Antibiotic Sales and Use Overview 2004 - 2009

Prepared for Approvals and ACVM Group

ISBN No: 978-0-478-38448-2 (online)

December 2010

Ministry of Agriculture and Forestry
Te Manatū Ahuwhenua, Ngāherehere

BIOSECURITY NEW ZEALAND

NEW ZEALAND FOOD SAFETY AUTHORITY

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Background

It is generally accepted that resistance to antibiotics in human pathogens is primarily due to the use and misuse of antibiotics in the human population. However, the food chain has been identified as a potential pathway by which humans might be exposed to resistant bacteria or resistance determinants of animal origin. Direct contact between humans and farm and/or companion animals may also represent a potential pathway for human exposure to resistant bacteria or resistance determinants. It is considered, however, that the likelihood of transfer in the latter case is low.

As part of the management of antibiotic resistance, registrants of restricted veterinary medicines (RVMs) containing antibiotics must provide an annual report of sales by month to MAF. These antibiotic sales data are summarised to approximate usage trends within different industries. This report focuses on the sale of antibiotics for use in food-producing animals, but sales data for antibiotic products used in companion animals are also recorded.

USE OF ANTIBIOTICS IN FOOD-PRODUCING INDUSTRIES

The food-producing industries in New Zealand that use a significant mass of antibiotics are the pig, poultry and dairy industries. These industry sectors have been invited to comment on the sales statistics and their comments are included throughout this report. The pig and poultry industries have previously provided a summary of antimicrobial use in their respective industries which may be viewed in appendices 1 and 2 of the 2004 antibiotic resistance report (see references at end for link).

Medication in the poultry industry and in grower pigs is primarily administered in feed and/or in water. As oral administration of antibiotics in food-producing animals is generally considered to be the most likely potential route to produce resistance that could be transferred to humans, this route is the focus of this and previous reports.

The New Zealand dairy industry is also a significant consumer of antibiotics, but intramammary and injectable antibiotic administration predominates. In their 2005 report on the impact of the use on antimicrobials in animals and the development of resistance in human pathogens the Expert Panel on Antibiotic Resistance noted that the strict controls in the dairy industry to regulate the quality of raw milk and routine pasteurisation mitigate against milk as a possible pathway for transfer of resistant organisms, though people who drink raw milk may have a higher risk profile.

The Expert Panel concluded that current New Zealand regulatory policy is prudent and conservative, and further restrictions beyond specific recommendations for limited antibiotics were not required.

The recommendations proposed in the report and progress on their implementation may be viewed on our website.

Antibiotic resistance recommendations: implementation update

Data collated between 2004-2009

This report includes data collated from 2004/05 to 2008/09. (The sales year is from 1 April to 31 March.) This data and industry comments on the data are presented as reported to MAF.

Data between 2004/05 and 2006/07 have been reported in the last sales report (Antibiotic Sales 2005-2007), which should be read for background information. However, due to revision of the data analysis methodology and correction of errors, sales figures in the earlier report differ slightly from those presented in this document.

The summary data do not include sales figures for antibiotics that are not managed as RVMs, including ionophores, avilamycin and quinoxalines. These products are not likely to be used in human medicine and there is no evidence to suggest that they could contribute to antibiotic resistance in humans.

DATA INTERPRETATION

Consider the following when interpreting data in this report:

- Using sales data over time as an indicator of individual animal treatments for a given antibiotic is inherently imprecise. An unknown amount of antibiotic sold within the nominated period will be used in the following year or years, depending on the product's shelf life. Some product may also be disposed of as damaged or expired.
- As different antibiotic classes are administered at different dose rates and for different treatment lengths, comparison of total active sales between classes must be made with care. This report has not attempted to convert sales data into an estimate of the number of animal treatments.
- Annual changes in national production animal numbers, while reported and briefly discussed, have not been allowed for in this analysis. Increased sales may only represent an increase in animal numbers within a population. Depending on the population changes, increased sales may occur when the percentage of animals treated within a population is actually declining. No data are available for companion animal numbers.
- The presentation of the data assumes products are used as indicated on the label and makes no judgement on known off-label uses. Significant quantities of antibiotics are used legally off label in species for which there are no registered label indications. This applies to species such as sheep and deer, which are significant in New Zealand but are 'minor use species' globally.
- Major disease outbreaks and inclement environmental conditions may cause a temporary increase in the use of specific antibiotics. Annual rotation of antibiotic classes in some industries may also contribute to apparent fluctuations in active sales. These should not be interpreted as long-term trends.
- This report only deals with antibiotics registered as veterinary medicines. Veterinarians can legally use human medicines and compound products for animals under their care subject to guidelines.

DATA PRESENTATION

The data are presented in a similar tabulated format to the 2005-07 report. The data were categorised based on antibiotic family and active ingredient, species, and administration route.

Species categories are defined as:

- Companion – cats and/or dogs

- Cattle – dairy and/or beef cattle
- Pigs/Poultry – pigs and/or chickens, turkeys and game birds
- Multiple species – all products registered for use in multiple species. This category includes products with claims for sheep or deer as there are few examples of antibiotics registered exclusively for use in these species.
- Other – currently includes horses, sheep, cage birds and ornamental fish.

