Antibiotic resistance: challenges and opportunities
Report to the New Zealand Veterinary Association

New Zealand Veterinary Association
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Foreword

Antibiotic resistance – an innovation opportunity for NZ

*Darwinian pressures mean it is not the strongest nor the smartest species that survive but ‘the species ... that is able best to adapt and adjust to the changing environment in which it finds itself’.*

Over the last century, human and veterinary medicine has made tremendous progress in the fight against infectious diseases. Remarkable advances in life sciences and innovations in healthcare have enriched our ability to overcome an increasing variety of public health challenges. The majority of the world’s human and animal populations now enjoy a significantly longer and better quality of life as a result. The strides made in human and animal health have been a catalyst for world economic growth, improved productivity and increased life expectancy.

Continued increases in physical wellbeing, however, is far from a given. A significant reason for this is that the medicines we use today to treat infections might not always work, due to the declining efficacy of antibiotics.

But rather than being seen solely as a threat – as it has been seen to date – this declining effectiveness can be an opportunity for New Zealand. It provides an opportunity to demonstrate our innovation and adaptability and the quality of our animal husbandry, while showcasing the natural benefits of our animal-based food systems. Rising to this challenge could reward New Zealand and New Zealanders with more resilient technology-based industries, more valuable export receipts, an enhanced international brand and an increased contribution to the wellbeing of the world in which we live.

From a more defensive perspective, it could also help ensure we are not locked out of valuable international markets, through future-proofing the supply chain in a world where antibiotics and resistance are likely to become an emerging consumer issue.

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The challenge
Antibiotics were a defining 20th century achievement – replacing them will be a major achievement of the 21st. The issue of antimicrobial resistance (AMR) and its potential impact on New Zealand agriculture has recently been given greater impetus. In July 2015 the NZVA, on behalf of the profession, announced the following vision statement:

By 2030 New Zealand Inc. will not need antibiotics for the maintenance of animal health and wellness

It is understood to be the first veterinary association in the world to make such a goal explicit. The NZVA has identified antibiotic resistance as a significant challenge to the health not only of animals but of humans and the environment. The three are ultimately inseparable, and the NZVA has set out to highlight this by drawing an aspirational line in the sand to promote urgency and action on this issue. Its goal is to preserve the efficacy of existing antibiotics through reduction, refinement and replacement of use so that they may be effective when most needed. In the meantime, the challenge is to find alternatives to problematic practices with antibiotic demand and supply.

The threats represented by growing resistance to antimicrobials (in particular antibiotics) are well recognised and have been publicised in several reports in the last few years. There has been less scrutiny in New Zealand, particularly in relation to the amount the country has to lose and, with the application of creativity, to gain as a result of addressing the issue. The available evidence suggests that some economically viable innovative therapies already exist and that the use of these and more new therapies can have an economic impact on animal production levels, while offering the potential to reinforce New Zealand’s credentials as a leading, safe producer of high quality animal-based food globally.

The opportunity
PwC has considered the NZVA’s positioning and its implications. Rather than solely a threat – as it has been seen to date – the declining effectiveness of antibiotics can be an opportunity for New Zealand to showcase its innovation, its adaptability and the quality of its animal husbandry. The most fundamental gain in doing so is likely to be in future-proofing the supply chain to overseas markets. Concern about antibiotics and resistance is an emerging consumer issue that could affect market access and overseas regulation.

With these sorts of issues, there is a temptation to estimate some big dollar figure to grab people’s attention. We decided that calculating the threat and the opportunity in dollar terms – generating some ‘magic number’ – required too many assumptions to be worthwhile. Nevertheless, New Zealand’s economy is underpinned by around $25 billion of animal-based exports annually, so animal health and market access are clearly relevant.

AMR should also been seen in the context of New Zealand’s growing high-tech industries (biotech in particular) and their potential to capitalise on the opportunity for innovation. New Zealand can build on existing, world-class research and production to develop clusters of upstream and downstream industries
based on pastoral specialisation. Such clusters could play an important role in the research and development of methods to replace or mitigate the need for current antibiotic use in the agricultural sector worldwide.

This new knowledge and capability could help meet the goals of the Government’s Business Growth Agenda (BGA). Three BGA goals that are directly involved are:

- **Export markets** – increasing the value of exports, including doubling the value of exports from the primary sector through increases in quantity and per-unit prices
- **Innovation** – making better use of existing and new technologies throughout the productive sector
- **Natural resources** – understanding the value of natural resources to New Zealand and working towards sustainability, which is often calling ‘farming within limits’.

### Achieving the NZVA goal

Capitalising on the innovation opportunity in developing replacements for antibiotics could foster world-leading capability in three inter-connected ways, the first two of which are already leading to encouraging results in New Zealand:

1. **High health husbandry** – demonstrating new farm animal husbandry techniques, including genetic selection to improve animals’ natural immune system and to breed more disease resistant animals.

2. **On-farm technology** – employing new technologies, such as sensor-based technologies that significantly increase early warning of changes and reduce management response times. The growth in the use of animal scanning technology over the past two decades demonstrates how technology can create fundamental (and sometimes unforeseen) flow-on benefits for animal management and health.

