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Culture of Resistance

Australia's response to the inappropriate use of antimicrobials.

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Summary

> *Unless we solve the problem of antimicrobial resistance to drugs, we will be facing a post-antibiotic era where things as common as a strep throat infection or a child's scratched knee could once again kill.*
>
> Margaret Chan, Director-General of the World Health Organization (WHO) 2012.

The term 'antimicrobial' includes antibiotics as well as compounds as diverse as alcohol, hypochlorites (bleach), triclosan, silver and quaternary ammonia compounds. Those of most medical significance are antibiotics, the discovery of which is one of the defining events in medicine in the 20th century, bringing about a massive reduction in the rate of human deaths from infectious bacterial diseases.

But bacteria are increasingly resisting these compounds, with a number of important antimicrobial agents no longer being effective in fighting the bacteria that cause serious illness. This phenomenon is called antimicrobial resistance (AMR). This is a major concern because resistant microorganisms can often multiply unchallenged and kill humans and animals, potentially spread to others, and ultimately impose huge costs to individuals and society. Of greatest concern is creation of disease-causing bacteria with resistance to multiple antimicrobial compounds – so called 'superbugs'. Resistant bacteria can spread from human to human, animal to animal, animal to human or human to animal through direct contact or via the food chain. Wind, water and contaminated soil can also spread resistant bacteria.

NPS MedicineWise made the point in 2012 that "Australians are among some of the highest users of antibiotics in the developed world. Around 22 million prescriptions are dispensed every year – that's a script for every man, woman and child in Australia each year".[1] Australia sits well above the OECD average in its use of antibiotics. Our use is more than double that of Scandinavian countries, but no obvious health benefits are apparent. There are warnings that by 2030 we may not have effective treatments for common illnesses, such as tonsillitis, let alone more serious illnesses like pneumonia; and that life-saving surgery such as bowel surgeries, appendix removal and organ transplants may no longer be able to be performed safely.

Given the gravity of the situation the uninformed observer could reasonably assume that Australian governments past and present would have made this threat to public health a high priority. This is far from the reality.

This policy brief looks at how Australian governments have responded to AMR since the problem became evident in the 1980s. Of particular importance in Australia's response was the 1999 establishment of the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR), which was set up to provide independent expert scientific advice on the threat posed by antibiotic-resistant bacteria to human health by the selective effect of agricultural use and medical overuse of antibiotics.[2] The JETACAR report provided a 'five point plan' covering regulation, monitoring and surveillance, infection prevention, education and research – the basics of which were equally applicable to human and veterinary medicine. The government generally accepted the recommendations of the report, stating that there was international concern about AMR and that Australia needed to respond with strategies that were "consistent with and complementary to global initiatives".

[1] Binns, P and Stowasser, D (2012). *Antibiotic resistance: the end of modern medicine?*
[2] Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) (1999). *The use of antibiotics in food producing animals: antibiotic-resistant bacteria in animals and humans.*

Initially there appeared to be strong commitment to implementing the recommendations of the 1999 JETACAR report, but many initiatives failed to result in any comprehensive systematic response to the issue. Committees, taskforces and groups were set up but disbanded, strategies were developed but not implemented, pilot programs failed to be anything other than pilot programs; undertakings were not carried out.

Of particular concern is the failure to develop a comprehensive national surveillance system of both usage and resistance to antibiotics, as recommended by JETACAR. Such a system provides an essential evidence base for management and appropriate regulation of AMR. Calls for a comprehensive surveillance monitoring system were made as early as the 1980s by the National Health and Medical Research Council (Working Party on Antibiotics). The 1999 JETACAR report recommended the same, and a strategy was developed in 2003. This strategy included a commitment to "ongoing evaluation to monitor progress against the strategy". This did not occur. Another strategy was developed for the then Expert Advisory Committee on Antimicrobial Resistance in 2006. Neither of these strategies appears to have been actioned in any meaningful way. In 2012 a new advisory committee on AMR was set up by the government and its first task was to oversee the production of a scoping study and the development of a business case for national surveillance of AMR and antimicrobial usage. This study was initially set up only to look at issues regarding human health and resistance.

It is of great concern that, despite the calls of the WHO and various other expert groups, so many years have passed and Australia still does not have a national comprehensive surveillance system of the use of and resistance to antimicrobials.

In fact, most of the underlying factors listed by the WHO as drivers of AMR are evident in Australia.[3] These include inadequate national commitment to a comprehensive and coordinated response; ill-defined accountability and insufficient engagement of communities; weak or absent surveillance and monitoring systems; potentially inappropriate and irrational use of medicines, including in animal husbandry; a need for improvement in infection prevention and control practices, as well as insufficient research and development on new products.

For a developed country like Australia this is a significant failure, not only in terms of protecting public health domestically but also in the global fight against AMR.

The Australia Institute's paper concludes that it is necessary to devise a much more accountable and transparent system of management of AMR in Australia if we are to avoid another largely wasted decade. Successful development and implementation of a comprehensive strategy and action plan to reduce AMR requires that there be:

- strong political awareness, leadership and will
- transparent and accountable public sector practice
- one government department or minister with overall responsibility for reducing AMR
- a long-term view and commitment with appropriate and ongoing resourcing
- a coordinated cross-sectoral approach including political, public, community and private interests
- a single independent management body with its own legislative base who reports regularly and directly to the parliament – the body should be empowered to self-initiate reports where necessary and should itself be reviewed, at a minimum, every three years by an independent expert individual or body.

Given the pressing nature of the problem and the catastrophic impact of antimicrobial resistance, effective action must be taken urgently. The current Senate Inquiry into AMR by

[3] World Health Organization (WHO) (2012a). *Antimicrobial Resistance.*

the Senate Finance and Public Administration Committees provides an opportunity for development of a strong and credible Australian response to this global public health threat.

