



**QUANTITY OF ANTIMICROBIAL PRODUCTS SOLD
FOR VETERINARY USE IN AUSTRALIA
1999/2000 - 2001/2002**

**THERAPEUTIC/PROPHYLACTIC, GROWTH PROMOTANTS
AND ANTICOCCIDIAL PRODUCTS**

**Australian Pesticides &
Veterinary Medicines Authority**

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QUANTITY OF ANTIMICROBIAL PRODUCTS SOLD FOR VETERINARY USE IN AUSTRALIA 1999/2000 - 2001/2002

Introduction

The emergence and spread of antimicrobial resistance has led to increasing Australian and international concerns about the use of antimicrobial products in humans, and animals. As a result of these concerns the Australian Government established in 1998 the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) to review the scientific evidence of the link between:

- the use of antibiotics in food-producing animals
- the emergence and selection of antibiotic-resistant bacteria
- their spread to humans, and
- to make evidence-based recommendations to Government for the appropriate future management of antibiotic use in food-producing animals.

The JETACAR report was released in September 1999. It highlighted the need for a coordinated and balanced approach to better manage the use of antimicrobials in humans and food-producing animals in Australia. The recommendations from the report formed the basis of an Australian antimicrobial resistance management (AMR) strategy. An important facet of this strategy is the collection of information on the quantity of antimicrobial products used in veterinary medicine and animal production in Australia. The quantity of antimicrobial used (or antimicrobial load) is one of four factors identified by JETACAR that influence the emergence and spread of antimicrobial resistance.

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government authority responsible for the registration of pesticides and veterinary medicines and their regulation up to and including the point of retail sale. The APVMA has contributed to the AMR strategy in a number of ways including the collection of information from registrants on the quantity of veterinary antimicrobial products sold in Australia in the period from 1999/2000-2001/2002. This information was voluntarily supplied by registrants (see Appendix 1).

There was incomplete reporting of the quantity of sales in 1999/2000 and 2000/2001. This incomplete reporting gives the impression, possibly erroneous, of considerable increase in the quantity of antimicrobials sold during 2001/2002. Hence the figures presented in this report should only be regarded, as indicative of overall trend in the quantity of sales for each individual period.

It is intended that this information will be collected annually, and will be used as a "baseline" which could assist regulatory authorities to:

- monitor changes in the overall use of antimicrobial products
- relate these to changes to antimicrobial resistance
- identify where reviews of prescribing practices might be appropriate and
- respond in a precise and targeted way.

1. Antimicrobial imports to Australia 1999/2000-2001/2002

All antimicrobials used in Australia must be imported because no antimicrobials are manufactured in Australia. Antimicrobials are prohibited imports under Customs legislation. Consequently, all antimicrobial active ingredients and formulated product imports require an import permit, issued by the Office of Chemical Safety of the Therapeutic Goods Administration (TGA). Information on the importation quantity of antimicrobials into Australia for the financial years 1999/2000 to 2001/2002 is set out in Table 1.

Table 1: Antimicrobial active ingredients (tonnes active ingredient) imported into Australia 1999/2000-2001/2002

	1999/2000	2000/2001	2001/2002
Total antimicrobials imported for veterinary use*	552	407	540

*Source Office of Chemical Safety antimicrobial permit statistics

2. Total quantity of sales of veterinary antimicrobials

The total quantity of antimicrobial products (in tonnes of active ingredient) sold in Australia in 1999/2000-2001/2002 is set out in Table 2. Table 2 shows that for each year under review approximately 36%-41% of the antimicrobials sold for use in food producing animals were for therapeutic/prophylactic purposes. Similarly, growth promotants accounted for 40%-43% whilst anticoccidial products represented 18%-21%. The proportion of antimicrobials used in non-food producing animals during this period remained stable at around 3% of the total quantity.

Table 2. Total quantity of sales (active ingredient in tonnes) of veterinary antimicrobials-therapeutic/prophylactic, growth promotants and anticoccidial products 1999/2000-2001/2002

	Analogues of human significance*	Quantity in tonnes		
		1999/2000	2000/2001	2001/2002
Therapeutic/prophylactic antimicrobials- food producing animals	Yes	154	159	172.5
	No	7	16.5	26.5
Growth promotants	Yes	0	8.5	15.5
	No	157	191	217.5
Total therapeutic/prophylactic and growth promotants - food producing animals		318	375	432
Anticoccidial products	No	71	100	115
Total antimicrobials -food producing animals		389	475	547
Therapeutic antimicrobials - non-food producing animals**	Yes	14	16	15
Total antimicrobials - food producing animals and non-food producing animals		403	491	562

* Analogue of human significance: Where a similar antimicrobial drug is used in humans and rated in the EAGAR document Importance Rating and Summary of Antibiotic Use in Humans in Australia to be of high/medium importance in human therapy

** Horses, dogs, cats

Anticoccidial products are antimicrobials used in the treatment and prevention of diseases caused by certain protozoa, especially Eimeria species in poultry. All the

antimicrobials used as anticoccidial products in food producing animals in Australia during the period in review are for animal use and have no human application.