3. **Substitution** – replacing existing antimicrobial treatments with innovative therapies.

New Zealand has a strong international reputation and global critical mass in some industries of the land-based sector, particularly dairy. Being among the lowest users of antibiotics on-farm in the OECD, New Zealand is in a relatively good position (as well as having considerable incentive) to take a lead in considering and acting on these innovations. Key to the country’s relatively light-handed use of antibiotics has been regulation, judicious antibiotic prescribing and dispensing for animals and our extensive agricultural systems.

Achieving the goal outlined by the NZVA requires:

- a co-ordinated response to the antibiotic use issue, including developing a scientific and research agenda – drawing on the concepts of One Health and support from other associated professional organisations

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• supporting the collection and analysis of data and engaging with policy makers to create the infrastructure necessary

• supporting the development of new techniques of animal care and innovative technologies to replace antibiotic use.

The NZVA’s position is timely. The AMR problem is exacerbated by (and could, in turn, itself contribute to) several global megatrends and is becoming an increasingly important issue for New Zealand’s land-based sector. Veterinarians’ training and their position at the nexus of the human-animal-environment interaction make them a critically important part of the answer.
Why the urgency?

A developing problem

Antibiotic resistance is a subset of antimicrobial resistance. AMR affects all pathogens against which antimicrobials are used, such as bacteria, viruses, fungi and parasites. AMR infections currently claim at least 50,000 human lives each year across Europe and the US, with possibly hundreds of thousands more dying in other areas of the world.\(^3\) The use and misuse of antibiotics is recognised as one factor in the development of these infections, leading to standard medical treatments becoming ineffective, infections persisting, simple infections becoming life threatening and infections spreading between people and animals.

Misuse of antibiotics is a key concern, contributing to selection pressure and allowing future generations of bacteria to develop resistance. With increased use of antibiotics or with poorly controlled use, the selection pressure increases and, worst case, people and animals can no longer fend off common infections.\(^4\)

According to the WHO, antibiotic resistance has a number of public health consequences with wide implications. Reduced productivity caused by sickness and higher costs of treatment is a drain on the global economy, while labour loss and the increased burden on health services will reduce productivity levels and have flow-on societal and cultural effects.

Economic development also creates new problems. Globalisation and intercontinental travel present new pathways for resistant microbes to spread. Resistance that develops in one organism or location can quickly spread and can have an impact on a range of treatments involving antibiotics.\(^5\)

Having said this, the goal-setting by the NZVA is timely. Although AMR is a developing problem, there is time to develop a sensible plan of action. The close links between animal health, human health and the environment mean the response needs to be cross-disciplinary, requiring considerable shared effort by those in human health, regulatory development, scientific research, pharmaceutical companies, the agricultural sector and, with time, the public.

Lack of exposure

Despite the challenges it poses, AMR has attracted considerably less attention (outside of the scientific community) than other concerns like global warming or poverty. The NZVA’s goal setting is consistent with the growth of the One Health movement in relation to antimicrobial resistance as well as food safety, food security, climate change and the human-animal relationship issues.

An indication of the lack of exposure to this issue is shown in Figure 1, which provides the frequency of the use of a few terms. ‘Global warming’ shows up as much more topical than ‘antibiotic resistance’.

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Figure 1. Google Ngrams for selected terms

The NZVA response
In July 2015 the NZVA, on behalf of the profession, announced the following vision statement:

By 2030 New Zealand Inc. will not need antibiotics for the maintenance of animal health and wellness

The NZVA has identified antibiotic resistance as a significant challenge to the health not only of animals but of humans and the environment. This aspirational line in the sand is a response by the NZVA to highlight the urgency of AMR and promote action on the issue. Its goal is to preserve the efficacy of existing antibiotics through reduction, refinement and replacement of use so that they may be effective when most needed. In the meantime, the challenge is to find alternatives to problematic practices with antibiotic demand and supply.
AMR in a global context

Introduction
Part of responding to the challenge of AMR is placing it in context. To do this, we review megatrends that are shaping our future, and then describe the interactions between the megatrends and the specific issue AMR.

Review of global megatrends
Major economic, cultural, social and scientific changes – pressures - are significantly affecting New Zealand and the world. Behind them are five global ‘megatrends’ that reflect society’s biggest challenges — and opportunities. These megatrends are:

1. Demographic and social change
2. Shifts in global economic power
3. Rapid urbanisation
4. Climate change and resource scarcity
5. Technological breakthroughs

PwC is working with the New Zealand veterinary profession to help understand the role of veterinarians in addressing the problems that these trends highlight. This reflects the profession’s increasingly three-dimensional ‘lens’ on the world, covering animals, the humans who own or care for them and the environment we share.

Three of these megatrends are particularly important as context for the issue of AMR:

- **Demographic shifts** – older people will need more healthcare and larger populations will require more food. Without change, these shifts will increase the use of antibiotics
- **Resource scarcity** – antibiotics are useful for animal production, which takes some pressure off land and water resources. As there will be more pressure on natural resources in the future, attempting to reduce antibiotic use at the same time will be challenging
- **Technological breakthroughs** – new technology around sensors, data, biological advances and information may allow more targeted disease treatment and improved animal production. Benefiting from these innovations will require smart, trained people.