Administration route categories are defined as:

- Oral – tablets, capsules, pastes, powders and suspensions for individual dosing
- Injectable – intravenous, subcutaneous and intramuscular
- Feed – in dedicated animal feed for the mass treatment of animals
- Water – in dedicated animal water supply for the mass treatment of animals
- Intramammary – 'lactating cow' and 'dry cow' products administered via the teat canal
- Other – topical, ophthalmic, ear preparations, intrauterine.

The weight (kg) of each antibiotic active ingredient within a product was calculated using the active concentration expressed on the label. Overages used in manufacturing and non-active salts are not included in the final mass.

Sales trends

Total antibiotic sales decreased from a peak of 62,883 kg in 2005/6 to 53,031 kg in 2007/8. Sales increased by 5% between 2007/8 and 2008/9. The annual fluctuations in total sales are principally driven by changes in sales of zinc bacitracin.

The following notes apply to tables 1-5 below.

Zinc bacitracin

Sales of in-feed zinc bacitracin were 35-47% by weight of all antibiotics sold between 2004 and 2009 and 71-80% of all antibiotics administered in feed and water. This antibiotic is used predominantly in the poultry industry and, to a much lesser extent, in the pig industry. It represented between 89-96% of all antibiotic sales for use in these industries over this time.

The poultry industry commented that annual fluctuations in sales of this active are correlated principally to the number of broilers. Broiler numbers peaked in 2005/06 at 85 million, which corresponds with peak sales of bacitracin, and have averaged approximately 80 million since then. Zinc bacitracin may also be administered at different dose rates and birds may be processed at different ages depending on market requirements. Both these factors also impacted on the total mass of active sold.

The pig industry commented that bacitracin use is insignificant. The industry estimates that less than 5% of bacitracin sales would be for use in pigs, and this represents less than 1% of total antibiotic use in pigs.

Macrolides/Lincosamides

Sales of these products decreased 19% between 2004/05 and 2006/07 to a low of 4,680kg. Sales increased 14.7% in 2007/08 and a further 1.3% in 2008/9 to 5,439kg, principally driven by sales of injectable tylosin.

In 2008/09, tylosin made up 82% of the total mass of macrolide/lincosamides sold, down from 89% in 2004/05. The percentage of tylosin administered in feed (principally in the pig/poultry industries) declined 41% over the survey period. Concurrent sales of tylosin and lincomycin sold for administration in water (used predominantly in the pig/poultry industries) also declined by 87%. Tilmicosin sales in pigs increased from approximately 200kg in the years 2004/05-2006/07 to 368kg in 2007/08 and 740kg in 2008/09.

Approximately 44% of tylosin sales in 2008/09 were injectable formulations compared to 19% in 2004/05. Injectable tylosin is registered for use in multiple species, but a significant, though unquantifiable, proportion of the sales is assumed to have been for administration in dairy cattle.

Sixty per cent of all macrolide/lincosamide sales in 2008/09 were products intended for in-feed and in-water medication (down from 71% reported in 2005-2007).

The poultry industry commented that the major use of tylosin in layers is for control of Mycoplasma. The rise in dedicated pullet rearers has resulted in a lot more pullets being seronegative to *Mycoplasma gallisepticum* and this combined with good biosecurity and eradication programmes, where feasible, has resulted in a marked reduction in the number of egg farms using tylosin in-feed or in-water. This has resulted in a steady decline in the use of macrolides/lincosamides in poultry between 2004/05 and 2008/09.

The pig industry commented that an increase in the dosage of tylosin has been required to meet prescribed therapeutic levels necessary to treat Mycoplasma arthritis. They note, however, that the use of vaccines where possible (such as a vaccine for ileitis) has displaced

the use of in-feed medication. Tilmicosin is used as part of partial depopulation regimes to enable eradication of Mycoplasma. It is sometimes used to treat specific challenges (for example, pleuropneumonia) and was also used to treat weaners impacted by Postweaning Multisystemic Wasting Syndrome (PMWS) before the availability of the vaccine in 2008.

Penicillins

Sales of penicillins increased 20% from 2004/05 to a peak of 16,383kg in 2007/08 and decreased 5% to 15,552 kg in 2008/09. These sales fluctuations were correlated to sales of intramammary preparations, specifically dry cow therapies for use in the dairy industry.

Penicillins are the most significant class of antibiotics used for treatment of individual animals across a wide range of species. The following comments can be made:

- Use in cats and dogs is primarily restricted to amoxicillin/clavulanic acid combinations. Most of these are administered orally.
- Approximately 95% of sales of penicillin products categorised for use in cattle are intramammary preparations. Dry cow therapies contributed 75% and 66% of these sales in 2007/08 and 2008/09 respectively.
- Most of the injectable amoxicillin, ampicillin and penicillin products have label claims for use in multiple species.
- A significant proportion of sales of these injectable penicillin products, especially the long-acting salts, were assumed to be for use in cattle in the dairy industry.
- Significant quantities were likely to have been administered to horses and pigs and, to lesser extent, sheep.
- Penethamate hydroiodide sales increased steadily from 580kg in 2004/05 to 1,026kg in 2008/09 as a result of increasing sales of an injectable product assumed to have been used primarily in cattle.
- Sales of amoxicillin and procaine penicillin remained relatively consistent.
- Sales of ampicillin were approximately 970kg between 2004 and 2007. Sales increased 65% to 1,618kg in 2007/8, declining slightly to 1,503kg in 2008/9. These changes were correlated to sales of dry cow therapies.
- Similarly, annual sales of cloxacillin fluctuated between approximately 3,000 and 4,000kg correlated to sales of dry cow therapies.