Table 2 also shows that most of the current antimicrobials used as growth promotants and as anticoccidial products have low to nil importance in human therapy according to the National Health and Medical Research Council's (NHMRC) Expert Advisory Group on Antimicrobial Resistance (EAGAR) antimicrobial ratings. A high EAGAR rating means that the impact of human pathogens which have antimicrobial resistance is high, as there are few alternative antimicrobial drugs.

There are several limitations in the collection and analysis of antimicrobial sales data. For example the figures do not take into account the relative potencies of the different active ingredients. In some instances as much as ten times the amount of one antimicrobial may be required to treat the same disease when compared with an equally efficacious alternative. In this document no correction is made for differences in potency (or intrinsic activity) between the various antimicrobials.

Secondly, for those antimicrobials with dual indications of use such as growth promotion and therapeutic/prophylactic uses, where the applicant did not provide the actual quantity used for each indication, an assumption was made that the quantity sold were divided evenly between the two uses. However, advice from veterinary experts in the poultry industry indicates that the main use of these products is for the control of necrotic enteritis caused by *Clostridium perfringens* in poultry.

Another area of limitation was assigning antimicrobial quantity where the product is used in food producing and non-food producing animals. In these situations, the assumption made was that three quarters of the quantity was assigned to food producing animals and the rest to non-food producing animals.

There was incomplete reporting of the quantity of sales in 1999/2000 and 2000/2001. This incomplete reporting gives the impression, possibly erroneous, of considerable increase in quantity of sales during 2001/2002. Consequently, the figures presented in this report should only be regarded, as indicative of overall trends in the quantity of sales and it is important that the figures are not misinterpreted.

3. Livestock in national herd

The table below (Table 3) shows the number of food producing animals recorded by the Australian Bureau of Statistics (ABS) for each of the three reporting years. All figures are quoted in thousands of animals.

Table 3. Numbers of livestock in the national herd (000s) Australia 1999/2000-2001/2002

	1999/2000	2000/2001	2001/2002
Cattle and calves	27,588	27,722	27,870
Sheep and lambs	118,600	110,930	106,170
Pigs	2,511	2,748	2,940
Poultry	401,600	397,200	428,200

Source Australian Bureau of Statistics

The ABS statistics shows that between 1999/2000 to 2001/2002 pigs recorded 17% increase in number, and poultry increased in number by 7%. Cattle number showed a modest increase of 1% whilst sheep recorded a 10% drop in number. The pigs and poultry production increase corresponds to the trend in sales of antimicrobials during this period. This may account for some of the increase in antimicrobial sales reported, since most of the antimicrobials used in food producing animals are primarily used in intensive animal production.

The National Residues Survey which monitors chemical residues in meat (beef, sheepmeat and pork) and grains with smaller programs for fish, poultry, honey etc reported that during the period under review, more than 99.5% of the meat samples tested complied with the maximum residues limit for antimicrobials used in food producing animals.

4. Therapeutic/prophylactic antimicrobials used in food producing animals

The quantity of sales for various groups of therapeutic/prophylactic antimicrobial products used in food producing animals from 1999/2000-2001/2002 is set out in Table 4. The table shows that two antimicrobial classes have analogues of human clinical significance, comprising the β -lactams, and lincosamides. EAGAR rates their importance in human therapy as either medium or low. Streptogramins used in animals are not currently included in the EAGAR rating because they are not used in humans. However, streptogramins have an analogue of human significance and consequently their use in food producing animals is now restricted to veterinary prescription only. β -lactams, lincosamides and streptogramins annually accounted for between 12%-25% of the total therapeutic/prophylactic antimicrobial products sold during the period under review.