AMR and megatrends – how they relate

**Demographic and social change**
By 2030, the global population is expected to reach 8.3 billion. The world will need 50% more energy, 40% more clean water, 35% more food and (broadly) commensurate increases in production animal numbers.⁶

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Population growth and the emerging middle class afford unique and significant opportunities for growth in New Zealand’s land-based sector to feed the expanding global population. However these growth opportunities also present ongoing challenges in relation to managing risks to the supply chain and risks to the ‘New Zealand Inc.’ brand.

Part of managing the food supply will be managing the use of antibiotics in animal medicine and agriculture, given that antibiotics have been part of the suite of technologies that have led to the large increases in productivity and animal welfare improvements over the last several decades. Meanwhile, concern about antibiotics and resistance has the potential to become a major consumer issue, and potentially even a market access or regulation issue. New Zealand exports nearly all of its milk and meat production, so maintaining the confidence of, and access to, overseas consumers is vital. The UN Food and Agriculture Organisation projects that the world will need 70 percent more food by 2050. Up to a third of the increase in animal production by 2050 will be met by shifting production practices to more intensive agricultural techniques.7

Resource scarcity

The demographic shift needs to be seen against the backdrop of increasing resource scarcity. It is not just that there will be more mouths to feed. We will need to do it with less land, less freshwater and less fossil fuel. In a standard production model, inputs are transformed into outputs. If we want to increase outputs while constraining inputs, we also need increases in productivity and improvements in technology. Antibiotics are one of these resources, and if we want to use them more efficiently – increase the output of food and health while reducing their use – new processes and technologies are needed.

Growing antibiotic resistance has similarities to other global issues such as climate change. This reflects its global scale, humans’ level of responsibility for its causation and the fact that one country’s practices can have a profound impact on the entire process.8

There have been calls to adopt a co-ordinated global approach to the AMR issue similar to that by the Intergovernmental Panel on Climate Change.9 AMR could potentially affect everybody, regardless of where they live, their health, economic circumstances, lifestyle or behaviour. The issue will affect sectors beyond human health, animal health, agriculture, food security and economic development and require

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The One Health perspective

The potential advantages of greater integration ‘across species’ have been identified and documented by individuals involved in the ‘One Health Initiative’ (www.onehealthinitiative.com)...

The mission of the One Health Initiative, as articulated on the group’s web-site, includes fostering joint educational efforts among medical, veterinary and public health schools; joint communication (in publications and conferences, and via networking); joint efforts aimed at clinical care and prevention, and efforts aimed at cross-species surveillance; fostering of comparative medical research; joint development of diagnostic methodologies; and joint advocacy aimed at educating leaders and the public.


One Health Initiative Mission Statement

Recognizing that human health (including mental health via the human-animal bond phenomenon), animal health, and ecosystem health are inextricably linked, One Health seeks to promote, improve, and defend the health and well-being of all species by enhancing cooperation and collaboration between physicians, veterinarians, other scientific health and environmental professionals and by promoting strengths in leadership and management to achieve these goals.

a range of experts including veterinarians, physicians, epidemiologists, microbiologists, pharmacologists, health economists, international lawyers and social scientists.

**Technological breakthroughs**

The pace of technological change is increasing, evidenced by advances in genetics, genomics and sensor technologies, among others. These are beginning to change the way that infections and new types of resistance are detected, diagnosed and reported worldwide.

Such technological advances can help in three ways. First, they may allow faster identification of bacterial infections in human and animal medicine. Secondly, these same technological advances could deliver diagnostic tools which improve the way we use antibiotics. Finally, they also represent potential replacements for antibiotics - innovative ways of dealing with problems that are currently solved with antibiotics.

In the meantime, efforts are being concentrated on maintaining effective and necessary antibiotics. Until new antibiotics or innovative therapies are available, conserving the existing antibiotic resource appears to be the best approach. Maintaining the efficacy of current antibiotics involves promoting and practicing their judicious use in both human and animal medicine, with doctors and veterinarians ensuring or advocating minimal use wherever possible.

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**What the NZVA’s leadership means**

**The NZVA position**

The NZVA has set a clear goal regarding antibiotic use, primarily aimed at the use of antibiotics in preventative treatment.

By 2030 the New Zealand veterinary profession aims to maintain the health and wellness of all animals for which they have duty of care without the need for antibiotics, other than in exceptional or emergency circumstances. The immediate focus is on addressing current usage in clinical, agricultural and environmental settings, which may expose pathogens to selective pressure for resistance.12

Part of this position is acknowledging that the use of antibiotics cannot be stopped overnight – hence the 2030 goal for the routine use of antibiotics in the maintenance of animal health and wellness. Restricting the routine use of antibiotics as a substitute for prevention by other means requires significant planning, research and application of research. This is particularly so given concerns that restricting the use of antibiotics could result in an increased presence of disease on farms, leading to trade issues around the possibility of disease outbreaks.