Cephalosporins

Sales increased from 1,202kg in 2004/05 to a peak of 1,739kg in 2007/08 and decreased to 1,528kg in 2008/09. Annual fluctuations were driven primarily by sales of dairy cattle intramammary preparations. Between 2004/05 and 2008/09 63% of all annual cephalosporin sales were intramammary preparations. Of these intramammary sales, 83% in 2007/08 and 92% in 2008/09 were cephalonium-based dry cow products.

Between 2004/05 and 2008/09 sales of oral cephalosporins (cephalexin products used in companion animals) were between 22% and 24% of total cephalosporin sales. Injectable cephalosporins sales contributed between 9% and 11%. The majority of the latter were sales of ceftiofur, registered for use in cattle, horses and pigs. Sales of this active ingredient increased 28% from 2004/05 to 2008/09. The third generation cephalosporin cefovecin, registered for treatment of serious infections in companion animals, had a low sales mass in 2008/09. The fourth generation cephalosporin cefquinome, approved for use in food-producing species, had very low sales for the last three years.

The pig industry commented that 3rd/4th generation cephalosporins are prescribed to a limited extent.

Tetracyclines

From 2004/05 to 2008/09, sales fluctuated between approximately 4,000 to 5,000kgs. About 60% of tetracycline sales during this period were products registered for use in feed and/or water in multiple species and were assumed to have been used primarily in the pig and poultry industries.

In-feed sales increased by 42% between 2005/06 and 2006/07, and remained approximately constant between 1,700 and 1,850kg to 2008/09. Injectable tetracyclines sales decreased slightly from 34% of total sales in 2004/05 to 30% in 2008/09.

The pig industry commented that in-feed dose rates of tetracyclines have increased to meet prescribed therapeutic levels for certain diseases such as Mycoplasma arthritis and pleuropneumonia. These diseases have been increasing problems in latter years.

The poultry industry notes that the use of tetracyclines in layers and broilers is extremely uncommon. Some use may occur in free range layer flocks on an 'as required' basis for health and welfare reasons.

Sulphonamides

Sales trended up (10%) between 2004/05 and 2005/06, and have remained relatively consistent since with the exception of a slight decline in 2007/08. Approximately 95% of the sales were orally administered products. Of sales in 2008/09, 2,507kg (51%) were oral 'scour' products registered for use in multiple species but most likely were used primarily in calves. Sales of these products declined slightly from 2,829kg in 2004/05. Of the remaining sales, 2,355kg (48%) were products registered for use in horses (up from 1,481kg in 2004/05).

Aminoglycosides

Aminoglycoside sales decreased from 1,898kg in 2004/05 to 1,217kg in 2008/09. This was primarily due to a reduction in dihydrostreptomycin sales from 1,057kg to 530kg. This decline was mostly due to the reduction in dihydrostreptomycin intramammary and injectable product sales. Additional sales trends for aminoglycoside products between 2004/5 and 2008/9 include:

- Total spectinomycin sales declined from 74kg to 43kg. This was driven by reductions in products sold for administration in water for use in the pig/poultry industries. Spectinomycin sales made up just 4% of total aminoglycoside sales in 2008/09.
- Neomycin sales declined from 356kg to 196 kg due to reduced sales of in-water products registered for use in multiple species, and intramammary products. Neomycin accounts for 16% of total aminoglycoside sales in 2008/09 with intramammary, oral and in-water administration accounting for 44%, 34% and 16% of sales respectively.
- Apramycin sales declined markedly from 75kg in 2005/6 to 0.4kg in 2008/09, principally because of reduced sales of products registered for in-feed use in pigs.
- There was a 10% reduction in sales of oral aminoglycosides used in combination with sulphonamides to treat bacterial enteritis (scour preparations). These products are used primarily in calves and, to a lesser extent, in piglets.
- Streptomycin sales remained static. These sales contributed 30% of the total sales in 2008/09. Of these, 60% were products administered orally and 40% by injection.

The drop in sales of intramammary and injectable aminoglycosides coincides with the formal reassessment conducted by MAF of products containing beta lactam and aminoglycoside combinations. (This review was conducted in response to a recommendation by the Expert Panel on Antibiotic Resistance in their 2005 report.) Products were required to show synergistic efficacy to retain registration. All intramammary and injectable products containing an aminoglycoside in combination with beta lactam antibiotics were either withdrawn prior to the commencement of the review or their registrations were declined after reassessment. This review was concluded in 2009, so aminoglycoside sales for these product classes will continue to fall as sales data in this report include many combination products that are no longer registered.

Fluoroquinolones

Despite remaining low, fluoroquinolone sales increased 50% over the last five years. Fluoroquinolones are registered for oral, parenteral and aural use in companion animals, parenteral use in cattle and pigs, and oral use in calves. Use of these products is limited to the treatment of individual sick animals and specific label statements are included to manage antibiotic resistance, particularly for products intended for use in production animals.

The increase seen is primarily a result of increased sales (142% between 2004/5 and 2008/09) of injectable marbofloxacin, registered for use in cattle and pigs. Oral sales of marbofloxacin for use in calves were 1.8kg in 2005/06 and did not exceed 0.2kg in any other year.

Fluoroquinolone sales in companion animals trended up (27%) between 2004/5 and 2007/8 to a peak of 20.9kg before declining 8.6% to 19.1kg in 2008/9. However, total sales were low.

