with any product.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
<p>Feline leukaemia virus</p> <p>And</p> <p>Feline panleucopaenia, rhinotracheitis and calicivirus vaccines</p>	Subcutaneous	1	1	Nil	<p>The cat was re-presented the afternoon following vaccination. The owner reported that the cat was unsettled, agitated, uncomfortable when handled, unwilling to move and anorexic. Clinical examination reportedly revealed a temperature of 39.9 degrees Celsius mild swelling in area of right shoulder and sensitivity and crying when touched.</p>	<p>Product-related</p> <p>Localised reaction – Type I hypersensitivity to the first vaccine.</p> <p>Systemic signs – Type I or III hypersensitivity to either vaccine.</p> <p>Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.</p>
Fipronil	External	1	1	Nil	<p>The treated cat became extremely itchy, began to scratch and constantly moved around. The owner was able to alleviate the symptoms by gently brushing the cat with a soft brush.</p>	<p>Possibly product-related</p> <p>There was a temporal relationship between the use of this product and the observed clinical signs. This product can cause hyperactivity of fleas prior to their death. This might cause symptoms as seen in this instance. This product is the subject to an ongoing monitoring process.</p>
Fipronil	External	2	1	Nil	<p>The cat went off its food, became lethargic and neglected washing its coat (which then became greasy) for a period of four days post-treatment. The cat continues to be lethargic and off its food.</p>	<p>Possibly product related</p> <p>There was a temporal relationship between the use of this product and the observed clinical signs. This product is the subject to an ongoing monitoring process.</p>

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Fipronil	External	1	1	1	Cat was treated with this product for a period of six months with no reported adverse effects. The cat had previously experienced one episode of tremors, lethargy and anorexia, which appeared to be unrelated to the use of this product. After this treatment, the cat started salivation excessively during the night. The attending veterinarian reported that the cat was distressed, hyperventilating but had a normal appetite and the salivation had stopped. The following day the cat began salivating again, hyperventilating, urinating around the house, was pyrexia and started champing at the mouth. The cat died later that night.	Possibly product-related The initial sign of hypersalivation might have been as a result of the cat licking some of the product and experiencing the unpalatable nature of the product. It would appear that the product was only involved with this initial clinical sign. Post mortem results revealed that the lungs were consolidated, there were subcapsular haemorrhages in the kidneys, myocarditis, vascular congestion of all organs but no obvious brain abnormalities. This product is the subject to an ongoing monitoring process.
Levamisole hydrochloride, Niclosamide And Feline panleucopaenia, rhinotracheitis and calicivirus vaccines	Oral Sub-cutaneous	1	1	Nil	The cat became lethargic and started vomiting soon after treatment. The cat remained unwell for some days after this. The attending veterinarian reported no abnormalities on clinical examination except possible mild anterior abdominal pain. The cat recovered over the following few days.	Product-related to the levamisole The label directions for this product contain a specific warning about the possibility of vomiting occurring.
Levamisole hydrochloride, Niclosamide	Oral	10	10	Nil	All treated cats vomited within half an hour of treatment.	Product-related The label directions for this product contain a specific warning about the possibility of vomiting occurring