The NZVA is not advocating for the removal of important disease management processes. Rather, its position is that the gradual removal of antibiotics from the maintenance of animal health and wellness should be promoted through the use of other effective technologies. They also support the use of critically important antibiotics as identified by the WHO only where essential and are promoting further studies to refine ‘essential use’.

Some antibiotics will continue to be necessary for therapeutic use in animals for the foreseeable future, especially because the unknown or unexpected can happen. New diseases arise periodically, and a small proportion of these are bacterial (e.g. Lyme disease, Q fever, food/environmental contamination). New Zealand will inevitably experience invasion by an as yet unknown disease pathogen or pathogens (as happened recently with a strain of the Theileria parasite). The NZVA believes that protecting the efficacy of key antibiotics will ensure their availability for an appropriate emergency response to such an event.

**Achieving the goal**

The NZVA is aiming to achieve minimum use of antibiotics on New Zealand animals based on a five ‘R’ structure: Responsibility, Reduction, Refinement, Replacement and Review. This assumes that the AMR issue is fully recognised.

- *Responsibility* has to be accepted by consensus. Acceptance does not imply any form of blame or guilt but simply understanding that a problem exists, is unsustainable and that a better system must be evolved. Strong partnerships have to be created among all stakeholders - this is not for the NZVA alone.

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• **Reduction** requires more science, innovation and adoption in diagnostics involving public and private investors and education for those involved in animal care: veterinarians, veterinary nurses, carers, owners, sellers, buyers, trainers and regulators.

• **Refinement** in use of antimicrobial treatment requires further study, expanding on learnings from the Reduction efforts. Quick, initial progress can be achieved by use of the 5 ‘Rs’ of Medication: right patient, right drug, right dose, right route and right time (duration as well as timeliness) and through developing and applying better husbandry, nursing and risk management.

• **Replacement** of antibiotic use is the final goal and hinges on determining where, how and when to use other approaches, such as immunity modulators, biologicals (vaccines), genetics and eradication programmes.

• **Reviewing** should be a constant throughout the programme.

Worldwide, the veterinary profession has promoted the concept of One Health to address food safety, food security, antimicrobial resistance, climate change and the human-animal relationship. The profession is well placed to help address antibiotic use because veterinarians work with people, animals and our environments, and often mediate the relationship between the three.

Veterinarians have a unique responsibility to improve the health and welfare of the animals they treat in a manner that also protects human health. There is no other profession dedicated to that function, who can assess the benefits and risks of antibiotic use in animals, and who can explain to their human clients the importance of their judicious use. This means striking a balance between maximising animal health and welfare and minimising AMR.

The principles involved are not new. Two of the Manhattan Principles of 2004, the basis for One Health thinking, call for the following:

- increasing investment in the global human and animal health infrastructure commensurate with the serious nature of emerging and resurging disease threats to people, domestic animals and wildlife
- (ensuring) adequate resources and support for global wildlife health surveillance networks that exchange disease information with the public health and agricultural animal health communities as part of early warning systems for the emergence and resurgence of disease threats.

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The economics of reduction

Where is New Zealand currently?

Early last decade, New Zealand adopted a prudential approach to the use of antimicrobial products in animals in order to address antimicrobial resistance. The New Zealand Food Safety Authority (now Ministry for Primary Industries):

- removed growth promotion as an acceptable use of critically and highly important anti-microbial active ingredients
- introduced veterinary authorisation on any active ingredient it considered to be relevant to antimicrobial resistance
- revised the information requirements for registering antimicrobial veterinary medicines to ensure that the potential for resistance was adequately addressed.

New Zealand has become a low user of antibiotics when compared with other OECD countries for which data are available – among the three lowest users. This level of use reflects regulation, control by veterinarians of prescribing and authorisation practices and how antibiotics are dispensed, and the country’s extensive agricultural systems.

The government’s Business Growth Agenda (BGA) includes a complex goal for agriculture, a key part of our land-based industries that together account for around 60% of New Zealand’s merchandise exports. To meet the targets, farms will need to produce higher quantities of products, and these products will have more value in overseas markets. At the same time, production methods will need to take more account of the limits of the natural environment to provide inputs and receive pollutants – the ‘source’ and ‘sink’ functions of the natural environment. Once we add in the concern about AMR, we are also consciously constraining our use of antibiotics, putting a further limitation on how to achieve the BGA goals.

Increasing agricultural outputs will mean more animals, more production per animal and a higher density of animals per hectare. Increases in animal care will also be required to keep up with the increased demand. With more animals per worker, new types of feed, new systems for feeding and better methods of animal management (such as housing, robotic milking, beef feedlots) may be required. Increased intensification of farming may lead to increased risk of infectious disease, a risk that will require an increased level of management.