Acronyms and abbreviations

ACSQHC Australian Commission on Safety and Quality in Health Care
AGAR Australian Group on Antimicrobial Resistance
AHMAC Australian Health Ministers' Advisory Council
AHPPC Australian Health Protection Principal Committee
AMR Antimicrobial resistance
AMRSC Antimicrobial Resistance Standing Committee
APVMA Australian Pesticides and Veterinary Medicines Authority
AQIS Australian Quarantine and Inspection Service
COAG Council of Australian Governments
CIJIG Commonwealth Interdepartmental JETACAR Implementation Group
DAFF Department of Agriculture, Fisheries and Forestry
DANMAP Danish Integrated Antimicrobial resistance Monitoring and Research Program
DIISR Department of Innovation, Industry, Science and Research
DOHA Department of Health and Ageing
EAGAR Expert Advisory Group on Antimicrobial Resistance
FAO Food and Agriculture Organization UN
FOE Friends of the Earth
FOI Freedom of Information
FSANZ Food Standards Australia and New Zealand
IDSA Infectious Diseases Society of America
JETACAR Joint Expert Technical Advisory Committee on Antibiotic Resistance
MRSA Methicillin-resistant Staphylococcus aureus
NHMRC National Health and Medical Research Council
NICNAS National Industrial Chemicals Notification and Assessment Scheme
NPS MedicineWise
OAIC Office of the Australian Information Commissioner
OECD Organisation for Economic Co-operation and Development
OIE World Organisation for Animal Health
PBS Pharmaceutical Benefits Scheme
TAI The Australia Institute
TGA Therapeutic Goods Administration
UN United Nations
WHO World Health Organization
WPA Working Party on Antibiotics
WTO World Trade Organization

Antimicrobial resistance (AMR) – why does it matter?

The discovery of antibiotics is one of the defining events in medicine in the 20th century, bringing about a massive reduction in the rate of human deaths from infectious bacterial diseases. Evolutionary processes, however, have ensured that bacteria have begun to resist these compounds, and that an increasing number of important antimicrobial agents are no longer effective in fighting the bacteria that cause serious illness. This phenomenon is called antimicrobial resistance (AMR).

The term microbe generally refers to an organism whose size means it can only be seen with a microscope. Many such microbes or microorganisms are essential for life and important for health, but some cause disease in humans, animals and plants. These mostly take the form of bacteria, viruses, fungi, or protozoa.[4] An antimicrobial is an agent which has the capacity to destroy particular microbes. Antimicrobials include not only antibiotics but compounds such as triclosan, silver and quaternary ammonia compounds. Antimicrobials are used for both humans and animals and in the agricultural sector.

Antimicrobial resistance occurs when populations of microorganisms – such as bacteria, viruses, fungi and parasites – change so that medications used to cure the infections they cause become ineffective. This is a major concern, because resistant microorganisms can often multiply unchallenged and kill humans and animals, potentially spread to others, and ultimately impose huge costs to individuals and society.

Overuse or misuse of antimicrobials is an important contributor to AMR in both human and animal medicine. Resistant bacteria can spread from human to human, animal to animal, animal to human or human to animal through direct contact or via the food chain. Wind, water and contaminated soil can also spread resistant bacteria.

Of greatest concern is the creation of disease-causing bacteria with resistance to multiple antimicrobial compounds – so called 'superbugs'. Bacteria have an extraordinary capacity to adapt to the different challenges presented by antimicrobials, and are theoretically able to develop and share resistance to any type of antimicrobial.[5] Indeed, a strain of the bacterium which causes gonorrhoea, *N. gonorrhoeae*, was identified in 2011 to be highly resistant to all known antibiotics. This strain may soon become a genuine superbug, causing untreatable gonorrhea.[6]

The World Health Organization (WHO), the authority responsible for directing and coordinating health within the United Nations, has been working on global containment of AMR since the late 1990s. The WHO *Global Strategy for the Containment of Antimicrobial Resistance* was the result of a World Health Assembly resolution in 1998.[7] The use of the word 'global' in this title does not refer to geography but rather to a cross-sectoral approach across human and animal health.[8] The WHO highlighted the threat posed by AMR on World Health Day 2011, announcing a six-point policy package to combat the spread of antimicrobial resistance. According to the WHO, AMR is a problem because:

[4] National Institute of Allergy and Infectious Diseases, *Antimicrobial (Drug) Resistance*, (website).
[5] McArthur, JV et al. (2012). *Antimicrobial Textiles.*
[6] Ohnishi, M et al. (2011). *Is Neisseria gonorrhoeae initiating a future era of untreatable gonorrhea? Detailed characterization of the first strain with high level resistance to ceftriaxone.*
[7] WHO (2001). *WHO global strategy for containment of antimicrobial resistance.*
[8] Tapsall, J (2007). *Recent World Health Organisation initiatives for antimicrobial resistance control.*

- infections caused by resistant microorganisms often fail to respond to the standard treatment, resulting in prolonged illness and greater risk of death
- AMR reduces the effectiveness of treatment because patients remain infectious for longer, thus potentially spreading resistant microorganisms to others
- AMR threatens a return to the pre-antibiotic era, with many infectious diseases at risk of becoming uncontrollable
- AMR increases the costs of healthcare as a result of more expensive therapies being needed and longer duration of illness and treatment
- the achievements of modern medicine are put at risk by AMR – without effective antimicrobials for care and prevention of infections, the success of treatments such as organ transplantation, cancer chemotherapy and major surgery would be compromised
- AMR threatens health security and damages trade and economies as the growth of global trade and travel allows resistant microorganisms to be spread rapidly to distant countries and continents.

The WHO states that the underlying factors that drive AMR include:

- inadequate national commitment to a comprehensive and coordinated response, ill-defined accountability and insufficient engagement of communities
- weak or absent surveillance and monitoring systems
- inadequate systems to ensure quality and uninterrupted supply of medicines
- inappropriate and irrational use of medicines, including in animal husbandry
- poor infection prevention and control practices
- depleted arsenals of diagnostics, medicines and vaccines, as well as insufficient research and development on new products.[9]

AMR is of particular concern when pathogens are resistant to antimicrobials, which are critically important in the treatment of human disease. In order to inform risk management strategies, the WHO has developed a list and categorisation of drugs according to their importance in human medicine. Antimicrobial drugs are categorised as critically important, highly important and important.[10]

Australia's response to AMR

In the early 1980s, the National Health and Medical Research Council (NHMRC) established a working party (WPA) to look at use of antibiotics in stockfeed. This came about because of concern in the UK about resistant and multi-resistant *Salmonella* species being selected in food animals and spreading to humans. A number of recommendations were made by the working party regarding resistance surveillance and scheduling, but none of the recommendations were directly adopted.[11] The group gave advice to government until 1997, when the NHMRC decided the work was no longer a priority. After this time the Therapeutic Goods Administration (TGA) took responsibility for the WPA and provided expertise on the issue. Evidence from Europe showing an association between a stockfeed containing an antibiotic, avoparcin, and vancomycin-resistant enterococci in humans resulted in the establishment of a Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) in 1999 by the then Minister for Health and Aged care Dr Michael Wooldridge and the then Minister for Agriculture, Fisheries and Forestry Warren Truss. The report of this

[9] WHO (2012a).
[10] WHO (2007).*Critically Important Antimicrobials for Human Medicine: Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use.*
[11] Turnidge, J (2007). *Australian Government attempts at regulatory and other control of antimicrobial resistance.*

committee*, The Use of Antibiotics in Food-Producing Animals: Antibiotic-Resistant Bacteria in Animals and Humans* ('the 1999 report') contained a broad set of recommendations aimed at reducing the incidence of AMR in Australia. It covered both the use of antibiotics in humans and in animals. In response to the recommendations of the 1999 report a number of committees were established and pilot surveillance programs initiated, but this effort was not sustained.