The pig industry commented that fluoroquinolones are prescribed to a limited extent.

Nitro-imidazoles

Total sales of dimetridazole, used as an in-feed medication for pigs and poultry, remained relatively low. Sales peaked in 2006/07 at 135kg but declined in subsequent years to reach 38kg in 2008/9. Off-label use in other food-producing species is not permitted because of the risks to trade. Metronidazole, used orally in companion animals, had consistent sales of 11kgs for the past four years.

Nitrofurans

Furazolidone sales decreased significantly between 2004/05 and 2005/06 and remained low in 2006/07. They increased by 110% in 2007/8 to 19kg before dropping to the lowest recorded sales of 6kg in 2008/9. Total sales of nitrofurans are now less than 3.5% of the 2002/03 levels. This coincides with increased constraints on use because of issues unrelated to antibiotic resistance. Furazolidone is used in relatively small quantities for the treatment of bacterial infections in pigs and poultry. Very small amounts of nitrofurazone are used for topical treatment in non food-producing animals.

Virginiamycin

Two virginiamycin products remain registered for therapeutic use -- one for the management of laminitis in horses and one for use in poultry. Sales for use in horses between 2004/05 and 2008/09 were very low (12-16kg). No sales have been reported for use in poultry for this period.

Other

This category includes carbadox administered in pig feed and florfenicol, used primarily for respiratory infections in young cattle. The apparent increase in this category in 2005/6 is because a carbadox product was classified as an RVM with the resultant requirement to report sales data.

Table 1: Total antibiotic sales (kg active ingredient) by antibiotic family 2004/5 to 2008/9

Antibiotic Family	2004/05	2005/06	2006/07	2007/08	2008/09
Aminoglycosides	1,898	1,658	1,620	1,253	1,217
Bacitracin	18,057	29,528	22,757	18,820	21,733
Cephalosporins	1,202	1,520	1,443	1,739	1,528
Clavulanic Acid	184	187	195	190	213
Fluoroquinolones	27	34	33	40	41
Fusidic Acid	2	4	4	2	2
Macrolides/Lincosamides	5,764	5,235	4,680	5,369	5,439
Nitrofurans	42	10	9	19	6
Nitro-imidazoles	61	72	146	108	49
Novobiocin	4	3	2	3	1
Other (includes carbadox, florfenicol and polymyxin)	9	461	615	478	336
Penicillins	13,765	14,979	14,676	16,383	15,552
Sulphonamides / Trimethoprim	4,702	5,251	5,219	4,615	5,187
Tetracyclines	4,298	3,923	4,788	4,002	4,492
Virginiamycin	16	16	16	12	14
Total	50,032	62,883	56,203	53,031	55,809

Table 2: Antibiotic sales (kg active ingredient) by active family and approved route of administration 2004/5 to 2008/9

Antibiotic Family	Administration Route	2004/05	2005/06	2006/07	2007/08	2008/09
Aminoglycosides	Feed	11.8	71.8	88.0	35.1	21.6
	Injectable	865.3	626.4	638.6	545.5	585.8
	Intramammary	550.6	503.1	449.6	343.4	255.0
	Oral	331.2	328.1	316.8	253.4	294.8
	Other	10.5	11.3	11.7	9.2	11.1
	Water	128.7	117.2	115.5	66.1	49.1
Aminoglycosides Total		1,898.1	1,657.9	1,620.3	1,252.7	1,217.4
Bacitracin	Feed	18,056.3	29,527.4	22,755.7	18,818.6	2,1731.8
	Other	0.8	1.0	1.1	1.1	1.1
Bacitracin Total		1,8057.1	2,9528.3	2,2756.8	18819.7	2,1732.8
Cephalosporins	Injectable	128.0	133.1	125.8	147.9	155.7
	Intramammary	755.1	957.4	901.9	1,138.9	955.8
	Oral	268.2	368.4	352.7	398.0	352.6
	Other	50.3	61.0	62.6	53.9	63.4
Cephalosporins Total		1,201.6	1,519.9	1,443.1	1,738.6	1,527.5
Clavulanic Acid	Injectable	4.6	4.9	6.2	5.3	6.5
	Intramammary	28.9	24.0	24.5	19.0	20.8
	Oral	151.0	158.5	164.4	165.4	185.3
Clavulanic Acid Total		184.4	187.4	195.2	189.6	212.6
Fluoroquinolones	Injectable	12.2	16.1	17.2	21.6	24.2
	Oral	14.6	17.7	16.3	18.4	17.0
	Other		0.0	0.0	0.0	0.1
Fluoroquinolones Total		26.8	33.8	33.4	39.9	41.3
Fusidic Acid	Other	2.4	4.2	4.0	1.8	1.7
Fusidic Acid Total		2.4	4.2	4.0	1.8	1.7
Macrolides / Lincosamides	Feed	4,483.6	4,153.7	3,231.8	3,667.9	3,288.7
	Injectable	1,020.5	892.1	1,232.6	1,533.3	1,975.3
	Intramammary	146.3	110.8	128.3	117.7	136.5
	Oral	33.1	33.7	34.6	38.5	28.9
	Water	80.7	45.1	52.6	11.7	10.1

