Overview of suspected adverse reactions to veterinary medicinal products reported in South Africa (March 2002 – February 2003)

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ABSTRACT

The Veterinary Pharmacovigilance and Medicines Information Centre is responsible for the monitoring of veterinary adverse drug reactions in South Africa. An overview of reports of suspected adverse drug reactions received by the centre during the period March 2002 to February 2003 is given. In total, 40 reports were received. This had declined from the previous year. Most reports involved suspected adverse reactions that occurred in dogs and cats. Most of the products implicated were Stock Remedies. The animal owner predominantly administered these products. Only 1 report was received from a veterinary pharmaceutical company. Increasing numbers of reports are being received from veterinarians.

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 2 Acts and are administered by 2 separate regulatory authorities:

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

Adverse drug reactions are addressed in both Acts. It is obligatory for Registration Holders (pharmaceutical companies with registered Stock Remedies) 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 (Regulations 34 and 37 of Act 90 of 1997) have been reviewed recently and have been expanded to include veterinary medicines (veterinary medicines were not included for the current period 2002–2003).

The Veterinary Pharmacovigilance and Medicines Information Centre was established on a formal basis within the Section of Pharmacology of the Faculty of Veterinary Science, University of Pretoria, in 2000. The Centre's role is to monitor adverse drug reactions to veterinary medicinal products in South Africa. The data-capture system makes use of Sentinel- Vet[†], a system developed and utilised by the French regulatory authority. 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 2002 to February 2003.

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, the general public, medical practitioners and Registration Holders.

Reporters are requested to complete and submit a form, which is published in the Index of Veterinary Specialities (IVS). Reports can also be faxed or e-mailed. Upon receipt, each report is provided with a date and given a sequential number. The minimum information to be provided in 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 asked to submit futher details.

Reports that contain all the above-mentioned information are entered into a computerised database. Thereafter the report is presented at the next meeting of the Veterinary Pharmacovigilance Working Group. At these meetings, 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 that they have not submitted themselves.

RESULTS

The Veterinary Pharmacovigilance and Medicine Information Centre received 40 reports of suspected adverse drug reactions for the period March 2002 to February 2003. These reports are summarised and classified according to the species in which the reactions occurred (Table 2), the registration of the implicated product under current South African legislation (Table 3), the person that administered 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[2]. Active ingredients implicated for the current period are also summarised by causality, and classified by the species in which the reactions occurred (Tables 6–10).

DISCUSSION AND CONCLUSIONS

There was a marked decrease in the number of reports received by the Veterinary Pharmacovigilance and Medicines

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[†]Sentinel-Vet® is a high-performance database, specifically prepared for veterinary pharmacovigilance. The program manages cases, assists the decision-making process and facilitates epidemiological studies.

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 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 re-challenge 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 meet 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 causal relationship improbable, and which other drugs, or chemicals or underlying disease provides plausible explanation.

Table 2: **Reports of suspected adverse drug reactions received for the periods March 2002 – February 2003 and March 2001 – February 2002 classified according to species.**

Species	March 2002 – February 2003 (*n* = 40)		March 2001 – February 2002 (*n* = 77)		Two-year total (*n* = 117)
	Number of reports	Percentage	Number of reports	Percentage	
Canine	25	62.5	31	40	56
Feline	6	15	21	27	27
Bovine	3	7.5	15	19	18
Equine	2	5	6	8	8
Ovine/caprine	2	5	2	3	4
Poultry	1	2.5	2	3	3
Human	1	2.5	0	0	1

Information Centre during the period March 2002 to February 2003 compared to the previous year (decreased from 77 reports to 40). As in previous years, most reports concerned products used either in small animal medicine or surgery[1,2].

Most of the reports also implicated products registered as Stock Remedies under Act 36 of 1947. These increased from 51 % to 62 % during the period under review.

During current period, animal owners administered most of the drugs, followed closely by veterinarians. The number of reports of adverse drug reactions to medicines administered by owners increased from the previous period (30 % to 50 %). It is still of concern that products to which owners have direct access, are frequently reported as causing adverse reactions. Client education to increase awareness of potential side-effects should remain a high priority.