The Australasian Society for Infectious Diseases and the Australian Society for Antimicrobials conjointly convened the Summit on Antimicrobial Resistance in 2011. It was pointed out that, while the JETACAR blueprint had initially resulted in action, the "effort (had) now dissipated and the committees disbanded" and "(t)he problem of resistance as a public health threat (had) increased significantly over the last decade and local solutions (were) needed more than ever".[12]

NPS MedicineWise has also been strong in its call for action, arguing that Australia sits well above the OECD average in its use of antibiotics. Our use is more than double that of Scandinavian countries, though no obvious health benefits are apparent.

> *Australians are among some of the highest users of antibiotics in the developed world. Around 22 million prescriptions are dispensed every year – that's a script for every man, woman and child in Australia each year.*[13]

It has warned that by 2030 we may not have effective treatments for common illnesses, from tonsillitis to the more serious illnesses such as pneumonia, and that life-saving operations such as bowel surgeries, appendix removal and organ transplants may no longer be able to be performed safely.[14]

Highly transmissible antibiotic resistant bacteria have developed not only in hospital settings but also in community settings. Resistant cultures of Methicillin-resistant *Staphylococccus aureus* (MRSA or 'golden staph') have almost doubled over the last ten years.

Professor Lindsay Grayson, Director of Infectious Diseases and Microbiology with Austin Health and the University of Melbourne, says significant changes in infection control are warranted because an increasing number of patients die as a result of multi-drug-resistant bacteria. He sees multi-resistance as 'almost unstoppable' and includes both the misuse of antibiotics in human and animals, and the abandonment of antibiotic research by the pharmaceutical industry in favour of more profitable 'lifestyle drugs' such as Viagra and anti-cholesterol medications as causes of the problem.[15]

While there is some disagreement about whether human use or animal use is the biggest cause for concern,[16] there appears to be general agreement that successive federal governments have failed to respond appropriately to recommendations of the 1999 report and that the threat to public health is very serious.

In 2012 the Federal Government announced the establishment of a new AMR advisory committee, the Antimicrobial Resistance Standing Committee (AMRSC). This new subcommittee will provide a voice on AMR directly to the Australian Health Ministers' Advisory Council. (Appendix A). The terms of reference and membership were endorsed by the Australian Health Minister's Advisory Council at a meeting in August 2012. It is funded by

[12] Australasian Society for Infectious Diseases, *Antimicrobial Resistance Summit,* (website).
[13] NPS MedicineWise (2012) 1 in 5 Australians expect antibiotics for coughs and colds:new NPS campaign
[14] Binns, P and Stowasser, D. (2012). *Antibiotic Resistance: The end of modern medicine?*
[15] Grayson, L (2012). *Smarter, cleaner approach needed to fight superbugs.*
[16] Duxfield, F (2012). *Superbug threat on the rise through farm animals.*

the Australian Commission on Safety and Quality in Health Care until 30 June 2013, after which time the arrangement will be reviewed.[17]

This paper provides a snapshot of progress since the release of the 1999 report, using information gained through interviews with experts, Freedom of Information (FOI) requests and publicly available information. It does not attempt to provide a technical assessment of AMR in Australia, nor does it claim to be a comprehensive assessment of the implementation of all the recommendations of the report. The first section looks at the report itself and at the committees established as a result of its recommendations. This is followed by an examination of how the use of antibiotics and resistance to them is monitored in both humans and animals and through the food chain. The wide use of antimicrobials such as nano-silver is also covered in this section. The paper then looks at the role of industry, how the broader community has been informed and engaged in the process and concludes with recommendations for ensuring greater accountability in future management of AMR in Australia.

1999: a good start

JETACAR was established in 1999 and comprised experts from the areas of human health, veterinary medicine and primary industry. It was set up to provide independent expert scientific advice on the threat posed by antibiotic resistant bacteria to human health by the selective effect of agricultural use, and medical overuse, of antibiotics. It was tasked with assessing the scientific evidence of a link between the use of antibiotics in food-producing animals and the emergence and selection of antibiotic-resistant bacteria and their spread to humans, and to recommend future risk management strategies.[18]

The report, released on 22 October 1999, provided a 'five point plan' covering regulation, monitoring and surveillance, infection prevention, education and research – the basics of which were equally applicable to human and veterinary medicine. The plan was underpinned by 22 recommendations for an antibiotic resistance management program. The government generally accepted the recommendations of the report, stating that there was international concern about AMR and that Australia needed to respond with strategies that were "consistent with and complementary to global initiatives". The 1999 report, while listed under the 'Historical Publications' archive on the website of the Department of Health and Ageing (DOHA), is still an important reference for Australia's response to AMR.[19]

Recommendations of the 1999 report did initially result in action, but it is difficult to get a clear picture of what exactly has happened since JETACAR was formed. Apart from a progress report in 2003, no overall and ongoing assessment of progress has been made available or, apparently, even undertaken. It appears the initial intention was that such assessment would occur and that progress would be made publicly available. An 'Implementing JETACAR' website was launched in March 2001 by the NHMRC – "to keep stakeholders informed" – but it no longer exists and it is unclear when or why it was taken down. Despite the JETACAR report including recommendations on communication (Recommendations 19 and 20), there has been no easily accessible and traceable record of implementation of the recommendations.

After the 1999 report was released there was a concerted effort to establish administrative structures that would support implementation of the recommendations. The range of committees established, strategies developed and pilot programs set up (Appendix B)

[17] Wright, P (2012). *Answers to Estimates Questions on Notice, Health and Ageing Portfolio,* p. 72.
[18] JETACAR (1999).
[19] Natale, R (2012) *Answers to Estimates Questions on Notice, Health and Ageing Portfolio*, Questions E12-276.

indicates that, at the time, there was recognition that cross-jurisdictional and interdisciplinary collaboration was essential. None of these committees still exist.