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Abamectin	Subcutaneous	80	30	2	On the day following treatment, approximately thirty percent of the herd were showing signs of ataxia and had become dull. Two animals had died overnight.	Product-related However it is noted that some of the cattle may have received an overdose.
Amitraz	External	12	12	Nil	Shortly following treatment a herd of twelve cattle showed signs of central nervous system depression and anorexia. The worst affected were treated with an antidote and recovered quickly. Blood analysis indicates that two of the affected animals had an acute inflammatory leukogram. The presence of a left shift suggests that this is more than just a stress-related neutrophilia.	Product-related The label directions for these products are currently under review.
Deltamethrin And Sulfadimidine sodium	External Injection	18	4	Nil	Four calves experienced severe skin reactions including focal skin necrosis and sloughing. The lesions were not only associated with the un-pigmented areas.	Possibly product-related (to the deltamethrin). This product is the subject to an ongoing monitoring process.
Deltamethrin	External	81	81	Nil	Soon after applying the product to the cattle the herded cows exhibited the following signs – nervous behaviour, tail twitching, biting each other, defaecating while being milked. The cows became calmer when in the paddock. The milk production of the cattle also decreased.	Product-related This product is the subject to an ongoing monitoring process.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Deltamethrin	External	240	120	Nil	Cows exhibited the following signs – tail twitching, nervous behaviour and scouring. The signs lasted for five days. There was also a recorded lack of efficacy against flies. The environmental conditions were very hot.	Product-related This product is the subject to an ongoing monitoring process.
Levamisole	External	6-8	2	1	Within one hour of treatment two cows began salivating and one died.	This incident was classified as product-related as there was a temporal relationship between the use of the product and the development of clinical signs. Hypersalivation is recorded in the toxicological data available for levamisole. This product is the subject to an ongoing monitoring process.
Monensin	Oral	Not recorded	1	1	A herd of steers were treated with this product and one steer died eighty-two days later. The steer had appeared unwell for one week prior to death, and had been frothing at the mouth. Neither a veterinary examination or post mortem were conducted, therefore the cause of death is uncertain. The capsule was retrieved from the dead steer and found to have fully paid out. The capsules are designed to pay out for at least one hundred days. In vitro testing of the formulation used in this batch of capsules indicated a release rate in the normal range.	Possibly product-related The reason for the increased rate of pay out of this product is unknown. Incidents similar to this have been published in previous NRA publications however the incidence of these types of reports is very low. This product is the subject to an ongoing monitoring process.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Monensin	Oral	14	1	1	Fourteen heifers were treated with this product and one died eighty-two days later. The suspected cause of death was bloat. The heifers had been grazing a high bloat-risk pasture, and had been showing signs of bloat several days beforehand. The capsule was retrieved from the dead heifer and found to have fully paid out. The product is designed to pay out for at least one hundred days.	Possibly product-related The reason for the increased rate of pay out of this product is unknown. Incidents similar to this have been published in previous NRA publications however the incidence of these types of reports is very low. This product is the subject to an ongoing monitoring process.
Oxytetracycline	Intramuscular	1	1	1	The cow had difficulty calving and was treated with this product to prevent post-calving infections. The cow died within two minutes of treatment..	Product-related Type 1 Hypersensitivity. Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.
Tylosin	Intramuscular	6	3	Nil	An orange, odorous vaginal discharge was noticed on the yard surface during milking from three of the treated cattle.	Possibly product-related Similar reactions have been reported previously in a very small number of cases both in Australia and overseas with this and other antibiotics. It does not however appear to cause any significant problems.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Zeta-cypermethrin	External	57	57	Nil	Signs of irritation were noticed the following morning. These included tail swishing, foot stamping, head turning, and trying to lick their backs, kicking cups off during milking and not feeding in the paddock. Cows are muddy from continual tail swishing and many also had sore udders due to continual tail swishing. All cows were affected to some degree. Signs of irritation continued for three days.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Zeta-cypermethrin	External	28	14	Nil	Twenty-four hours after treatment approximately half the mob were showing signs of extreme irritation. Signs included stomping, tail swishing, runny eyes, rubbing and restlessness. Most recovered within four days, however a small number of cattle took five to seven days to recover and one cow took ten days. The product was applied from the withers to the tail not from poll to the tail as per label directions, and cattle were slightly underdosed.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	150	150	Nil	Signs of irritation were observed in all cattle within twenty-four hours post-treatment. The clinical signs included tail swishing, arching of the back and licking the back. Signs settled down in most animals within seventy-two hours, but some were still showing signs for five days.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	18	18	Nil	Signs of irritation were observed the next day and included tail swishing, shaking the head, licking the back and restlessness. Signs continued for three days.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Zeta-cypermethrin	External	145	18+	Nil	A dairy herd was treated with this product for lice control. Cows were of mixed ages and lactation. One hundred of the cattle were dried off at the time. Signs of irritation were noticed at the next milking. These included tail swishing, foot stamping, general irritation/nervousness and kicking cups off during milking. Approximately forty percent of the lactating cows were affected. The owner did not observe the one hundred cattle that had been dried off. Signs of irritation continued for three to five days.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	234	234	Nil	The morning following treatment all cattle were showing signs of irritation. These included tail swishing, kicking at their bellies and general restlessness. These signs lasted less than twenty-four hours. Feed intake and milk production also decreased.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	75	60	Nil	Signs of irritation were observed twenty-four hours after treatment and included kicking, tail swishing, agitation and difficulty in milking. Signs continued for two days and eased following rain.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Zeta-cypermethrin	External	160	90+	Nil	Cattle had a very heavy lice infestation. The morning following treatment all lactating cattle were showing signs of irritation including stamping, kicking cups off, restlessness, tail swishing and licking their backs.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	90	90	Nil	All treated cattle began to show signs of irritation within twelve hours. Signs included watery eyes and severe restlessness.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	110	90	Nil	Signs of irritation were noticed in most cattle the day following treatment and included tail swishing, kicking and difficulty in milking. There was also a drop in milk production.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.
Zeta-cypermethrin	External	180	170	Nil	Signs of irritation were noticed the day following treatment and included restlessness/agitation, tail swishing and licking their backs.	Product-related This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATTLE (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Zeta-cypermethrin	External	500	120	Nil	<p>Of the five pens treated in the feedlot, two showed signs of irritation, which commenced on the afternoon of treatment. In one of the pens, the cattle appeared restless on the afternoon of treatment and by the next day were very agitated. Feed intake decreased for two days. Other signs observed included tails swishing and licking their backs.</p> <p>In the second pen the cattle showed signs of irritation the next morning. The signs were very mild and the feed intake was unaffected.</p>	<p>Product-related</p> <p>This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.</p>
Zeta-cypermethrin	External	60	60	Nil	<p>Signs of irritation were noticed in all treated cattle the day following treatment and included tail swishing, kicking, licking their backs and restlessness.</p>	<p>Product-related</p> <p>This does not normally cause a significant problem, however the cattle can become restless when being milked. A label change has been made to this product to warn users of this potential side effect.</p>