Table 4: Quantity (active ingredient in tonnes) of sales of antimicrobials used for therapeutic/prophylactic purposes in food producing animals 1999/2000-2001/2002 (Anticoccidial products not included)

Antimicrobial class	EAGAR Rating*	Quantity in tonnes		
		1999/2000	2000/2001	2001/2002
Tetracyclines	Low	55	55	52
Polypeptides	-	34	32	42.5
β -lactams	Medium/Low	18	23	32
Macrolides	-	24	27	25
Streptogramins	-	0	8.5	15.5
Trimethoprim/Sulphonamides	Low	15	16	15
Aminoglycosides	Low	5	4	4
Lincosamides	Medium	2	2	2
Others**	-	8	8	9
TOTAL		161	175.5	199

* Rating of importance of antimicrobial agent in human therapy by the EAGAR document: Importance Rating and Summary of Antibiotic Use in Humans in Australia to be of high/medium importance in human therapy

** Others= ionophores, novobiocin and thiostreptan, tiamulin fumarate

0 No amount reported or <100kg

- Not rated

Tetracyclines, macrolides, trimethoprim/sulphonamides and β -lactams together accounted for approximately 62-70%% of the quantity of sales of therapeutic/prophylactic antimicrobials each year, with tetracycline sales accounting for between 26%-34% of the total amount. The quantity of sales of tetracyclines, macrolides and trimethoprim/sulphonamides saw modest changes during the period under review while β -lactams increased in sales by 78%.

5. Quantity of sales of antimicrobials used as growth promotants

A summary of the quantity of antimicrobials sold as growth promotants for use in poultry, pigs and beef cattle between 1999/2000-2001/2002, is provided in Table 5. All the growth promotants used in Australia during this period have low to no significance in human therapy except streptogramins, which have analogues of human significance.

Table 5: Quantity (active ingredient in tonnes) of sales of antimicrobials used as growth promotants in food producing animals) 1999/2000-2001/2002

Antimicrobial class	Quantity in tonnes		
	1999/2000	2000/2001	2001/2002
Ionophores	78	120	138
Quinoxalins	24	15	15
Macrolides	14	14	11
Others **	41	50.5	69
TOTAL	157	199.5	233

** Others= Roxarsone, Aminoglycoside, Bambermycin, Polypeptides, Streptogramins, Everninomicin
0 No amount reported or <100kg

There was incomplete reporting of the quantity of sales of growth promotants in 1999/2000 and 2000/2001. For example, there were no sales figures reported for streptogramins in 1999/2000 and ionophores sales were considerably lower than in subsequent years.

More than half of the quantity of antimicrobials sold as growth promotants are not related to any antibiotic used in human therapy. These antimicrobials include ionophores (monensin, narasin, salinomycin, lasalocid sodium), olaquinox avilamycin and roxarsone.

6. Quantity of sales by major route of administration

The quantity of sales of therapeutic/prophylactic antimicrobials (active ingredient in tonnes) in food producing animals by major route of administration is provided in Tables 6.1 and 6.2. Medicated feed additives accounted for approximately 57-62% of the therapeutic/prophylactic antimicrobials sold for use in food producing animals each year while other oral medications averaged around 29%. Most of these products were used in pigs and poultry to treat respiratory and gastro-intestinal infection.

Tetracyclines, macrolides and polypeptides contributed on average about 85% of the total medicated feed additive sales annually. Similarly tetracyclines, trimethoprim/sulphonamides and β -lactams accounted for over 80% of the in-water medication product sales. Tetracyclines sales ranged between 14-45% of the total in-water medication sales, while sales of β -lactams ranged from 9% in 1999/2000 to 34% by 2001/2002. Trimethoprim/sulphonamides sales remained relatively stable at around 23-26% of the total sales during the period in review.

Table 6.1: Quantity (active ingredient in tonnes) of sales of therapeutic/prophylactic antimicrobials used in food producing animals by route of administration 1999/2000-2001/2002 (Anticoccidial products not included)

Route of administration and or function	Quantity (tonnes)			Antimicrobials sold for use in food animals (as a %)		
	1999/2000	2000/2001	2001/2002	1999/2000	2000/2001	2001/2002
Medicated feed additive	92	100.5	124	57	57	62
In-water medication	49	50	56	31	29	28
Injectable	16	21	15	10	12	8
Intramammary	4	4	4	2	2	2
TOTAL	161	175.5	199	100	100	100

Table 6.2: Quantity (active ingredient in tonnes) of sales of therapeutic/prophylactic antimicrobials used in food producing animals by route of administration and antimicrobial group 1999/2000-2001/2002 (Anticoccidial products not included)