In answer to a question on notice submitted by Senator Richard Di Natale, it was stated that the AMR-related committees referred to above had been wound up because "… they had essentially done their job and as a result of other emerging health protection priorities" and because "Many committees are time limited … the department … conducts reviews of its committees structure to improve efficiency."[20]

The answer also stated that the work of the original committees was not handed on because "existing committee structures were used to provide advice on AMR-related issues as matters have arisen."

No detail or evaluation of this approach was provided with this answer to Senator Di Natale's question. Given the concerns of expert groups about the lack of progress since JETACAR,[21] it is arguable that the department's approach has not been effective and its optimism about continued action is misplaced.

If 'efficiency' is assessed against the benchmark of establishing effective coordination, comprehensive monitoring and surveillance and reduction of AMR in Australia, it is questionable that the committees have "done their job". It is also questionable that departmental reviews have improved efficiency. The reference to "other emerging health protection priorities" casts doubt on how seriously the threat of AMR is taken by DOHA and the Australian government. It is not clear which emerging issues the government thinks are more important than AMR; but Margaret Chan, Director-General of WHO, made the point earlier this year in a speech she gave at an EU conference:

> *Unless we solve the problem of antimicrobial resistance to drugs, we will be facing a post-antibiotic era where things as common as a strep throat infection or a child's scratched knee could once again kill.*[22]

Given that the government has recently established an AMR advisory committee, in the form of the AMRSC, it is interesting to note that a similar advisory committee was set up in 2001 – the Expert Advisory Group on Antibiotic Resistance (EAGAR). This committee was tasked with providing advice to Commonwealth, state and territory and Commonwealth statutory organisations and was to work closely with other newly established committees to develop and implement the national antibiotic resistance management program. During 2001, EAGAR developed and commenced the use of a protocol to assess the risk of antibiotic resistance developing in new and existing antibiotics. EAGAR was discontinued after two NHMRC triennial cycles, according to Professor Mary Barton of the School of Pharmacy and Medical Sciences at the University of South Australia:

> *EAGAR worked hard to drive the implementation of the recommendations (although it was not EAGAR's brief to do so) but was discontinued after two NHMRC triennial cycles. Now there is no Australian focus on antibiotic resistance and the issue has dropped off the political agenda.*[23]

[20] Natale, R (2012). Questions E12-277.
[21] Antimicrobial Resistance Summit (2011).
[22] Chan, M (2012), Keynote address.
[23] Barton, M (2010). *Antibiotic Resistance in Australian Animals in 2010 - What lies ahead?*

The new advisory committee, AMRSC, unlike EAGAR, does not appear to have any direct role in current regulatory processes.[24]

A positive initiative, in 2006, was the establishment of the Australian Commission on Safety and Quality in Health Care (ACSQHC). It is funded by the Commonwealth, state and territory governments to develop a national strategic framework and associated work program that will guide its efforts to improve safety and quality across the healthcare system in Australia. According to the answer provided in Budget Estimates to Senator Di Natale, ACSQHC has supported activities to reduce AMR under its Healthcare Associated Infections Prevention Program through a number of initiatives, all of which are related to human health.[25] Unfortunately, the Commission does not appear to have a leadership role in ensuring overall coordination of an Australia-wide AMR reduction strategy. The 1999 report stressed the importance of such an overall approach, including in monitoring and surveillance. The following section looks in more detail at this aspect of government responses to the 1999 report.

Monitoring and surveillance of use of antibiotics and antimicrobial resistance

Surveillance of AMR is regarded by the WHO as a fundamental requirement for any control of the problem. It also stresses the need not only for surveillance of resistance in bacteria but also for monitoring of the use of antimicrobials and how well this use is applied.

According to the 1999 report, an internationally acceptable and scientifically defensible Australian continuous surveillance program is essential to facilitate management of bacterial antibiotic resistance.[26] The report stipulated that, for effective action and development of strategies to deal with AMR, there has to be comprehensive monitoring of both usage and resistance patterns and argued that interpretation of resistance trends was difficult in the absence of reliable data on use of antibiotics. While some data can be relatively simple to collect, such as the volume of antibiotics imported into Australia, the collection of other data requires multiple sources. Multiple sources are accessed for human medicine but few of these sources exist in veterinary medicine and livestock production.

The 1999 report called for an improvement in monitoring and surveillance not only of the medical area but also food-producing animal and veterinary areas with emphasis on establishment of food chain – including imported food – and environmental connections such as groundwater, as well as molecular studies of resistant genes. It was also pointed out in the 1999 report that the federal government did not have the legislative power or resources to collate information held by states and territories or, increasingly, information held by the private sector; and that the effects of deregulation and a ‘user pays’ approach meant new cooperative systems had to be devised. It is unclear whether progress has been made in developing the above recommended cooperative systems, or any other systems which could remedy the situation. But it is clear that there is still no comprehensive system of continuous surveillance of usage and resistance patterns in Australia.

The 1999 report was not the first time an expert advisory committee had recommended that an Australian government establish a surveillance system for antibiotic resistance. As early as the 1980s, the NHMRC’s working party on antibiotics had made such recommendations.

[24] Senate Community Affairs Committee (2012), *Answers to Estimates Questions on Notice, Health and Ageing Portfolio.*
[25] Di Natale, R (2012). Questions E12-276.
[26] JETACAR (1999).

According to Professor John Turnidge, Australian National University Professor of Infectious Diseases and Chair of JETACAR, "none of these recommendations were adopted directly".[27]

In response to the 1999 report, a surveillance strategy was released by the Australian government in 2003: Strategy for Antimicrobial Resistance Surveillance in Australia.[28] In its introduction it stressed the importance of national surveillance and a coordinated cross-sectoral approach. It recognised the need to strengthen existing networks across a number of sectors including human and animal health, industry and other stakeholders. The strategy also included a statement on the need for ongoing evaluation.

> *An ongoing evaluation process should monitor progress against the strategy. The performance of the strategy will be monitored against performance indicators that will be outlined in the detailed action plans for each of the four surveillance areas. Progress against the Strategy will be regularly reported by CIJIG on the Implementing JETACAR website, to the Communicable Diseases Network Australia, the Public Health Laboratory Network and other relevant bodies including the Australian Health Ministers' Conference and the Primary Industries Standing Committee, as required.*

Despite this commitment to undertake evaluation, the answer to a question on notice asked by Senator Di Natale reveals that there has been no such evaluation of this strategy produced by any government since that time.[29] In that answer it was stated, however, that regular surveillance updates were provided to the EAGAR. The answer did not go into detail about dates of these surveillance updates, their public availability, what has happened since EAGAR's funding ceased or what happened to the 'Implementing JETACAR' website.