A final link between the BGA and antibiotic use concerns overseas markets. Concern about AMR is increasing overseas. Given the rising concern, it may be prudent to take a proactive approach to its effects on the New Zealand Inc. brand. This may involve creating a demonstrable, verifiable commitment to reduced antibiotic use as an effort to future-proof our supply chain. This effort may become necessary just to preserve market access to our preferred export markets. In addition, making a public commitment to addressing AMR could also allow better positioning of New Zealand Inc. products, allowing them to gain or maintain premium prices. Higher prices are one way to achieve the doubling of exports from the primary sector that is sought.

Compared with most other countries it has been relatively easy so far because we have been a relatively low user of antibiotics for animals. Pressure to increase production by more intensification will increase

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pressure for more antibiotic use. The NZVA’s position on antibiotics will counter this pressure, challenging New Zealand to further reduce, refine and replace current antibiotic use in animal health and wellness. This will be, in part, by considering carefully how we increase productivity, and the ultimate sustainability of any and all attempts to do so.

**The economic opportunity**

Economic research on potential impacts of reducing antibiotic use is limited. What evidence is available suggests that economically viable alternatives do exist in agriculture and that the use of these in New Zealand would have a minimal negative economic impact on animal production. However, the benefits of maintaining the effectiveness of antibiotics and protecting market access for agricultural exports are significant for both individual stakeholders and New Zealand as a whole.

Focusing just on replacing antibiotics in agriculture misses the larger opportunity. Addressing AMR could be a chance for New Zealand to innovate and create a competitive advantage, both for the country’s agricultural exports and, more widely, for the science and high-tech sector.

Given New Zealand’s strength as an agricultural exporter and as a relatively low user of antimicrobials in agriculture, the country is well placed to develop and implement innovative alternatives to the use of antibiotics in agriculture, novel approaches which can be used to create higher-value products for export. They can also be the basis for additional technology exports for use in other countries’ agricultural sectors. Meeting the challenge of antibiotic resistance has clear links to the Government’s Business Growth Agenda.

The innovation literature has found that increased connectivity promotes knowledge generation. A place like New Zealand, with a small, connected population, could use its existing networks to great advantage to develop solutions to antibiotic resistance through vaccines, advances in genetics and genomics, sensor technologies, materials technology, improvements in current farm systems and development of animal husbandry. Experience with agricultural innovation in New Zealand suggests that the solution will lie in a combination of techniques and technologies.

Innovation to cope with antibiotic resistance will require people with different skillsets working together to understand the problem, develop solutions and implementing processes and policy. It will also require a willingness by different stakeholder groups to engage in the process. The challenge is not likely to be solved by the science system, private sector or policy makers in isolation. All stakeholders can contribute to create new products, knowledge and technology, and to build the capability and capacity to rapidly adopt and work with them. The NZVA, as a key organisation working at the intersection of people, animals and the environment can serve an important role in co-ordinating activities, promoting agricultural research to produce scientific and economic evidence, supporting the collection and analysis of data and engaging with policy makers. Minimising ‘distance’ between end-users, scientific research and technological development enables end users to express their needs whilst being encouraged to consider opportunities that arise from new scientific knowledge, products or technology – driving further innovation within the end-user value chain.

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A closer look at antibiotic use and reduction

Uses of antibiotics

Use of antibiotics for animals is becoming recognised as a contributor to the development of resistant organisms that result in life-threatening diseases affecting all species. The NZVA is advocating for reduction, refinement and replacement of the use of antibiotics on animals in New Zealand. To understand the implications of the NZVA’s position, it is important to have a perspective on current uses of antibiotics for animals and the possible impacts of changing those uses.

Antibiotic use in animals falls within three broad categories:

- **Therapeutic** - the treatment of an existing medical issue. Continuing this use of antibiotics prudently is consistent with the NZVA’s aspirational vision statement.

- **Preventative** - the control of a disease when it is likely to occur or has started to occur. The NZVA is advocating for reducing preventative forms of antibiotic use and, when possible, substitution. The consequences of continued use are high.

- **Growth promotion** - the use of antibiotics at sub-therapeutic doses to promote growth. This category of use is not considered a problem in New Zealand as antibiotics are not prescribed for this purpose.

These categories of use do not have strictly defined boundaries but blend into each other and require further scientific research and economic evidence to better understand the risks to human health and the benefits to animal health, welfare and production when compared with viable alternatives.

Use of antibiotics for animals contributes to the development of resistant organisms that result in life-threatening diseases in all species (for more detail, see Appendix A). Livestock systems are often seen to be the major contributor. In New Zealand, most antibiotics used in food animals are used in the poultry, pig and dairy industries. However, the degree to which livestock systems contribute to AMR is likely to depend on a number of factors. Increasing problems with use of antibiotics in companion animals are also being reported.

Reducing antibiotic use

A key aspect of the NZVA’s goal to reduce the need for therapeutic use of antibiotics on domesticated animals is reducing disease incidence. Veterinarians can contribute by educating animal farmers and carers on:

- infection risks
- animal management and husbandry
- infection control
- hygiene and biosecurity practices.