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

DOGS

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Amoxicillin trihydrate, Clavulanic acid And Carprofen	Oral Oral	1	1	Nil	This dog was treated with these two products for suspected pancreatitis. The day following initial treatment, the dog exhibited extreme pruritus and small circular, inflamed and erosive lesions (a few millimetres in diameter) over the base of the tail, back and sides.	Possibly product-related
Amoxicillin, Clavulanic acid	Subcutaneous	2	2	Nil	Both dogs developed tennis ball sized lumps at the sites of injection. These lumps reduced in size within two to three days. No systemic reaction or ill health was observed.	Product-related Site reactions such as these can occur with any injectable product.
Bordetella bronchiseptica inactivated Distemper, hepatitis, parvovirus and parainfluenza living	Subcutaneous	1	1	Nil	Within one hour of vaccination the dog started licking its feet, rubbing its muzzle and became agitated. The attending veterinarian treated the dog with an antihistamine and cortisone. The dog recovered uneventfully within the next twelve hours. The owner also noticed that the dog was unusually depressed.	Product-related Type I hypersensitivity. Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.
Combined living and inactivated viral components	Subcutaneous	1	1	Nil	Within one hour post-vaccination the dog developed bilateral periocular swelling and erythema, pruritus at the site of injection and excessive panting. The swelling and panting resolved after treatment with cortisone and antihistamine. The dog continued to appear depressed for approximately eighteen hours post-vaccination but then made complete recovery.	Product-related Type I hypersensitivity. Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.