Given the lack of any publicly available record of action on this strategy it is therefore of interest to note that EAGAR itself had a separate report prepared in August 2006, entitled: 'A comprehensive integrated surveillance program to improve Australia's response to antimicrobial resistance'.[30]

In answers to an FOI request submitted by The Australia Institute seeking access to any response – formal or informal – from DOHA to this report, the department replied, "despite an extensive search, the Department has been unable to identify any documents relevant to your request".[31]

It was also stated that the August 2006 report was not an official NHMRC publication, it did not complete the NHMRC formal approval processes and that the NHMRC accepted the report as advice from EAGAR and did not release it for public use: "However the NHMRC did release the report to a number of interested agencies, including the Department, for information only."[32]

The Australia Institute sought clarification as to whether this meant there was in fact "any discussion at all" about this report, even if it was, as explained, "for information only". The response from the department to this request from The Australia Institute was as follows: "In response to your request for clarification, we didn't identify any documents through the FOI search which discussed the report and its recommendations".[33] This response indicates that

[27] Turnidge, J (2007).
[28] Hundy, R and Roche, P (2003). *Strategy for Antimicrobial Resistance Surveillance in Australia Communicable Diseases Intelligence.*
[29] Natale, R (2012). Question E12-281.
[30] Webber, J (2006). *A comprehensive integrated surveillance program to improve Australia's response to antimicrobial resistance.*
[31] Email to TAI from DOHA, May 25, 2011 (correspondence pertaining to FOI request).
[32] Email to TAI from DOHA, June 28, 2011 (correspondence pertaining to FOI request).
[33] Email to TAI from DOHA, June 22, 2011 (correspondence pertaining to FOI request).

the August 2006 report was accepted by the government as "information" from EAGAR, the appointed expert advisory group, but that no action was taken by the department to respond to this work, or even, apparently, to discuss its contents or possible use in policy development. It is unclear why the report did not undergo the formal approval process of the NHMRC.

It is also unclear why the above mentioned 2003 report, 'Strategy for Antimicrobial Resistance Surveillance in Australia' or the 2006 'A comprehensive integrated surveillance program to improve Australia's response to antimicrobial resistance', did not result in a comprehensive and coordinated system of surveillance in Australia as recommended in the 1999 report. The first initiative of the recently established AMRSC is to oversee the production of a scoping study and development of a business case for national surveillance of AMR and antimicrobial usage. This study will initially look only at issues regarding human health and resistance.[34] It is unclear when or how a broader examination of related animal and environmental issues will be undertaken. While such research is critical, the above documented history indicates that the development of such strategies is no guarantee of the system change recommended in the 1999 report.

The following section looks in more detail at some examples of past and present monitoring and surveillance programs in both the human and animal sectors and in food.

Human use of antibiotics

Australia has undertaken a number of initiatives to support prudent use of antimicrobials – including through regulation, antimicrobial stewardship programs,[35] therapeutic guidelines and education programs – but the rate of usage remains high. NPS MedicineWise has been strong in its call for action on AMR, making the point that Australia sits well above the OECD average in its use of antibiotics. Our use is more than double that of Scandinavian countries – but there are no obvious health benefits arising from the higher usage.

> *Australians are among some of the highest users of antibiotics in the developed world. Around 22 million prescriptions are dispensed every year – that's a script for every man, woman and child in Australia each year.*

At the time of the 1999 report, basic information on human use of antibiotics was collected by the TGA through importation data (no antibiotics are produced in Australia) and human use was recorded under the Pharmaceutical Benefit Scheme (PBS). Other information was available through sales data, prescriber surveys and specific projects. According to the 1999 report, "antibiotic resistance of bacteria isolated from medical sources was surveyed in a series of loosely connected programs established by a variety of interested groups".[36] The report also found that while there was "no overall coordination", the information formed the basis for an integrated national program of surveillance of resistant bacteria in combination with animal and environmental data.

A number of these programs continue to collect data, including the Australian Group on Antimicrobial Resistance (AGAR), the Australian Hospital Morbidity Database managed by the Australian Institute of Health and Welfare, the National Antimicrobial Utilisation Surveillance program (NAUSP) managed by the South Australian Department of Health, the National Enteric Pathogen Surveillance Scheme (NEPSS) managed by the Microbiological Diagnostic Unit at the University of Melbourne and the SENTRY program. The human use of antibiotics is a significant cause of the development of AMR. According to Marilyn

[34] Senate Community Affairs Committee (2012).
[35] Duguid, M and Cruickshank, M (2011). *Antimicrobial stewardship in Australian hospitals.*
[36] JETACAR (1999). p. 125.

Cruickshank from ACSQHC, Australia still does not have a coordinated approach to antimicrobial resistance and antibiotic usage.[37]

This point was powerfully made recently by Thomas Riley, Professor of Microbiology at the University of Western Australia, when he said the extent of the presence of a newly arrived deadly superbug known as 244 is unknown, due to inadequate testing, and that up to 40 per cent of serious cases are possibly being missed in New South Wales. Prof Riley suspects imported food could be responsible for spreading the bug.[38]

It is useful to note that when appropriate action is taken, the incidence of AMR can be reduced. For example, the Australian policy limiting access to quinolones has been acknowledged internationally as a successful policy intervention.[39] Restrictions on the use of quinolones in humans occur through the PBS and the use of quinolones is not permitted in food-producing animals. These restrictions have been associated with low rates of resistance to this important antimicrobial drug class in Australia.[40] This example shows regulation of supply can have a positive impact on AMR and that, if leadership is shown, changes for the better can be made.

Over the decade since JETACAR was established, it has become apparent that the risk associated with widespread use of antimicrobials in disinfectants and antiseptics also needs to be carefully examined. In particular there is concern that widespread use of antimicrobials such as nano-silver can further build on multiple resistance in bacteria.

Nano-silver

The rapid rise in antibiotic-resistant bacteria has required the increased usage of other antimicrobials in disinfectants and antiseptics within clinical settings – such as hypochlorites, quaternary ammonium compounds, silver and triclosan. Of these antimicrobials, the use of silver at the nano scale (nano-silver), currently plays the additionally important role in the control of infection in particular clinical settings – particularly lining wound dressings and implants (such as catheters and stents). Given the widespread recognition of the value of nano-silver to clinical applications, particularly in light of growing AMR, it is of concern that nano-silver is increasingly being used in household consumer goods, often marketed as 'odour-controlling' or 'antimicrobial'. Nano-silver is used in everyday household items such as toothbrushes, hairbrushes, socks and shoes, sports clothing and towels, cleaning products, computer keyboards, fridges, washing machines, baby bottles and more. It is particularly concerning that widespread household use of products that release lower levels of silver ions, for example dish cloths, baby mats or computer keyboards, may be especially problematic breeding grounds for bacterial resistance.