Antimicrobial class	Medicated feed additive			In-water medication			Injectables			Intramammaries		
	99/00	00/01	01/02	99/00	00/01	01/02	99/00	00/01	01/02	99/00	00/01	00/02
Polypeptides	34	32	42	0	0	0	0	0	0	0	0	0
Tetracyclines	30	28	40	22	21	9	3	6	3	0	0	0
Macrolides	19	21	17	3	4	8	1	2	1	0	0	0
Streptogramins	0	8.5	16	0	0	0	0	0	0	0	0	0
Lincosamides	1	1	1	1	1	1	0	0	0	0	0	0
Aminoglycoside	0	0	0	4	3	3	0	0	0	0	0	0
Trimethoprim/Sulphonamides	1	2	0	13	14	12	2	2	2	0	0	0
β -lactams	0	0	0	5	7	20	10	11	9	4	4	4
Others*	7	8	8	1	0	3	0	0	0	0	0	0
TOTAL	92	100.5	124	49	50	56	16	21	15	4	4	4

* Others= ionophores, novobiocin and thiostreptan, tiamulin fumarate

0 No amount reported or <1000kg

7. Quantity of sales by food producing animal species

The quantity of sales of antimicrobials used in different species of food producing animals is shown in Table 7. The figures indicate that on average approximately 41% of antimicrobial products sold for use in food producing animals are registered for use in more than one species.

Most of the products are used in pigs and poultry but at this stage it is impossible to determine the exact usage in different species. A separate study will be required to provide further data on this aspect of the use of antimicrobials in food animals.

Table 7. :Quantity (active ingredient in tonnes) of sales of therapeutic antimicrobials by species 1999/2000-1999/2002 (Anticoccidial products not included)

Species	Quantity (tonnes)			Antimicrobials sold for use in food animals (as a %)		
	1999/2000	2000/2001	2001/2002	1999/2000	2000/2001	2001/2002
Cattle & Sheep	6	15.5	25.5	4	9	13
Pigs	37	30	31	23	17	16
Poultry	50	53	64.5	31	30	32
Multi-species*	68	77	78	42	44	39
Totals*	161	175.5	199	100	100	100

* a combination of two or more of the following species- cattle, pigs, sheep and poultry



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Dear Registrant

Collection of Animal Antimicrobial Supply Data From Registrants

The NRA announced its intention to collect animal antimicrobial supply data from registrants in February 2003 in the NRA Gazette. As you may be aware, following the JETACAR Report the Government is developing a comprehensive strategy to address antimicrobial resistance in order to maintain the effectiveness of antibiotic products. A key element of this plan is the collection of information on the amounts of antibiotic products used in veterinary medicine and animal production in Australia.

This information would assist the regulatory authorities to monitor changes in the overall use of antibiotic products, relate these to changes in antibiotic resistance and identify where reviews of prescribing practices might be appropriate and respond in a precise and targeted way.

Please supply the APVMA, figures in kg of active of your registered antimicrobial products for the previous three financial years (i.e. 1999/2000, 2000/2001 and 2001/2002) using the table below. You may wish to provide your best 'guess estimate' in the last two columns if hard data is not available. Please complete a separate table for each financial year. The process of calculating supply is based upon the current method for calculation of the APVMA levy.

Product name	Registration number	Names of actives	No. of specific pack sizes sold	Kilogram active constituent	Species	Purpose: Non growth promotion/ Growth promotion
<i>Completed by NRA</i>	<i>Completed by NRA</i>	<i>Completed by NRA</i>	<i>To be completed by registrant</i>	<i>To be completed by registrant</i>	<i>To be completed by registrant</i>	<i>To be completed by registrant</i>

To expedite the process, we have attached a list of your antimicrobial products currently registered with the APVMA. Please add to the list any other products that have been inadvertently left off the list.

Please ensure that your antimicrobial supply data reaches the APVMA by 30 June 2003. The data can be submitted by mail, or by email using Excel spreadsheet. For further information please contact me on 02 6272 5916 or by email via jowusu@apvma.gov.au

Yours sincerely
 John Owusu
 Vaccines and Antibiotics Manager
 1 May 2003

Active ingredients (of a veterinary product)

The substance(s) in a formulated veterinary product that is responsible for the primary biological effect of the product.

Antimicrobial

A chemical agent that, on application to living tissue or by systemic administration, will selectively kill or prevent or inhibit growth of susceptible organisms. This definition *includes* antibacterials (including ionophores), antiprotozoals, and antifungals, but *excludes* antineoplastics antivirals, immunologicals, direct-fed microbials and enzyme substances.