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DOGS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Distemper, hepatitis, parvovirus and parainfluenza virus vaccine	Subcutaneous	8	3	3	Two pups started gasping for air, became blue and salivating within thirty minutes post-vaccination. A third pup showed similar signs one day later. All pups were treated with adrenalin, cortisone and antihistamine. One pup died the following day, another the following day and one was euthenased.	Possibly product-related The pathology reports for two of the pups noted that there was an underlying infectious disease present.
Fenthion	External	1	1	Nil	This dog developed generalised urticaria and oedema of the lips and ears. Signs resolved over several days.	Possibly product-related This product is the subject to an ongoing monitoring process.
Fipronil	External	1	1	Nil	The dog developed diarrhoea approximately one week after being treated with this product. The dog also began vomiting and became slightly ataxic some time later. This report was classified as possibly product-related, however the causality association was considered to be unlikely.	Possibly product-related (unlikely) Both oral and transcutaneous absorption of fipronil is very low and owing to the timing of the clinical signs (one week post-treatment), it was considered unlikely that there was a causal relationship between the use of this product and the clinical signs observed.
Fipronil	External	1	1	Nil	The dog became lethargic and went off its food within days of treatment. It then became pyrexia and developed papules and erythema over the dorsal skin of the neck and shoulders.	This report was classified as possibly product-related and may have been the result of a hypersensitivity reaction. Hypersensitivity reactions to these products have been reported to the NRA previously and as a result the label now warns against using the product if the user or animal has a known hypersensitivity to alcohol or insecticides.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

DOGS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Gentamicin, Clotrimazole, Betamethasone	External (Ear)	1	1	Nil	The dog developed ulceration of the treated ear within a few days of treatment. One week after the treatment was stopped, the ear healed.	Product-related The product label carries a warning statement that this is a potential side effect.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

DOGS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Gentamicin, Clotrimazole, Betamethasone	External	1	1	Nil	After using the treatment for seven days, the dog appeared to become deaf in one ear. The condition improved within one week of cessation of the treatment.	Possibly product-related The product label for this product states that treatment should be discontinued if hearing dysfunction occurs.
Ivermectin, Pyrantel embonate	Oral	2	1	Nil	Within twelve hours of treatment, the dog became weak in the hind legs. The owners searched the dog for a paralysis tick but did not find one. By the following day the dog had recovered. On two subsequent treatments, a similar series of events was observed.	Product-related This product is the subject to an ongoing monitoring process.
Levamisole hydrochloride, Niclosamide	Oral	3	3	Nil	All three dogs began vomiting within hours of treatment. Dogs recovered uneventfully.	Product-related The product label carries a warning statement that gastrointestinal upsets may occur after use of this product. One of the dogs was given a relatively high dose.
Melarsomine hydrochloride	Intramuscular	1	1	1	The dog was diagnosed with sub-clinical heartworm disease. The dog was treated with prednisolone for three weeks then given the recommended two doses of this product twenty-four hours apart. No pain was observed at the time of injection and the dog appeared to be fine while in the veterinary hospital. Three days post-treatment the dog developed dyspnoea, depression, bloody diarrhoea and died later in the day. The post mortem revealed adult heartworm in the right atrium of the heart and blood stained fluid throughout the gastrointestinal tract.	Product-related. A temporal relationship existed between the treatment and the development of clinical signs. It is however recognised that the prognosis of such treatments is guarded.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

DOGS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Meloxicam	Oral	1	1	1	The dog became depressed, lethargic and dyspnoeic for three to four weeks post-treatment. Fluid was present in the pleural space and lung parenchyma. A thoracic tap revealed frank blood on both sides. Blood profile indicated a regenerative anaemia. A differential diagnosis included cancer and rodenticide poisoning. The dog improved slightly with supportive treatment. The dog became anorexic and dyspnoeic again after re-treatment with anti-inflammatory some days later.	Possibly product-related The veterinarian suggested that the most probable cause of the clinical signs was neoplasia. The dog had received ibuprofen, administered by the owner prior to veterinary treatment, and also received pentosan polysulphate at the same time as NSAID treatment. The impact of concurrent treatment could not be established. In vivo studies suggest meloxicam has negligible effects on blood clotting.
Parvovirus, hepatitis, distemper and parainfluenza virus vaccine	Subcutaneous	3	3	Nil	The dog collapsed, vomited and urinated shortly after vaccination. It had an increased respiratory rate and became cyanotic. Another two puppies treated at the same time presented four hours later with swelling and pain at the sites of vaccination.	Product-related Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.
Parvovirus, hepatitis, distemper and parainfluenza virus vaccine	Subcutaneous	1	1	Nil	On the way home in the car soon after the vaccination was given the dog vomited. The dog was returned to the veterinarian and treated with an antihistamine.	Product-related Type I hypersensitivity reaction. Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