The Australia Institute submitted an FOI request to DOHA seeking access to documents relevant to the development of policy in relation to the regulation of nano-silver, including any assessment of risk to public health from its increased use. DOHA refused this request on the grounds that the request was too broad and transferred the request to the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) one of the responsible regulatory agencies. This correspondence suggests that DOHA does not have a publicly available risk assessment or policy on the widespread use of nano-silver in products.

[37] Parnell, S (2013). *Superbug onslaught.*
[38] Corderoy, A (2012). *Deadly superbug hits Australia.*
[39] WHO (2012b). *The evolving threat of antimicrobial resistance – options for action.*
[40] Cheng, AC et al. (2012). *Control of Fluoroquinolone resistance through successful regulation.*

This transfer was accepted by NICNAS, with the caveat that "NICNAS is a regulatory agency and will therefore not be able to provide documents relating to the overarching policy of the Australian Government with regard to nano-silver".[41]

Microbiology experts interviewed for the report of Friends of the Earth (FOE) agreed that the widespread use of nano-silver in consumer settings was likely to breed further antimicrobial resistance. Professor Hatch Stokes (UTS), former President of the Australian Society for Microbiology warned:

> *[T]he use of antimicrobials outside of the clinical context indirectly facilitates and further raises the possibility that such resistance genes are going to make their way into very serious pathogens, and at that point, it becomes a major health problem … and if we start using nano-silver quite broadly in the environment, then not only will we have bacteria that are resistant to nano-silver, then I would bet that they'll already be multi-drug [antibiotic] resistant as well.*[42]

Such statements have recently been echoed by the German Federal Institute for Risk Assessment (BfR), calling for greater regulation of the widespread consumer use of nano-silver in consumer goods in order to minimise the spread of antimicrobial resistance.[43] Nanomaterials such as nanoalumina and nano-titanium dioxide have also recently been demonstrated to promote the transfer of resistance genes to multiple antimicrobial compounds between different types of bacteria.[44]

Both laboratory experiments and environmental observational studies have demonstrated that the exposure of bacteria to silver (along with other metals such as mercury) results in an increase in the proportion of bacteria resistant to both those metals and antibiotics.[45]

In 2008, the Minister for Innovation, Industry, Science and Research, Senator Kim Carr, released the Australian Government's 'Objectives for the Responsible Management and Oversight of Nanotechnology'.[46] This document claimed the Australian government would "protect the health and safety of humans and the environment", by continuing to "apply a precautionary approach consistent with Australia's international obligations, including the Rio declaration". However, in spite of these commitments, the management of nano-silver in Australia as a household antimicrobial has been anything but precautionary, as nano-silver remains effectively unregulated.

Given the fact that there is a growing body of evidence that suggests greater caution is needed in relation to the regulation of nano-silver, it interesting to note that FOI documents retrieved from the Department of Innovation, Industry, Science and Research (DIISR) by The Australia Institute reveal a reliance on supportive industry-based evidence rather than independent testing. In December 2010, the Assistant Manager of the Enabling Technologies Section, DIISR, stated to the Health, Safety and Environment (HSE) [nanotechnology] working group:

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[41] Email to TAI from NICNAS, July 27, 2011 (correspondence pertaining to FOI request)
[42] Crocetti, GR and Miller, G (2011) 'Nano-silver: Policy failure puts public health at risk', pp. 10.
[43] German Federal Institute for Risk Assessment (2011). 'Safety of nano silver in consumer products: many questions remain open'.
[44] Qiu, Z et al. (2012). 'Nanoalumina promotes the horizontal transfer of multiresistance genes mediated by plasmids across geners'.
[45] McArthur, JV et al. (2012).
[46] Department of Innovation, Industry, Science and Research (2008). 'Australian Government Objectives for the Responsible Management and Oversight of Nanotechnology'.

> *I am interested in whether we can assertively state that nano-silver is not a nanomaterial of concern based on existing evidence. A recent presentation and submission by a silver industry group to the USEPA is attached. These documents support the argument that nano-silver is well understood and existing oversight is satisfactory.*[47]

Use in animals

Antibiotics are used in both food-producing animals and in companion animals for therapeutic and other reasons. The Australian Pesticides and Veterinary Medicines Authority (APVMA) registers veterinary antibiotic products before they can be supplied, distributed or sold in Australia. The APVMA also has responsibilities after a product is registered, including monitoring use and undertaking reviews when appropriate. A number of such reviews occurred as a result of the JETACAR recommendations. Post-marketing surveillance of resistance for newly registered antimicrobials is not required for drugs in humans or animals.[48] Veterinary use of antibiotics is regulated by label restraints imposed in the federal registration process and by state and territory governments' control of use legislation. The point was made in the 1999 report that this was a concern because there were considerable differences in veterinary chemicals legislation, as well as considerable overlap of responsibilities. This was seen to be a particular problem, "allowing differences in application of off-label prescribing … which can sometimes be inappropriate".

'Off-label' use is defined in the 1999 report as "a use practised by, or prescribed by, a registered veterinarian where the label directions … are varied. For example, use on a different species … or by varying the dose regime".[49]

Regarding progress on this issue, in answer to a question on notice, the Department of Agriculture Forestry and Fisheries (DAFF) stated that:

> *Proposed harmonisation of state and territory veterinarian prescribing and compounding rights is an element of the current Council of Australian Governments' (COAG) reforms for a single national framework for the regulation of agricultural chemicals and veterinary medicines is due to be delivered to COAG by end of 2012.*[50]

The 1999 report stated there was "an urgent need for harmonisation of State/Territory legislation".[51] Why this serious regulatory gap identified 12 years ago is only now being addressed is unclear, but it builds on the argument that implementation of the recommendations of the 1999 JETACAR report has not been given the attention the WHO suggests is warranted.