Macrolides Lincosamides Total		5,764.2	5,235.5	4,679.9	5,369.1	5,439.4
Nitrofurans	Feed	41.0	8.0	6.0	16.8	3.0
	Other	0.9	0.8	0.9	0.8	0.8
	Water		1.6	1.8	1.1	1.8
Nitrofurans Total		41.9	10.5	8.7	18.7	5.6
Nitro-imidazoles	Feed	42.8	49.5	126.1	78.8	24.8
	Oral	11.9	12.3	13.8	13.0	12.0
	Water	6.0	9.8	6.6	16.6	12.6
Nitro-imidazoles Total		60.7	71.6	146.4	108.4	49.4
Novobiocin	Intramammary	4.5	3.0	2.0	3.2	0.6
Novobiocin Total		4.5	3.0	2.0	3.2	0.6
Other	Feed		450.0	598.8	471.3	326.3
	Injectable	8.7	10.7	15.6	6.5	9.6
	Other	0.2	0.3	0.3	0.3	0.3
	Water		0.0	0.0	0.0	0.0
Other Total		8.9	461.0	614.6	478.0	336.1
Penicillins	Injectable	7,774.6	7,882.5	8,341.2	8,174.1	8,293.8
	Intramammary	5,400.7	6,493.6	5,700.2	7,520.4	6,662.8
	Oral	542.4	565.6	574.4	617.3	556.6
	Other	29.1	30.2	26.9	5.6	32.4
	Water	17.7	7.0	33.0	65.6	6.4
Penicillins Total		13,764.5	14,978.9	14,675.6	16,383.0	15,552.0
Sulphonamides/Trimethoprim	Feed	119.5	28.0	14.0	7.0	1.0
	Injectable	183.9	164.6	151.4	172.0	173.5
	Oral	4,342.2	4,929.6	4,871.3	4,394.9	4,937.9
	Other	56.4	128.7	182.0	40.6	74.9
	Water	0.3	0.0	0.0	0.0	0.0
Sulphonamides/Trimethoprim Total		4,702.2	5,250.9	5,218.7	4,614.5	5,187.2
Tetracyclines	Feed	1,391.0	1,206.0	1,714.1	1,855.6	1,720.0
	Injectable	1,452.4	1,343.2	1,425.1	1,264.1	1,372.8
	Intramammary	115.4	110.9	131.7	154.8	194.5
	Oral	23.2	28.4	26.7	25.0	25.2
	Other	166.6	218.4	201.3	190.7	208.7

	Water	1,149.7	1,016.5	1,289.3	511.2	970.6
Tetracyclines Total		4,298.2	3,923.4	4,788.2	4,001.5	4,491.8
Virginiamycin	Feed	16.1	16.4	16.3	12.4	13.8
Virginiamycin Total		16.1	16.4	16.3	12.4	13.8
Total		50,032	62,883	56,203	53,031	55,809

Table 3: Antibiotic sales (kg active ingredient) by approved label species and antibiotic family 2004/05 to 2008/09

Label Species	Antibiotic Family	2004/05	2005/06	2006/07	2007/08	2008/09
Cattle	Aminoglycosides	467.7	429.8	358.0	273.5	171.8
	Cephalosporins	805.4	1,018.4	964.5	1,192.8	1,019.2
	Clavulanic Acid	28.9	24.0	24.5	19.0	20.8
	Fluoroquinolones		1.9	0.2	0.2	0.1
	Macrolides/ Lincosamides	78.0	48.8	50.8	47.9	53.3
	Novobiocin	4.5	3.0	2.0	3.2	0.6
	Penicillins	5,738.4	6,787.4	6,008.3	7,829.9	7,115.9
	Sulphonamides/ Trimethoprim	84.1	192.2	255.5	113.4	150.5
	Tetracyclines	7.8	16.2	12.5	15.7	28.7
Cattle Total		7,214.8	8,521.8	7,676.3	9,495.5	8,560.8
Companion	Aminoglycosides	5.9	8.7	9.0	6.9	6.8
	Bacitracin	0.5	0.6	0.7	0.7	0.7
	Cephalosporins	268.2	368.4	352.7	398.0	353.7
	Clavulanic Acid	125.7	127.5	133.7	143.5	163.9
	Fluoroquinolones	16.4	17.7	18.2	20.9	19.1
	Fusidic Acid	2.4	4.2	4.0	1.8	1.7
	Macrolides/ Lincosamides	33.1	33.7	34.6	38.5	28.9
	Nitro-imidazoles	11.9	11.3	11.2	11.2	11.0
	Other	0.2	0.2	0.2	0.2	0.2
	Penicillins	449.6	450.4	459.1	529.7	470.9
	Sulphonamides/ Trimethoprim	0.0	0.0	0.0	0.0	0.0
	Tetracyclines	23.2	28.4	26.7	25.0	25.2
Companion Total		937.2	1,051.2	1,050.2	1,176.6	1,082.1
Multiple	Aminoglycosides	1,342.5	1,065.5	1,106.6	909.5	995.6
	Bacitracin	0.3	0.4	0.4	0.4	0.4
	Cephalosporins	128.0	133.1	125.8	147.9	154.7
	Clavulanic Acid	29.8	35.9	37.0	27.2	27.9