Antibiotic

In this report, the term antibiotic has been used to mean a subset of antimicrobial agents (see above) that include antibacterial agents (including ionophores).

Anticoccidial product

An antimicrobial agent that kills the protozoan parasites (*Eimeria* spp.) that cause the disease coccidiosis in chickens. Some coccidiostats are also antimicrobial (eg the ionophore coccidiostats are also polyether antimicrobial).

Antimicrobial resistance

A property of bacteria that confers the capacity to grow in the presence of antimicrobial levels that would normally suppress growth or kill susceptible bacteria. An organism is said to have become resistant to an antimicrobial when the minimum inhibitory concentration (MIC) is significantly higher (> 4 times) than the sensitive parent or than the range of MICs found in the same species not previously exposed to that antimicrobial.

Emergence of antimicrobial resistance

In this report this term is used to mean the appearance of antimicrobial-resistant bacterial strains in clinical or veterinary laboratory isolates.

Food-producing animals

Animals reared for the production of meat or other food products (eg eggs, milk).

Growth promotants

Substances used to increase weight gain and/or reduce feed requirements in food producing animals/

Growth promotion

The use of substances to increase the rate of weight gain and/or the efficiency of feed utilisation in animals by other than purely nutritional means. The term does not apply to the use of antimicrobial for the purpose of inhibiting specific pathogens even when an incidental growth response may be thus obtained. (The above notwithstanding, growth promotants appear to act by virtue of their antimicrobial effect since they do not work in germ-free animals.

Medicated feed additive

In the Australian context, medicated feed additive is an antimicrobial product manufactured for incorporation into the feed of animals (as distinct from administration or application of antimicrobial to animals by other routes such as water medication, oral dosing, injection, dermal application or infusion). In Australia, antimicrobial substances are added to animal feed for therapeutic, prophylactic, growth promotion and anticoccidial purposes.

Intensive farming

Livestock rearing and production methods in which large cohorts of animals are raised in close proximity in feedlots (cattle), or rearing sheds (pigs or poultry).

Maximum residue limit (MRL)

An MRL is defined as the maximum concentration of a residue resulting from the officially authorised safe use of an agricultural or veterinary chemical that is recommended to be legally permitted or recognised as acceptable in or on a food, agricultural commodity or animal feed. The concentration is expressed in milligrams per kilogram (mg/kg) of the commodity (or milligrams per litre in the case of a liquid). Although MRLs are not directly based on any health criteria, they are only established after a comprehensive risk assessment process, where the known toxicological risks are not considered to constitute an undue hazard to human health based on dietary exposure.

Veterinary prescription only antimicrobial product

Antimicrobial that must be prescribed by a registered veterinarian for animals under their care (also known as poisons schedule S4). Persons distributing, wholesaling or retailing PARs (S4s) must be licensed by the relevant State/Territory health department. All antimicrobial used therapeutically in animals are classified as PARs (eg penicillins, neomycin, tetracyclines). Poisons schedule definitions are given in the *Standard for the Uniform Scheduling of Drugs and Poisons*

Prophylaxis/prophylactic

The use of antimicrobial (by any route of administration) to prevent infection with a pathogen(s) that is anticipated to challenge the host during the treatment period; that is, initiating treatment in advance of an actual infection or disease condition because such a condition is expected to occur if treatment is withheld. For example, some animals may be treated on reaching a particular age because a disease condition usually occurs at that age.

Registration of agricultural and veterinary chemicals

The process whereby the Australian Pesticides and Veterinary Medicines Authority approves the sale and use of a formulated agricultural or veterinary chemical product after the evaluation and assessment of appropriate scientific data demonstrating that the product is effective and not unduly hazardous to human health, the environment or target plants and animals and that it will not adversely affect trade.

Residue (in food)

The remains of a chemical product persisting in or on food (including the active constituent and relevant derivatives, metabolites and degradation products).

The probability of an agent (hazard) causing an adverse effect and the magnitude of that effect (expressions of risk can be quantitative or qualitative, and should include consideration of any uncertainties).

Therapeutic use

The use of antimicrobial for the purpose of inhibiting a pathogen(s) which already infects the host; that is, initiating treatment because there is a disease condition.

**Glossary of terms adapted from the Report of the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR), The Use of Antibiotics in Food-producing animals: antibiotic-resistant bacteria in animals and humans. September 1999*