There was a marked decrease in the

Table 3: **Comparison of the registration of products implicated in reports of suspected adverse drug reactions for the periods March 2002 – February 2003 and March 2001 – February 2002.**

Product registration	March 2002 – February 2003 (*n* = 58)		March 2001 – February 2002 (*n* = 114)		Two-year total (*n* = 172)
	Number of products	Percentage	Number of products	Percentage	
Stock Remedies (Act 36/47)	36	62	58	51	94
Veterinary Medicines (Act 101/65)	11	19	41	36	52
Product used extra-label	11	19	15	13	26

Table 4: **Reports of suspected adverse drug reactions received for the periods March 2002 – February 2003 and March 2001 – February 2002 classified according to persons that administered the drugs.**

Person administering	March 2002 – February 2003 (*n* = 40)		March 2001 – February 2002 (*n* = 77)		Two-year total (*n* = 117)
Drugs	Number of reports	Percentage	Number of reports	Percentage	
Veterinarian	16	40.0	47	61	63
Owner	20	50.0	23	30	43
Other	3	7.5	5	6	8
Paraveterinary professional	1	2.5	2	3	3

Table 5: **Reports of suspected adverse drug reactions received for the periods March 2002 – February 2003 and March 2001 – February 2002 classified according to the origin of the report submitted to the Veterinary Pharmacovigilance and Medicines Information Centre.**

Person submitting report	March 2002 – February 2003 (n = 40)		March 2001 – February 2002 (n = 77)		Two-year total (n = 117)
	Number of reports	Percentage	Number of reports	Percentage	
Pharmaceutical Company	1	2.5	29	38	30
Veterinarian	35	87.5	28	36	63
Paraveterinary professional	1	2.5	12	16	13
Veterinary specialist	1	2.5	7	9	8
Other	2	5	1	1	3

Table 6: **Active ingredients implicated in dogs.**

Active ingredient	Number of reports	Certain	Probable	Possible	Unlikely	Unclassifiable
Atropine	1		1			
Carprofen	4	1	2	1		
Complementary remedies	2					2
Cypermethrin	1		1			
Diminazene	7			7		
Doramectin	2			2		
Ethinyl oestradiol	1		1			
Lufenuron	1				1	
Meloxicam	3		3			
Piperonyl butoxide	1		1			
Piroxicam	2		2			
Potentiated sulphonamides	1		1			
Praziquantel	1				1	
Prednisolone	3			1	2	
Viral antigens	12		4	8		
Xylazine	1	1				

number of reports submitted by the pharmaceutical industry (from 38 % to 2.5 %). During the preriod under review, pharmaceutical companies were not legally bound to submit reports to the Medicines Control Council. With current amendments to Act 101/65, companies will in future be required to submit reports to the Pharmacovigilance Centre. A contributory factor to the low submission rate could have been the perception that the centre may provide negative publicity for a particular product and/or company. Such a written complaint was filed by a pharmaceutical company. It must be noted, however, that the registered names of products and company details are treated with strict confidentiality.

As mentioned above, a separate governmental body administers Act 36/47. According to the Act, companies are obliged to submit all reports of adverse drug reactions to the registrar of the Act. Thus, it is not necessary for pharmaceutical companies to submit these reports *via* the Pharmacovigilance Centre.

The number of reports submitted by

Table 7: **Active ingredients implicated in cats.**

Active ingredient	Number of reports	Certain	Probable	Possible	Unlikely	Unclassifiable
Levamisole	1			1		
Methoprene	3				3	
Niclosamide	1			1		
Permethrin	2		2			
Praziquantel	3		3			
Pyrantel pamoate	3		3			
Viral antigens	1			1		

Table 8: **Active ingredients implicated in cattle.**

Active ingredient	Number of reports	Certain	Probable	Possible	Unlikely	Unclassifiable
Closantel	1				1	
Manganese	1				1	
Moxidectin	1		1			
Viral antigens	1				1	
Vitamin A	1		1			
Zeranol	1				1	
Zinc	1				1	

Table 9: **Active ingredients implicated in horses.**

Active ingredient	Number of reports	Certain	Probable	Possible	Unlikely	Unclassifiable
Anica	1		1			
Camphor	1		1			
Eucalyptus oil	1		1			
Menthol	1		1			
Methyl salicylate	1		1			

Table 10: **Active ingredients implicated in sheep.**

Active ingredient	Number of reports	Certain	Probable	Possible	Unlikely	Unclassifiable
Ivermectin	1			1		
Viral antigens	2		2			

veterinarians in the field has increased (from 36 % to 87 % during the current period). It is hoped that this trend will continue. In the interest of patient safety, I appeal to the profession to increasingly make use of the services provided by the centre.

The number of reports of suspected adverse reactions following the extra-label use of products (*i.e.* not registered for use in animals) has also increased, from 13 % to 19 %. The could be ascribed to the larger number of reports submitted by veterinarians rather than by pharmaceutical companies. During the period under review, the pharmaceutical industry was not legally bound to submit such reports, but the amended legislation will oblige companies to report adverse drug reactions following extra-label drug use. The aim of this amendment is to increase general awareness of drug reactions following such use of human medical products, and would would hopefully lead to enhanced safety in both humans and animals.

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