	Fluoroquinolones	10.3	14.2	15.0	18.8	22.0
	Macrolides/ Lincosamides	5,213.0	4,831.9	4,283.2	4,189.5	4,156.6
	Nitrofurans	0.5	0.5	0.5	0.4	0.5
	Other	8.8	10.8	15.7	6.5	9.7
	Penicillins	7,499.0	7,649.1	8,000.5	7,846.1	7,863.1
	Sulphonamides/ Trimethoprim	3,017.0	2,940.0	2,849.2	2,434.5	2,680.4
	Tetracyclines	4,267.1	3,877.0	4,745.3	3,518.6	3,622.1
Multiple Total		21,516.4	20,558.3	21,179.2	19,099.4	19,533.0
Other	Aminoglycosides	4.7	5.4	5.3	0.0	4.2
	Nitrofurans	0.4	2.0	2.2	1.5	2.1
	Nitro-imidazoles		1.0	2.6	1.8	1.0
	Penicillins	59.8	85.0	174.8	111.6	95.7
	Sulphonamides/ Trimethoprim	1,481.6	2,090.7	2,100.1	2,059.7	2,355.4
	Tetracyclines	0.1	1.7	3.7	2.2	0.9
	Virginiamycin	16.1	16.4	16.3	12.4	13.8
Other Total		1,562.6	2,202.2	2,304.8	2,189.1	2,473.0
Pigs/Poultry	Aminoglycosides	77.3	148.5	141.3	62.7	38.9
	Bacitracin	18,056.3	29,527.4	22,755.7	18,818.6	21,731.8
	Macrolides/ Lincosamides	440.1	321.1	311.3	1,093.2	1,200.6
	Nitrofurans	41.0	8.0	6.0	16.8	3.0
	Nitro-imidazoles	48.8	59.3	132.6	95.4	37.4
	Other		450.0	598.8	471.3	326.3
	Penicillins	17.7	7.0	33.0	65.6	6.4
	Sulphonamides/ Trimethoprim	119.5	28.0	14.0	7.0	1.0
	Tetracyclines	0.0	0.0	0.0	440.0	815.0
	Virginiamycin	0.0	0.0	0.0	0.0	0.0
Pigs/Poultry Total		18,800.6	30,549.2	23,992.7	21,070.5	24,160.4
Total		50,032	62,883	56,203	53,031	55,809

The following comments apply to tables 4 and 5 below.

Label species versus route of administration

- Sales of companion animal products increased 26% between 2004/05 and 2007/08 as a result of increased oral product sales. Oral products sales also accounted for the 8% decline in sales between 2007/08 and 2008/09.
- Sales of products registered for use only in cattle increased 24% between 2006/07 and 2007/08, and then declined 10% in 2008/09. These fluctuations were driven by sales of intramammary products, specifically dry cow products used in the dairy industry. There were increases in the sales of injectable products (33%) and the 'other' use category (35%) between 2004/05 and 2008/09 but these numbers were proportionately much

lower. 'Other' use includes predominantly sales of intrauterine products with a smaller mass of topical preparations. The injectable data will not accurately reflect sales for use in cattle as a significant proportion of sales of injectable products categorised for use in multiple species will be used in dairy cattle.

- The Dairy Cattle Veterinarians of the New Zealand Veterinary Association provided the following comments:
  - The total cattle antibiotic use is less than (or about equal to) the pig and poultry industries.
  - The vast majority of antibiotic used in cattle is penicillin-based (of limited human impact). Of that, a huge proportion is intramammary, and this route could be argued as lower risk with regard to residue and resistance development because it is more locally targeted and active. Of that, the majority is dry cow therapy (DCT), which is a preventative approach when the cow is not being milked, further reducing any risk to the food chain.
- Sales in the pig and poultry industries trended down from a peak of 30,549kg in 2005/06 to 24,160kg in 2008/09, reflecting reduced sales of in-feed bacitracin preparations administered to poultry. Over 99.7% of sales categorised for use in pigs and poultry are administered in feed or in water.
- The poultry industry notes that less than 0.003% of flocks per year in the New Zealand poultry meat industry are administered any class of therapeutic antibiotics.
- Total sales of antibiotics registered for use in multiple species declined by 9.2% between 2004/05 and 2008/09. This was driven by a 46% decrease in sales of in-feed antibiotics and a 17% reduction of in-water antibiotics, (most of which are used in the pig and poultry industries), and a 11% reduction in oral antibiotics which represent 'scour' treatments used primarily in calves. Corresponding increases in sales were recorded in injectable products (9%), intramammary products (27%) and other category (20%) (intrauterine and topical preparations). A significant proportion of the latter products are likely to have been sold for use in dairy cattle.
- Sales for other species increased 58% between 2004/05 and 2008/09 as a result of increased sales of oral products, primarily used in horses.

Use pattern by route of administration

Tables 4 and 5 tabulate the route of administration by use pattern. These data illustrate that the routine method of administration varies significantly between companion animals, pigs/poultry and cattle.

Sales of oral products in the 'other' species category represent predominantly sulphonamides and trimethoprim intended for use in horses, plus a very small amount of other actives used in cage birds and lambs.

The significant sales of antibiotics categorised for use in multiple species make interpretation of these data difficult. However, analysis of the specific product registrations enables the following assumptions to be made:

- Sales of *oral* products, which trended downwards, represent predominantly anti-diarrhoeal preparations, most of which are used in neonates, more specifically calves. An unquantified amount is administered to piglets with neonatal scours. A small quantity (approximately 108kg in 2007/08 and 2008/09) represents 500mg amoxicillin/clavulanic acid tablets, which can be used in dogs or calves.