Initially, Australian regulation of the use of antibiotics in animals was aimed at minimising residues on food, but by the 1980s the potential was recognised for the transfer of resistant bacteria and genes from animals to humans. As a consequence a number of antibiotics were not registered for use in food animals, including fluoroquinolones and gentamicin, and limitations on use for food-producing animals were placed on some other antibiotics. Despite this relatively conservative approach, the extent and seriousness of AMR in both food animals and companion animals is unclear due to poor surveillance systems. Where food animals are intensively reared, antibiotics can be given routinely in food as a preventive

[47] Email to Health, Safety and Environment working group from Assistant Manager Enabling Technologies, Policy Section DIISR, January 29, 2010 (correspondence pertaining to FOI request).
[48] Cheng, A et al. (2012).
[49] JETACAR (1999) pp. 221.
[50] Natale, R (2012). Question E12-280.
[51] JETACAR (1999) pp.97.

measure. The 1999 report agreed there was evidence for the development of resistance in bacteria in animals following antibiotic use, the spread of resistant animal bacteria to humans and the potential for resistant bacteria to be able to cause human disease. A significant number of the recommendations of the 1999 report deal directly with the use of antibiotics in animals. They call for reviews of the use of certain drugs, the tightening of access generally and improved national surveillance. Professor John Turnidge made the point that:

> *Australian antibiotic use in farming, medicine and veterinary medicine is high. During 1992-7 an annual average of 399 tonnes or 56 per cent of all antibiotics by weight was used in stock feed. Humans consumed 251 tonnes or 36 per cent, while 54 tonnes or 8 per cent were used in veterinary therapeutics.*[52]

He also said that while good food hygiene could slow the transfer of resistance it would not completely stop it and that antibiotics should therefore only be given to animals when necessary and for the shortest effective duration.

The regular use of antibiotics in animals is particularly concerning if the antibiotics used belong to the same classes as those used for humans and select for cross-resistance to human antibiotics. The second recommendation of the 1999 report called for a review of glycopeptides (avoparcin), streptogramins (virginiamycin) and macrolides (tylosin, kitasamycin and oleandomyci). Avoparcin and virginiamycin can select for resistance to drugs that are reserved for infections caused by bacteria resistant to multiple other antibiotics (`last-line' drugs). The European Union suspended the use of avoparcin and other drugs including virginiamycin as an in-feed antibiotic. In Australia, the pharmaceutical company Roche voluntarily withdrew avoparcin from the market in mid-2000, but the use of virginiamycin (a streptogramin) continues.

The review of macrolides still appears not to have been completed, despite the 2003 Progress Report[53] on implementation of the recommendations of the 1999 report stating that a review of the use of macrolide antibiotics had begun in 2001. In 2012, committees of the TGA considered a referral from the medicines and chemicals scheduling delegate to consolidate the scheduling of all uses of tylosin in Schedule 4.[54] However they agreed that they were “unable to provide the scheduling delegates informed advice at this stage”. Reasons given in the ‘Delegates Consideration’ included that the APVMA review on macrolides was yet to be completed and that there was insufficient information to make an informed decision. It is also interesting to note that one of the reasons to defer the decision was that a late public submission included “information relevant to determining the risk of antibiotic resistance development, a key issue in the re-scheduling decision”.

This suggests that the failure to complete this review continues to impede regulatory decisions.

Third and fourth generation cephalosporins are last-line drugs for a number of infections and are designated by the WHO as a critical class of drug for which comprehensive risk management strategies are needed most urgently. Despite the concerns of the WHO, third generation cephalosporins such as ceftiofur are currently used in food animals, registered for cattle and used off-label for pigs. Professor Peter Collignon from the Australian National University has recently argued that he is not convinced by claims made by the poultry and cattle farming sector that the use of ceftiofur is minimal. He cites as reasons for his scepticism the lack of any rigorous surveillance and monitoring of use and resistance, as well

[52] Turnidge, J (2001). *Antibiotics in animals - much ado about something.*
[53] Commonwealth Interdepartmental JETACAR Implementation Group (CIJIG) (2003). *Facilitating the Implementation of a National Antimicrobial Resistance Management Program*.
[54] Therapeutic Goods Administration (2012). *Reasons for scheduling delegates' final decisions.*

as the fact that advertisements in trade magazines continue to promote inappropriate use of ceftiofur. A study in 2009 showed a quarter of Australian pig herds were given ceftiofur for treatment of diarrhoea.[55]

The monitoring and surveillance of use of antibiotics in animals was cited as a concern in the 1999 report. At the time of the report there was

> *… no comprehensive national coordinated or standardised collection and collation of animal or environmental antibiotic resistance data. Currently resistant bacteria are selected from the veterinary and medical areas on an ad hoc basis. Environmental isolates are infrequently included.*[56]

In response to JETACAR, the APVMA produced a report in 2005: 'Quantity of Antimicrobial Products Sold for Veterinary Use in Australia, 1999/2000-2001/2002'.

In the introduction to this report the APVMA stated that the JETACAR recommendations

> *… formed the basis of an Australian antimicrobial resistance management (AMR) strategy. An important facet of this strategy is the collection of information on the quantity of antimicrobial products used in veterinary medicine and animal production in Australia. The quantity of antimicrobial used (or antimicrobial load) is one of four factors identified by JETACAR that influence the emergence and spread of antimicrobial resistance. … The APVMA has contributed to the AMR strategy in a number of ways including the collection of information from registrants on the quantity of veterinary antimicrobial products sold in Australia in the period from 1999/2000-2001/2002. This information was voluntarily supplied by registrants.*[57]

The APVMA also stated that it was intended that the information would be collected annually and used as a baseline, which could assist regulatory authorities to:

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

Despite the above commitment for annual collection of this information in order to establish a baseline, no subsequent review has been produced.

[55] Duxfield, F (2012).
[56] JETACAR (1999), p125.
[57] Australian Pesticides and Veterinary Medicine Authority (2005). *Quantity of Antimicrobial Products Sold for Veterinary Use In Australia 1999/2000 - 2001/2002: Therapeutic/Prophylactic Growth Promotants and Anticoccidial Products*. p. 2.

The Australia Institute submitted a FOI request seeking access to any information that had been gathered. In an email dated 1/7/2011 from the APVMA it was explained that: "The APVMA is currently in the process of generating a similar report which covers the period 2005–2010. This report is expected to be completed by October 2011 (for publication / presentation at a conference in November 2011)."

In another letter dated November 2011, the APVMA explained that it had no "statutory obligation" to produce another report.[58]

> *I consider it was the intention at the time that further reports would be published using subsequently collected data. However this has not happened and it is this data that is being sought in this FOI Request. There is no statutory obligation on the APVMA to collect or publish the data. … The APVMA is the custodian of the sales data, owned by private companies. … The data is owned by each registrant of veterinary microbial products and are [sic] providing information on a voluntary basis to the APVMA. The data was originally collected as part of one of the JETACAR report's recommendations to monitor trends in the use of antibiotics in humans and animals.*

Finally, on 26th March 2012, the APVMA provided a draft report, with a letter explaining the context to the material provided.