DOGS (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Parvovirus, hepatitis, distemper and parainfluenza virus vaccine	Subcutaneous	1	1	Nil	One month after the vaccination was given a firm lump was noticed at the site of injection. The lump was approximately two to three centimetres in diameter. The lump increased in size and was removed surgically after another month. Histopathological examination of the sample revealed that it was a mesenchymal tumour composed of plump spindle cells interspersed by moderate amounts of collagen. The spindle cells showed considerable variation in nuclear size and the mitotic rate was quite high in some areas.	Possibly product-related Reactions such as this have been reported previously in the veterinary literature and are rare, but unavoidable. They occur in a very small percentage of the very large number of animals that are vaccinated yearly.
Permethrin	External	1	1	Nil	The day following treatment the dog became lethargic, ataxic and depressed.	Product-related This product is the subject to an ongoing monitoring process.
Permethrin	External	1	1	Nil	The dog continued to scratch for two weeks after the product was applied. Fleas were still noticed on the dog and red circles appeared on the skin at the site of application.	Possibly product-related This product is the subject to an ongoing monitoring process.

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HORSES

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Flunixin meglumine	Intravenous	1	1	Nil	Approximately one minute after the horse was injected with this product, it staggered and flipped over backwards. It became recumbent and remained so for twenty minutes. It was non-responsive and developed moderate nystagmus. It tried twice to get up but staggered and fell. Eventually was able to get up and was disorientated for some time.	Product-related. Anaphylactoid reaction.
Penethamate hydriodide	Intramuscular	1	1	Nil	Immediately after the injection was given the pony collapsed into lateral recumbency and began to thrash in tetanic spasms. The thrashing lasted for two to three minutes. The pony then recovered within five minutes.	Product-related Anaphylactoid reaction. This is the only report the NRA has on record of this type of report for this product, so it would appear to be a very rare and unusual, however unavoidable reaction.
Permethrin	External	4	1	Nil	A superficial corneal ulcer developed within hours of treatment with this product.	Product-related As a result of this a change was made to the label of this product to emphasise the need to take care when applying the product on the head.
Procaine penicillin	Intramuscular	1	1	Nil	The owner reported that the horse developed excitation and incoordination within one minute of injection.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.

HORSES (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Procaine penicillin	Intramuscular	1	1	Nil	Within thirty seconds of administration the horse reacted violently, running around the box and thrashing around the floor. The reaction lasted one to two minutes.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.
Procaine penicillin	Intramuscular	1	1	1	Within seconds of administration the horse developed severe signs of excitation such as running around the stable, collapsing and thrashing around the floor. The reaction lasted only a few minutes.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.
Procaine penicillin	Intramuscular	1	1	1	This horse died after fracturing its skull when thrashing around the stable after being treated with this product.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.
Procaine penicillin	Intramuscular	1	1	Nil	Central nervous system stimulation occurred soon after treatment and lasted approximately two minutes.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.
Procaine penicillin, Benzathine penicillin	Intramuscular	1	1	1	Within two minutes of treatment the horse began to stumble, collapsed and had convulsions. It also developed dyspnoea. Within one minute the heart stopped. The post mortem results revealed a profuse, frothy nasal discharge and dark red patches in the lungs.	Product-related It is recognised that these types of excitation reactions can occur in a small percentage of horses treated with products containing procaine penicillin.