- The *injectable* product data have trended up 10% between 2004/05 and 2008/09 and principally include sales of penicillins, tetracyclines, macrolides, and aminoglycosides. A smaller sales mass of cephalosporins, sulphonamides, fluoroquinolones and florfenicol are included. A significant percentage of these sales are likely to have been for administration in dairy cattle whose numbers have increased 14% over the same period. Significant sales of some antibiotic classes would have also been for use in horses and pigs and, to a lesser extent, deer and sheep. The amount sold for administration in companion animals will be small due to the comparatively smaller body weight of dogs and cats, classes of antibiotics involved and the general preference to administer antibiotics orally in these species.
- The *in-feed* data have declined by 46% between 2004/05 and 2008/09 and consist of sales of oxytetracycline and tylosin products. These products are predominately used in the pig and poultry industries. Tylosin is registered for use in feed lot beef cattle to reduce the incidence of liver abscesses. Oxytetracycline may also be used in feed for cattle. Because of the predominance of pastoral farming in New Zealand, these use patterns are relatively uncommon.
- The *in-water* medication data chiefly represent sales of oxytetracycline (97% in 2008/09). The remaining sales are neomycin. In-water medication is used most commonly in the poultry industry, but may be used in the pig industry if facilities allow. Minimal amounts of oxytetracycline may be used in milk to medicate calves.
  - The pig industry commented that New Zealand pig farms are generally not set up for in-water medication. However, they consider that in-water medication is probably preferable, if feasible, and that its use has increased over the last couple of years. Water soluble antibiotics may also be administered in feed.
- The *intramammary* data represents sales of an intramammary product that also has a label indication for topical treatment of dermatological conditions in cats and dogs. Most of this product will be used in cattle. Intramammary products are normally registered only for treatment of mastitis in cattle, but small amounts could be used to treat sheep and goats.
- The *other* category consists mainly of topical products, which are frequently approved with multiple species claims. It also contains a small amount of intra-uterine product for use predominantly in cattle.

Table 4: Antibiotic sales (kg active ingredient) by approved label species and administration route 2004/05 to 2008/09

Label Species	Administration Route	2004/05	2005/06	2006/07	2007/08	2008/09
Cattle	Injectable	339.6	293.8	308.1	309.5	453.1
	Intramammary	6,740.3	7,972.1	7,049.7	9,018.0	7,893.3
	Oral	32.0	70.4	73.7	72.9	75.7
	Other	102.4	184.7	244.6	94.5	138.2
	Water	0.5	0.8	0.3	0.6	0.5
Cattle Total		7,214.8	8,521.8	7,676.3	9,495.5	8,560.8
Companion	Injectable	1.8	1.9	2.2	2.7	3.2
	Oral	926.5	1,035.5	1,034.1	1,164.2	1,069.4
	Other	8.9	13.7	14.0	9.7	9.6

Companion Total		937.2	1,051.2	1,050.2	1,176.6	1,082.1
Multiple	Feed	5,519.0	5,085.3	4,690.1	4,006.4	3,003.5
	Injectable	11,045.1	10,691.3	11,465.8	11,441.9	12,044.9
	Intramammary	261.2	230.8	288.6	279.4	332.7
	Oral	3,272.6	3,239.1	3,154.6	2,624.9	2,904.6
	Other	205.4	257.1	231.8	199.4	246.2
	Water	1,213.1	1,054.7	1,348.3	547.4	1,001.1
Multiple Total		21,516.4	20,558.3	21,179.2	19,099.4	19,533.0
Other	Feed	16.1	16.4	16.3	12.4	13.8
	Injectable	59.8	85.0	174.8	111.6	95.7
	Oral	1,486.0	2,097.1	2,107.9	2,061.5	2,360.6
	Other	0.4	0.4	0.4	0.4	0.3
	Water	0.4	3.4	5.5	3.2	2.6
Other Total		1,562.6	2,202.2	2,304.8	2,189.1	2,473.0
Pigs/Poultry	Feed	18,626.9	30,409.1	23,844.4	20,944.7	24,113.6
	Injectable	3.8	1.5	2.9	4.4	0.4
	Oral	0.8	0.3	0.7	0.5	-
	Water	169.1	138.3	144.7	121.0	46.4
Pigs/Poultry Total		18,800.6	30,549.2	23,992.7	21,070.5	24,160.4
Total		50,032	62,883	56,203	53,031	55,809

Table 5: Antibiotic sales (kg active ingredient) by administration route 2004/05 to 2008/09

Administration Route	2004/05	2005/06	2006/07	2007/08	2008/09
Feed Total	24,161.9	35,510.8	28,550.7	24,963.4	27,130.9
Injectable Total	11,450.1	11,073.5	11,953.7	11,870.2	12,597.2
Intramammary Total	7,001.5	8,202.9	7,338.2	9,297.4	8,226.0
Oral Total	5,717.9	6,442.4	6,371.0	5,923.9	6,410.3
Other Total	317.1	455.9	490.8	304.0	394.4
Water Total	1,383.0	1,197.2	1,498.8	672.2	1,050.6
Total	50,032	62,883	56,203	53,031	55,809

Variations in animal populations

Between June 2004 and June 2009 (according to Statistics NZ figures), the total number of dairy cattle increased 13.8% from 5,152,000 to 5,861,000 while beef cattle, sheep and deer numbers fell 11.7%, 17.5% and 34.8% respectively.

