Overview of suspected adverse reactions to veterinary medicinal products reported in South Africa (March 2001 – February 2002)

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ABSTRACT

An overview of reports of suspected adverse drug reactions received by the Veterinary Pharmacovigilance and Medicines Information Centre during the period March 2001 to February 2002 is given. A total of 77 reports were received. The majority of reports involved suspected adverse reactions that occurred in dogs and cats. Most products implicated in the reports were Stock Remedies. The products were predominantly administered either by veterinarians or trained paraveterinary professionals. Although the majority of reports were received from veterinary pharmaceutical companies, the proportion of reports received directly from veterinarians increased compared with previous years.

Key words: spontaneous reports, suspected adverse drug reactions, veterinary medicinal products, veterinary pharmacovigilance.

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INTRODUCTION

Veterinary medicinal products in South Africa are currently registered under two Acts and are administered by two separate regulatory authorities:

- The Medicines and related Substances Control Act, 1965 (Act No. 101 of 1965), administered by the National Department of Health. These products are called Veterinary Medicines.
- The Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act 36 of 1947) administered by the National Department of Agriculture. These products are called Stock Remedies.

Veterinary Medicines are grouped into various schedules (unscheduled – Schedule 9) based on their safety, use and habit-forming potential[2]. Unscheduled medicines and Stock Remedies are over the counter products and are legally available directly to the public from any retail outlet. Pharmacists may supply any medicine up to Schedule 2 and Stock Remedies directly to clients for use in animals without a veterinary prescription. A veterinary prescription is required for all other scheduled substances[2].

Adverse drug reactions are addressed in both Acts. It is obligatory for Registration Holders (pharmaceutical companies with registered veterinary medicinal products) to forward to the registrar reports of suspected adverse reactions of products registered under Act 36/47 that come to their attention. The regulations of Act 101/65 pertaining to adverse drug reactions (Regulation 12 (3) (a) to (j)) have been recently reviewed and expanded to include veterinary medicines.

The Veterinary Pharmacovigilance and Medicines Information Centre was established on an informal basis within the Section of Pharmacology of the Faculty of Veterinary Science, University of Pretoria, South Africa, in 1998. A formal system of recording reports was implemented in 2000. Since then, the Centre's role in the monitoring of adverse drug reactions to veterinary medicinal products has grown and a new data-capture and retrieval programme is currently being implemented to better manage the increasing number of reports. One of the Centre's main functions is to record spontaneous reports of suspected adverse drug reactions on behalf of both regulatory authorities. This paper presents an overview of the reports of suspected adverse drug reactions received by the Centre during the period March 2001 to February 2002.

MATERIALS AND METHODS

The Veterinary Pharmacovigilance and Medicines Information Centre relies on spontaneous reports of suspected adverse drug reactions. Reporting is voluntary and reports may be received from veterinarians, paraveterinary professionals, pharmacists and the general public. Legally, Registration Holders are required to submit all reports of suspected adverse drug reactions that come to their attention to the relevant regulatory authority. These are then recorded in the computerised database of the Veterinary Pharmacovigilance and Medicines Information Centre.

Reporters are requested to complete and submit a form (Appendix A in ref. 1), which is published in the Index of Veterinary Specialities (IVS). Reports can also be faxed or e-mailed on request. Upon receipt, each report is marked with a date and given a sequential number. The minimum information required to appear on each report is: an identifiable source (name and contact details of reporter), animal details (species, sex, age), suspected product (name and/or registration number) and reaction details. If some of this information does not appear on the report, the reporter is contacted and requested to submit these details.

Reports that contain all the above-mentioned information are entered into a computerised database. Thereafter, it is presented at the next meeting of the Veterinary Pharmacovigilance Working Group (constituted by staff members of the Department of Pharmacology and Toxicology, Faculty of Veterinary Science). At these meetings, which are held weekly, each report received since the previous discussion is evaluated and assigned a causality classification (Table 1).

Reports are then forwarded to the relevant regulatory authority together with an evaluation and recommendation. The Registration Holder is also informed of any report of a suspected adverse reaction to one of their products, which they have not submitted themselves.

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Table 1: **Criteria used for assigning causality.**

Causality classification	Criteria
Certain	There is a plausible time relation between the administration and the adverse event, which cannot be explained by the concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (de-challenge) is clinically plausible and the event is definitely pharmacological or phenomenological, using a satisfactory rechallenge procedure if necessary.
Probable	There is a plausible time relationship between the administration of the drug and the adverse event, unlikely to be attributed to concurrent disease or other drugs or chemicals and which follow a clinically reasonable response on withdrawal. A positive re-challenge is not required to fulfil this definition.
Possible	There is a plausible time relationship between the administration of the drug and the adverse event, but the event could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.
Unlikely	An adverse event with a temporal relationship to drug administration that would make a casual relationship improbable and for which other drugs, chemicals or underlying disease provide a plausible explanation.