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HORSES (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Propantheline bromide	Intravenous	5	3	Nil	Five mares were brought in from the paddock singularly or in pairs, treated, examined and returned to paddock. Temperature approximately 32° Celsius. The mares appeared normal when returned to paddock. Within hours the three nursing mares had developed colic and vulval swellings. The two dry mares were not affected.	Product-related The product label carries a warning statement that this is a potential side effect.
Trimethoprim, Sulfadiazine	Intravenous	1	1	1	The horse died soon after treatment with this product. The pathology results were consistent with anaphylaxis.	Product-related There is a clear temporal relationship between the use of this product and the clinical signs observed. The pathology findings are also consistent with anaphylaxis.
Xylazine	Intravenous	1	1	Nil	Approximately thirty seconds after intravenous administration of this product, the horse began to toss its head in the air, followed by rearing up and throwing itself over backwards, violently thrashing all four legs and throwing head. Approximately 1-2 minutes after this it began to stagger to its feet and was reluctant to move. Following this was apparently normal sedation.	Product-related It is possible that the reaction was related to intra-carotid injection, however we recognise that these types of reactions have occurred after intra-venous injection of xylazine products as well.

HORSES (cont.)

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Xylazine hydrochloride	Intravenous	1	1	Nil	This product was given intravenously into the right metacarpal vein using fine gauge needle. Some of the product went perivascularly. A swelling developed shortly after the injection was given and oedema of the leg from the mid cannon region to the hoof was present within a few hours.	The cause of the swelling in the leg was most likely to have been as a result of a haematoma after leakage from the punctured vein.

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SHEEP

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Diazinon	External	1600	320	240	Seven days later many of the lambs experienced severe blow fly strike, particularly on the shoulders. Approximately two hundred and forty lambs died.	Based on this report and other similar reported adverse experiences the label directions for ovine ectoparasiticides will be re-evaluated. The findings of this will be used to improve the label directions for use of these products.
Diflubenzuron	External	488	488	34	Four hundred and eighty-eight sheep were treated with a product containing diflubenzuron to control lice and blowflies. The farmer noticed that the applicator gun was not working properly and that the product did not spray out over the backs of the sheep as expected. Some of the sheep were noticed to have lesions along their back lines at the site of application approximately one month post-treatment.	Product-related Although this was classified as product-related it highlights the need to ensure all equipment used when treating animals in such situations is working properly and effectively
Diflubenzuron	External	2500	12-15	Nil	A small proportion of the treated lambs developed lumpiness in the wool on the back line. This report was classified as possibly product-related but other factors may have been involved in causing this (such as skin infections unrelated to the use of the product).	Possibly product-related This product is the subject to an ongoing monitoring process.
Diflubenzuron	External	3300	495	Nil	A small proportion of the treated lambs developed scabs in the wool on the back line. This report was classified as possibly product-related but other factors may have been involved in causing this (such as skin infections unrelated to the use of the product).	Possibly product-related This product is the subject to an ongoing monitoring process.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

SHEEP

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Levamisole hydrochloride, Albendazole oxide	Oral	420	3	3	A very small proportion of the treated sheep showed signs (within 10-20 minutes of treatment) of head shaking, lip licking, salivation, frothing at the mouth, muscle tremors, agitation and three sheep died.	Possibly product-related Many environmental factors may have contributed to these problems such as extreme temperatures and stress factors involved with mustering and handling.
Levamisole hydrochloride, Oxyclozanide	Oral	660	5	4	A very small number of sheep treated developed signs of muscle tremors, agitation and died soon after treatment.	Product-related This product is the subject to an ongoing monitoring process.

5 SECTION 5

5.1 Summary of Suspected adverse experience reports 2000 – Lack of Efficacy Category

All reports of lack of efficacy received in 2000 are presented in this appendix that have been classified as product-related or possibly-product-related.

As stated for the previous category, this summary table is intended only to provide general information about the types of reactions that veterinarians, animal owners and others have voluntarily reported to the NRA or the manufacturer after use of the product. The information in the tables is not by itself a basis for determining the safety and efficacy of a given product or for comparing one product with another, nor can it be used to predict the frequency of occurrence of a reaction.