Horse numbers were recorded as approximately 77,000 in 2004, 66,000 in 2007, 62,000 in 2008 and 65,000 in 2009. (Horse numbers were not available for 2005 and 2006.)

Pig numbers increased 4.5% from approximately 340,000 in 2004 to around 355,000 in 2005 and increased again to 367,000 in 2006. Since then numbers have declined 11.5 % to 325,000 in 2008 and a further 1% to 322,000 in 2009.

Broiler numbers peaked between 2005 and 2007 at approximately 85 million and declined to 81 million in 2008 and 78 million in 2009. The standing population of broilers is about 13 million at any one time. Layer numbers remained relatively stable at approximately 3 million for 2006 and 2007 and increased to 3.4 million and 3.3 million in 2008 and 2009 respectively. There are approximately 1 million replacement pullets each year (Poultry Industry Association).

These figures suggest that antibiotic sales for cattle products, while fluctuating between years, have increased as dairy cattle numbers have increased. Product sales coded for use in multiple species but assumed to be used prominently in the dairy sector have also increased with increasing dairy cattle numbers. Sales of oral sulphonamide/aminoglycoside scour preparations used significantly in calves have declined despite increasing dairy cattle numbers.

Sales in the pig and poultry category decreased from a peak in 2005/6, driven by decreased sales of bacitracin used prophylactically in the poultry industry. These data roughly correlate to the number of broilers. Sales of other in-feed and in-water antibiotics used therapeutically in the pig and poultry industries have also generally decreased or remained consistent.

The only category where sales increased despite apparent falling numbers of animals was the ‘other’ category which includes horses. These sales include predominantly oral sulphonamide/trimethoprim products.

Antibiotic use in horticulture

One product containing streptomycin is registered for the following uses:

- pipfruit (fireblight)
- stonefruit (blast and bacterial spot)
- seedling tomatoes (bacterial diseases).

Off-label use of this product is not allowed without express permission from MAF. Sales of streptomycin in horticulture have increased between 2006/07 and 2007/08 and declined again to levels similar to 2006/07 in 2008/09. Sales fluctuations are predicted to be correlated to varying disease incidence and climatic factors.

Table 6: Reported streptomycin sales for use in horticulture

Sales	2004/05	2005/06	2006/07	2007/08	2008/09
Kilograms	281.35	281.42	393.92	449.21	384.34

Report summary

These data provide approximate information regarding annual sales of restricted veterinary antibiotics. This summary focuses on antibiotics used in food-producing animals.

IN FEED/WATER ADMINISTRATION

Administration of antibiotics in feed and/or water in food-producing animals has been identified as a potential pathway by which humans might be exposed to resistant bacteria or resistance determinants of animal origin.

The majority of the sales of in-feed and in-water products will be used in the poultry and pig industries. A limited number of antibiotic families identified by the Expert Panel on Antibiotic Resistance as highly significant in human medicine are registered for administration via these routes. These include the aminoglycosides, macrolides/lincosamides, and streptogramins.

Sales of aminoglycosides have declined 65% to 71kg in 2008/09 from a peak in 2006/07 of 204kg. Sales of macrolides/lincosamides have also decreased 28% to 3,299kgs from 4,564kgs recorded in 2004/05. No virginiamycin (streptogramin) has been sold for use in poultry over the survey period.

The percentage decrease in sales is greater than the corresponding decrease in the pig and poultry population recorded between 2006/07 and 2008/09. These trends indicate the pig and poultry industries are prescribing these antibiotics prudently with the desired outcome of reducing dependence on active ingredients of high human health significance.

PARENTERAL OR ORAL ADMINISTRATION

Antibiotics registered for parenteral or oral administration in food-producing animals that have been identified by the Expert Panel on Antibiotic Resistance as significant in human medicine include the aminoglycosides, 3rd and 4th generation cephalosporins, fluoroquinolones, macrolides, anti-mycobacterial antimicrobials and the streptogramins.

Sales of aminoglycosides have declined following a MAF review of combination aminoglycoside/beta-lactam products and sales are expected to fall further in subsequent reports.

Sales of cephalosporins have increased 26% between 2004/05 and 2008/09, possibly because of new product registrations and increased dairy cattle numbers. Sales of 4th generation cephalosporins were very low in 2008/09.

Sales data for injectable fluoroquinolones, which have specific label restrictions to manage antibiotic resistance, have increased 114% between 2004/05 and 2008/09 but total sales mass is still very low at 22kgs reported in 2008/09. Oral sales of marbofloxacin registered for use in calves were very low between 2006/07 and 2008/09.

Parenteral and oral macrolide sales have increased by 81%, driven primarily by increased sales of injectable tylosin. Injectable tylosin is likely to be administered most frequently in dairy cattle. (Dairy cattle numbers have increased significantly over the survey period.) Tylosin may also be used in pigs. Some limited use may occur in sheep and goats.

Sales of the anti-mycobacterial antibiotic streptomycin have remained relatively static over the survey period. Sales will decline significantly in subsequent reports as this aminoglycoside was in aminoglycoside/beta-lactam combination scour products that are no longer registered following the MAF review. An injectable product containing streptomycin has specific and limited use indications.

The streptogramin virginiamycin is registered for use in horses with laminitis. The sales mass remains very small. A small number of horses are processed for export in New Zealand. There is no domestic market.

Conclusion

There are no reported trends that would indicate antibiotics are not being used as intended or outside their registration conditions.

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