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A healthy animal is production-efficient and poses no risk to other animals or carers. Economic benefits (through increased health, production and reduced costs) will flow from better diagnostic processes whereby only infected animals are treated, using the most effective antibiotics judiciously. New Zealand uses approximately 57,000 kg antibiotics annually to treat animals. The exact proportion used for therapy compared with prevention is not known but is likely to be a ratio of approximately one-third for therapy and two-thirds for prevention. New Zealand is probably the third lowest user of antibiotics for animals, for countries that supply data, a consequence of farm systems that promote healthy animals. New Zealand largely farms animals extensively, in low-input-low-output outdoor systems. A low production pressure and lack of high risk internal (housed) environments results in generally healthy animals.

The greatest progress in reducing the antibiotic usage will come from:

- further improving the use of low risk systems for both farm and companion animals
- managing the adoption of any more intensive systems
- applying preventative therapy judiciously
- adopting innovative therapies to replace the use of antibiotics
- using veterinary expertise to educate farmers and carers better.

The economic impacts of changes are important. The impacts may not all be positive, and the affordability of changes could be an issue. Social expectations and demands from customers and value chains may also have an impact, and possibly outweigh simple monetary considerations.

**Companion animals and horses**

Use of antibiotics for companion animals is often overlooked when considering AMR. In New Zealand only 0.5% of antibiotics for animals are used on pet species. This low usage rate is predominantly related to the small biomass of companion animals when compared with production animals rather than reflecting overall health status. The proportion increases slightly when horses are included because of their size. Antibiotic resistance, including to potential human pathogens, is not new in pets and, increasingly, multi drug resistance is being reported in New Zealand from animals such as horses.

Given the low usage rate, it is practical and economic to treat and prevent disease in companion animals with antibiotics. There is also the consideration of the social value: these animals have closer contact with more people than any other animals, wild or farmed.

No assessment of the economic impact of this source of resistance appears to have been made so far, and no assessment of the economic costs of changing antibiotic use seems to have been made.

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23 Ministry of Agriculture and Forestry (2010).
Production animals in New Zealand

Poultry

The poultry sector has revenues of $185 m (2015) and is mainly focused on the domestic market.

New Zealand poultry meat and egg production follows strict guidelines in the use of antibiotics with most use being in intensive production systems. Although many poultry diseases are now controlled by vaccination as opposed to medication, certain diseases including some critical intestinal infections still require metaphylactic control (see Appendix A for an explanation of metaphylaxis). In the poultry industry this involves the administration of antibiotics that are not generally considered critically important to human health (and mostly antibiotics not used at all in humans and not implicated in AMR), in food and water.

Poultry in New Zealand generally have a high health standard and the management of production is hygienic. This is illustrated by falling food-linked human Salmonellosis infections and Campylobacter contamination arising from animal product consumption.

The economic impact of removing antibiotics for all but therapeutic uses is unknown and does not appear to have been studied in a New Zealand context.

Pigs

The pig sector has revenue of $193 m (2015) and is domestically focused.

New Zealand pig production is switching from intensive, housed systems to extensive outdoor systems. Antibiotics are often used in pig/swine production overseas and in New Zealand, with majority of the antibiotics being administered in feed and/or water. The disease spectrum differs between the two systems; however, both systems require complicated health management that necessitates some metaphylaxis.

The occurrence of AMR in bacteria from pigs has been widely reported from intensive systems, with humans involved in the farming enterprise more likely to carry resistant bacteria. The means of any transmission to humans is still unclear, whether by direct contact or via food contamination. With respect to the general population, transfer can only be via food that is improperly handled in production, in retail or in final food preparation. The initial source of resistant bacteria is in animal production, hence the current need for prudent use of antibiotics and increasingly urgent need for non-antibiotic solutions.

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31 Ministry for Primary Industries (2015).


As with poultry, the economic impacts of removing antibiotics in New Zealand pig production do not appear to have been assessed.

**Dairy**

The dairy industry had revenues of $10b in 2015 and supported $14b in exports. It represented nearly one-half the revenue of agriculture, so is a major part of the industry.\(^{34}\)

Dairy animals make up nearly half the national total domesticated animal biomass. Nevertheless, the amount of antibiotics used is somewhat less than 40% of the national total\(^{35}\) even though large dairy cows require large doses.

The largest use of antibiotics for dairy animals is to treat mastitis, a bacterial infection of the mammary gland, although it is only the second most (29% or $273m per year) costly health disorder affecting dairy cows, after metabolic disease.\(^{36}\) New Zealand has one of the lowest incidence rates of mastitis internationally, approximately 20 cases per 100 cows per year. This compares with 45 and 30 cases per 100 cows per year in the UK and USA, respectively.\(^{37}\) New Zealand’s extensive, pasture-based dairy herd has a high health status, one of the main reasons that New Zealand is the third lowest user of antibiotics for animals.