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BIRDS

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Avian encephalomyelitis	NR	NR	NR	Nil	Birds were vaccinated at twelve weeks of age. Four weeks later, serological testing (ELISA) failed to detect antibodies. This test is used by the farmer and has demonstrated sero-conversion previously and since. No details were provided regarding storage or transportation of vaccine.	Possibly product-related This product is the subject to an ongoing monitoring process.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

CATS

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Selamectin	External	1	1	Nil	The mother was treated twice with this product for an ear mite infestation. The attending veterinarian reported that the ear mites had resolved within a week. She was subsequently re-infected by her own kittens. The kittens could not be treated until six weeks of age. The owner was informed that the product would be effective after fourteen days. The kittens were born three weeks after their mother was treated. Subsequently when the owner treated the kittens there were no instructions about how to or whether to prevent their mother licking the product once it had been applied to the kittens. The owner isolated the kittens from their mother for approximately nine hours.	Possibly product-related This product is the subject to an ongoing monitoring process.

DOGS

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Oxantel embonate, pyrantel embonate, praziquantel	Oral	10	10	2	Pups were treated with this product at eight and ten weeks of age. The pups were found to be very weak soon after treatment and were taken to a veterinarian. Parvovirus was diagnosed. Two of the pups died before presentation and faecal material from these pups was found to have substantial numbers of hookworm eggs. Faecal material taken from the pups in the clinic showed no such infestation.	Possibly product-related This product is the subject to an ongoing monitoring process.

National Registration Authority for Agricultural and Veterinary Chemicals, Australia

SHEEP

Active constituent	Route of administration	No. Treated	No. Affected	No. Died	Reported Adverse Experience	Classification and comments
Triflumuron	External	4200	NR	NR	Sheep were treated immediately after shearing. Approximately four months later the owner noticed considerable numbers of sheep affected by lice. Wool samples were taken and owner advised that the concentration of active in the wool was insufficient to control lice.	Possibly product-related This product is the subject to an ongoing monitoring process.
Albendazole	Oral	441	441	43	A total of four hundred and forty-one fine wool merino weaners were treated with this product. The flock developed clinical signs of scouring, weight loss, lethargy and forty-three sheep died.	Product-related As a result of this incident, the registrant of this product has been requested to consider a change in the label directions particularly those relating to anthelmintic resistance.

REFERENCES

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2. Toxicology, edited by Gary D. Osweiler 1996, Williams & Wilkins.
3. Saunders Comprehensive Veterinary Dictionary Second Edition, edited by D.C. Blood & V.P. Studdert 1999, WB Saunders.
4. The National Registration Authority for Agricultural and Veterinary Chemicals. Report of Adverse Experiences 1997 and 1998.

GLOSSARY AND ABBREVIATIONS

Analgesic	pain relieving treatment
Anaphylaxis/ anaphylactic	an exaggerated allergic reaction of an animal to a foreign protein or other substances
Anthelmintic	an agent destructive to worms
Antimicrobial agent	an agent that kills micro-organisms or suppresses their multiplication or growth
Ataxic	unsteady walking action due to muscular incoordination
Colic	a general term for abdominal pain
Cyanotic	blue discolouration of the mucous membranes and other tissues due to a lack of circulating oxygen in the blood
Erythema	abnormal redness of the skin due to local congestion, as in inflammation
Folliculitis	inflammation of the follicles
Hypersalivation	excessive salivation
Hypersensitivity	an excessive reaction to an allergen
Intramammary	within or into the mammary gland
Oedematous	abnormal accumulation of fluid in body cavities and under the skin
Parasiticide	an agent that is destructive to parasites
Parvovirus	viral infection of dogs that is characterised by diarrhoea, dehydration and pyrexia
Pruritus	irritation and itching
Pyrexia	animal suffering from a high fever
Registrant	the commercial party which according to the national legislation is legally responsible for the marketing of the product
Urticaria	vascular reaction of the skin as a result of contact with a chemical or may be immunologically based
Withholding period	the time interval after the withdrawal of a drug from the treatment of an animal before the animal or its products can be used for human food