RESULTS

The Veterinary Pharmacovigilance and Medicine Information Centre received 77 reports of suspected adverse drug reactions from March 2001 to February 2002. These reports are summarised and classified according to the species in which the reactions occurred (Table 2), the registration of the implicated products under current South African legislation (Table 3), the person administering the implicated product to the animal (Table 4) and the source of the report submitted to the Veterinary Pharmacovigilance and Medicines Information Centre (Table 5). These results are compared with those of previous years.

Table 2: **Reports of suspected adverse drug reactions received for the periods March 2001 – February 2002 and January 1998 – February 2001 classified according to species.**

Species	March 2001 – February 2002 (n = 77)		January 1998 – February 2001 (n = 57)	
	Number of reports	Percentage	Number of reports	Percentage
Canine	31	40	19	33
Feline	21	27	15	26
Bovine	15	19	7	12
Equine	6	8	2	4
Ovine/caprine	2	3	6	11
Poultry	2	3	4	7
Porcine	0	0	3	5

DISCUSSION AND CONCLUSIONS

There was an increase in the number of reports received by the Veterinary Pharmacovigilance and Medicines Information Centre during the period March 2001 to February 2002 compared with previous years (increased from 57 over 3 years to 77 reports over 1 year). This could be attributed to an increased awareness of the Centre's activities. As in previous years, the majority of reports received pertained to those products used in either small animal medicine or surgery[1].

Trained veterinarians or paraveterinary professional persons administered most drugs. Some reports were received of suspected adverse reactions following treatment that was rendered to animals by owners, who had not consulted a veterinarian. Current legislation allows owners direct access to some potentially toxic drugs with narrow margins of safety. Proper client education on potential side-effects may enhance the prudent use of these drugs.

There was a decline in the proportion of reports received directly from the pharmaceutical industry (decreased from 56 % to 38 % of reports). The legal requirement for pharmaceutical companies to submit reports to the regulatory authorities is not currently being enforced under the Medicines and related Substances Control Act (Act 101 of 1965) and companies may be hesitant to forward reports to the Centre if there is a possibility that opposition companies do not comply. It can also be speculated that an increased awareness of the Centre and its function amongst members of the veterinary profession has led veterinarians to report suspected adverse reactions directly to the Centre and not the Registration Holders.

The majority of products implicated in the reports were registered as Stock Remedies under Act 36 of 1947. The proportion of reports of suspected adverse reactions to products used extra-labelly (*i.e.* not registered for use in animals) increased from 7% for the period January 1998 – February 2001 to 13% for the period March 2001 – February 2002. The reason

Table 3: **Comparison of the registration of products implicated in reports of suspected adverse drug reactions for the periods March 2001 – February 2002 and January 1998 – February 2001.**

Product registration	March 2001 – February 2002 (n = 114)		January 1998 – February 2001 (n = 59)	
	Number of products	Percentage	Number of products	Percentage
Stock Remedies (Act 36/47)	58	51	34	58
Veterinary Medicines (Act 101/65)	41	36	21	35
Products used extra-labelly (Act 101/65)	15	13	4	7

for this could be that a larger proportion of the reports were received directly from veterinarians and not from pharmaceutical companies. Documentation of adverse reactions following the extra-label use of products can contribute toward the safer use of these products in animals.

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Table 4: **Reports of suspected adverse drug reactions received for the periods March 2001 – February 2002 and January 1998 – February 2001 classified according to persons administering the drugs.**

Person administering drugs	March 2001 – February 2002 (*n* = 77)		January 1998 – February 2001 (*n* = 57)	
	Number of reports	Percentage	Number of reports	Percentage
Veterinarian	47	61	31	54
Owners	23	30	24	42
Other	5	6	2	4
Paraveterinary professional	2	3	0	0

Table 5: **Reports of suspected adverse drug reactions received for the periods March 2001 – February 2002 and January 1998 – February 2001 classified according the origin of the report submitted to the Veterinary Pharmacovigilance and Medicines Information Centre.**

Person submitting report	March 2001 – February 2002 (*n* = 77)		January 1998 – February 2001 (*n* = 57)	
	Number of reports	Percentage	Number of reports	Percentage
Pharmaceutical company	29	38	32	56
Veterinarian	28	36	18	32
Paraveterinary professional	12	16	0	0
Veterinary specialist	7	9	5	9
Others	1	1	2	3