Therapeutic use of antibiotics for mastitis is pragmatic. Antibiotics are the largest component of mastitis costs at 30%.\(^{38}\) Lost milk due to potential antibiotic residues is 19% of the overall cost of the disease. For economic reasons, cows are not treated unnecessarily during lactation, but only treated for health and welfare reasons. Most new infections of the mammary gland occur in the non-lactating season, before the next calving. The most common preventive mechanism for 50 years has been infusion of the udder with a long acting antibiotic preparation immediately after the last milking of the season. This dry cow therapy (DCT) applied to all cows to calve and return to the herd (blanket dry cow treatment) has been long understood to prevent at least 80% of new infections and to cure up to 80% of existing infections.\(^{39}\) DCT accounts for about 4,500 kg of antibiotics annually in New Zealand, or nearly 8% of the total used. This use contributes to the low rate of mastitis in New Zealand, which is up to 60% lower than in other developed dairy countries.

Although blanket DCT is effective, it is indiscriminate. Many animals that are treated are either not infected or unlikely to become infected. This is the kind of widespread, non-therapeutic antibiotic use that the NZVA is aiming to replace. This may soon become important to maintain competitiveness because the European Commission has draft guidelines recommending that no DCT is the default option.

Non-antibiotic alternatives are available and appear to be as good at preventing new intramammary infections during the dry period as DCT in cows that do not have infections at dry off. For example, an internal teat sealant is reported to be clinically effective and economically viable under specific

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\(^{34}\) Ministry for Primary Industries (2015).


\(^{38}\) Buijs (2015).

conditions. One tentative conclusion is that the growing use of non-antibiotic approaches to dealing with mastitis combined with the continuation of therapeutic uses for infected cows is likely to allow farmers to maintain current levels of control. As a result, the dairy sector can probably restrict antibiotic use without a major economic impact.

**Overseas experience**

In researching this report, we found that there were few examples of economic analysis of the potential costs of restricting antibiotic use, and they tended to focus on a few examples. They are instructive because they show that industries overseas have been resilient in the face of changes to permitted antibiotic use. An objection to these examples is that the production systems are different and the starting points for regulations are different. Nevertheless, they show that industries can make changes and still survive.

The experiences of Denmark and the United States provide some indication of the impact of restricting antibiotic use in poultry production. The research suggests that the poultry industries in Denmark and the United States experienced minimal economic impact when antibiotic growth promoters were restricted.

- Denmark was an early adopter of antimicrobial control policies. In 1998, the Danish poultry industry voluntarily stopped using antibiotic growth promoters. For the broiler industry, mortality rates, average weight gains and productivity were not affected by restricted use of antibiotics. However, a small decrease in feed efficiency was observed, this was offset by savings in the previous cost of antibiotics. There have been fluctuations in total antibiotic use since 1998, with 2014 showing the highest use in more than a decade due to increased treatment of disease.

- In the United States, economic research suggested that suspending the use of antibiotic growth promoters did not affect production in broiler operations. A second cost-benefit assessment of growth-promoting antibiotic (GPA) use found that gains produced were not large enough to compensate for the increased cost of feed. There is also evidence that growers not using antibiotic growth promoters were getting paid higher contract prices due to the ability to sell products as ‘antibiotic free’.

Information from overseas producers may also be helpful in understanding potential impacts on pig production:

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• Sweden banned antibiotic growth promoters in food animal production in 1986. Pig producers did report seeing some initial negative results from the ban. While the health of finishing pigs and the cost of producing them remained unchanged, there were negative impacts among weaning pigs.\textsuperscript{46}

• In Denmark, the use of antibiotic growth promoters was banned in finishing pigs in 1998 and in weaning pigs in 2000. The ban had no major effect on productivity or feed efficiency in finishers, but resulted in some loss of productivity in weaners. Production in the sector continued to increase after the ban, suggesting that the ban on antibiotic growth promoters did not harm long-term productivity.\textsuperscript{47} The use of antibiotics has grown as the sector has grown, but total consumption of antibiotics is still below the 1997 level.\textsuperscript{48}

The experiences of Denmark and Sweden suggest that the removal of antibiotics had a small, negative impact on producers, but that the industries learned to accommodate the changes.

\textsuperscript{46} Graham, et al. (2007).
\textsuperscript{47} Graham, et al. (2007).
Acknowledgement

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Appendix A Details on AMR and antibiotic use in animals

What is antibiotic resistance?

In 1928, Sir Alexander Fleming discovered that mould produced a substance that killed bacteria; he later identified this substance as penicillin. By 1940, penicillin had become a revolutionary new drug used to address bacterial infections. As other forms of antibiotics were discovered, these new drugs became the foundation for ground-breaking advances in healthcare. Antibiotics enabled the effective treatment of life-threatening illnesses and infections and reduced the dangers of routine surgery and childbirth. Antibiotics have been equally successful in safeguarding the food supply and preventing, controlling and treating diseases in animals.\textsuperscript{49}

When Fleming first isolated penicillin he was identifying a natural process. A 2011 article in the respected science journal \textit{Nature} showed that natural or inherent resistance to common antibiotics exists in bacteria captured in permafrost 30,000 years ago.\textsuperscript{50} However, acquired resistance, developing in response to exposure to antibiotics, is now allowing some bacteria to survive. The survivors reproduce to create the next generation, producing a population that tends to be less susceptible (or more resistant). Over time, the use of antibiotics can cause selection pressure that can lead to an antibiotic resistant strain of bacteria.

As a result of acquired resistance, standard medical treatments can become ineffective, allowing infections to persist and even spread in the population. Some highly resistant strains of bacteria are leaving health care professionals with limited treatment options for their patients.

While some antibiotic resistance is a natural phenomenon, certain human actions have accelerated the development and spread of resistance. Humankind has made three major contributions to antibiotic resistance:

- the undisciplined use of antibiotics in human clinical settings and their inappropriate use in some parts of animal agriculture
- novel bacteria emerging in new environments as a result of increased human mobility and the frequency of interspecies contact due to urbanisation and changing environmental conditions
- expanding technological capabilities create an enabling environment for microorganisms to more readily and rapidly acquire mutations that can transform them into more virulent and resistant strains.

These trends have created an environment that allows common infectious microorganisms to acquire mutations more quickly and easily, potentially making them deadlier and able to spread rapidly. In essence, these trends are accelerating the Darwinian natural selection of resistance.

Resistance mechanisms are embedded in the genetics of the bacteria. These resistance genes can be transferred between different strains of individual species of bacteria and between different species of bacteria. A resistant strain of bacteria may transfer between host species, such as human to animal or animal to human. The causes and mechanisms of antibiotic resistance are debated widely. However,

\textsuperscript{49} Van Boeckel, et al. (2015).

selection pressure as a general principle is well understood. Every time an antibiotic is used, it can select for the survival of bacteria that have some tolerance to it, and this creates resistance.

In addition, the epidemiology of antimicrobial resistance and antibiotic resistance, and the mechanisms of transfer among humans, animals and the environment are complicated and require a significant level of continued research. At the moment, the science of antibiotic resistance is not fully understood and there are areas of scientific disagreement. There are a number of different pathways for AMR transmission to companion animals, production animals and humans, and for their interaction with the environment (Figure 3).

![How Antibiotic Resistance Happens](http://www.cdc.gov/drugresistance/about.html)

Some research evidence suggests the spill-over of resistant microbes from food animals into human populations.\(^{51}\) There is also recognition that the use of antibiotics in food animals can contribute to human infections by resistant bacteria. However, there is still a lack of evidence that use practices present significant risk to human health.

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\(^{51}\) Teillant & Laxminarayan (2015).
Antibiotics are detectable in the environment as well. Antibiotics have been detected in wastewater, including treated wastewater, sludge and effluent, and soils. There are several sources for these substances: medicines that pass through human patients and are excreted in an active form, waste medicines that are flushed into wastewater systems, and antibiotics that pass through livestock and end up in effluent. In addition, antibiotic resistant bacteria, and even multi-resistant bacteria, have been detected in wastewater and sewage treatment plants.\textsuperscript{52}

Compounding the problem of increasing resistance is a lack of new antibiotics. Resistant infections require alternative and effective antibiotics for successful treatment. However, the pace at which we are discovering novel antibiotics has slowed drastically; no new clinically viable antibiotics have been discovered in the last 30 years. With no new antibiotics available, the existing ones have to do the work – and to work they will need to be used differently.

**Antibiotic use in animals**

The misuse of antibiotics in some parts of animal agriculture is a concern. Most OECD countries have regulatory systems in place to counter the spread of antibiotic resistance, but these systems are not universal. The antibiotic use issue in animals has four components:

- **Therapeutic use** - The treatment of an existing bacterial infection. Continuing this use of antibiotics prudently is consistent with the NZVA’s positioning statement and essential for animal health and welfare.

- **Metaphylaxis** - In any population at any time, a proportion of individuals suffer infection but show no obvious signs of disease. They are not treated because they cannot be diagnosed. These individuals expose all others to infection and can lead to significant episodes of disease. Antibiotics are used in some species and husbandry systems to prevent such events: this is metaphylaxis. The criticism is that these animals and bacteria are exposed to relatively low doses of antibiotics and this can lead to resistant bacterial populations. In many instances such use has been removed by development of vaccines and changes to husbandry systems but significant use of antibiotics still exists primarily with housed animals.

- **Prophylaxis** – Treatment of animals totally in the absence of disease is prophylaxis. It is a preventative form of use where the probability of disease is considered to be particularly high. It has been highly successful in reducing the incidence of certain diseases (for example, mastitis in the dairy cow by use of dry period antibiotics protection, called DCT). However, this practice also treats animals that may not suffer infection. Research is under way and more is needed on, for example, identifying cows at risk of infection or using teat sealants even more effectively. Note that this may also become a possible trade or market access issue: the European Commission has recently proposed that the default position in its dairy industry will be no DCT.

- **Growth promotion** – The growth-promoting properties of antibiotics in farm animals were discovered in the late 1940s. The practice of feeding sub-therapeutic doses of antimicrobials over long periods of time was readily adopted and soon became an integrated part of the production systems developed in industrialised animal husbandry. Concern about the spread of antibiotic resistance through the use of growth promotion techniques was first addressed in the United

Kingdom by the 1969 Swann Report on antibiotics. Antibiotics are not prescribed for this purpose in New Zealand.
\textbf{Appendix B Disclaimer} \\

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