It was explained that the APVMA was still preparing to publish a report on the sales of antibiotics for the five-year period from 2005 to 2010, (the report that was previously to be have been completed in October 2011), but that it was delayed because, due to an oversight, registrants had not asked whether the antibiotics were used as growth promotants or for therapeutic purposes, and that because information is provided on a voluntary basis, it was "difficult for the APVMA to give a definite commitment for the date of publication of the final report".

The Australia Institute was told the draft report provided was not to be taken "to represent the APVMA's opinions or conclusions in relation to the information contained within it".

The most recent commitment from the APVMA was that the report would be ready by the end of 2012,[59] though at the time of writing, January 2013, the report has still not been made available.

The answers raise a number of issues. First is the fact that, despite an initial commitment to follow through with annual reports of antibiotic sales data in order to assist with the monitoring and surveillance of antibiotic usage in animals, there has been no regular release of such information. It is concerning that the reason given for this failure was that "there was no statutory obligation to collect or publish the data".

The commitment made in the initial review is consistent with the recommendations of the JETACAR report and basic to effective implementation of Recommendation 11: "That a comprehensive monitoring and audit system for antibiotic usage be established that covers all areas of antibiotic use."

It is unclear why the initial commitment to collect data annually was not followed up.

[58] Letter to TAI from APVMA, November 2011 (correspondence pertaining to FOI request).
[59] Natale, R (2012). Question E12-276.

Given the WHO's view on the importance of comprehensive monitoring and surveillance of both use and resistance to antibiotics, it is also concerning that the APVMA must rely on data provided by industry on a voluntary basis. If pharmaceutical companies continue to have the power to decide when and whether information will be provided, even though there is a clear public health interest in comprehensive collection of data, an evaluation must be made of the voluntary system in terms of both the accuracy and timeliness of data provision.

This could assist in informing policy relating to whether an alternative approach is necessary. For example, meaningful data could be collected if veterinary surgeons were required to record all usage of antimicrobials, including in companion animals, and provide that data to a central authority for collation. Recommendation 3 of the 1999 report suggests that "a much stronger audit trail for antibiotics from the importer to the end-user be implemented".

Once again it seems very little has changed since the 1999 report. Various laboratories, private and public, retain data which can be collected and analysed, but there is no comprehensive surveillance of AMR or antimicrobial use in animals. This results in a lack of data and evidence on which to determine risk and, if necessary, make appropriate regulatory changes in order to minimise inappropriate use and development of AMR and protect the Australian community.

While compared to some countries Australia has taken a conservative approach to the use of antibiotics in food animals, there is general agreement that resistance to some antimicrobials has developed in animals in Australia and that careful monitoring and surveillance is urgently needed.[60] More recently, Professor Lindsay Grayson expressed concern about several patients who had come in from country towns in Victoria with multi-resistant infections, concluding that, as they had not been travelling out of Australia, the source was most likely the local food chain.[61]

Intensively farmed food animals and antibiotic use

The use of antibiotics for extensively grazed animals and pets is usually similar to use in humans – that is, antibiotics are used to treat individual sick animals when necessary. However for most intensively farmed animals such as pigs, poultry, feedlot cattle and some fish, antibiotics are given to groups of animals in feed or water.[62] The 1999 report points out that such use can have animal welfare and disease prevention benefits and also that intensive farming can have environmental benefits such as reduced pressure to clear land. It also looks at alternatives to antibiotics including vaccination.

A 2010 UK report found that use of antibiotics in the intensively farmed pig sector in the UK was 115 times higher than in sheep farming, where grazing was the common production method.[63]

A recent systematic review of over 200 research articles comparing the health effects of organic and conventional foods found that conventional chicken and pork have a higher risk for contamination with bacteria resistant to three or more antibiotics than the organic alternatives. The review concluded by noting that this "increased prevalence of antibiotic resistance may be related to the routine use of antibiotics in conventional animal husbandry".[64]

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[60] Barton, M (2010).
[61] Duxfield, F (2012).
[62] JETACAR (1999) pp. xviii.
[63] Friends of the Earth (2010). *Factory Farming's Hidden Impacts*.
[64] Smith-Spangler. C et al. (2012). *Are Organic Foods Safer or Healthier Than Conventional Alternatives?: A Systematic Review.*

The WHO considers that routine prophylactic use of antimicrobials should never be a substitute for good animal health management, and prudent use guidelines internationally support the principle that antimicrobial use should not be used to compensate for poor or deficient husbandry methods.[65] If one of the aims of an AMR strategy is to reduce unnecessary use of antibiotics, an analysis of the relationship between Australian farming methods and antibiotic use would seem to be a relevant area of interest, as would regular auditing of the adequacy of animal husbandry methods**.**

Any such auditing would require there be clear information about the purpose of the use of antibiotics. For example in its glossary of terms the JETACAR defined:

- therapeutic use as, "The use of antibiotics for the purpose of inhibiting a pathogen(s) which already infects the host; that is, initiating treatment because there is a disease condition", and
- prophylactic use as, "The use of antibiotics … to prevent infection with a pathogen(s) that is anticipated to challenge the host during the treatment period; that is initiating treatment in advance of an actual infection or disease condition before such a condition is expected to occur if treatment is withheld".

However DAFF, in answer to a question on notice from Senator Richard Di Natale[66] regarding collection of data on use of antibiotics, stated that "the boundary between 'prophylactic use and therapeutic use' is not always clear". In later questioning through Estimates[67] in October 2012, Dr Bryce from the APVMA agreed that the distinction between prophylactic and therapeutic use was clear, but that there can be a 'grey area' between prophylactic and growth promotion use in some products. Some countries such as Sweden have banned the use of antibiotics for growth promotion.

DAFF also stated that it "has not conducted an analysis of antibiotic use for different farming systems".[68]

Aquaculture

Aquaculture is a growing industry in Australia, as pressure on wild fish numbers limits fishing opportunities. Common species now being farmed include salmon, tuna, prawns and oysters as well as abalone, barramundi, yellowtail kingfish, mulloway and mussels. Methods often involve high-density farming in sea cages or off-shore pontoons, onshore or estuarine ponds, racks and ropes or onshore tanks, dams and ponds. This intense farming increases the risk of disease and thus the pressure to use antibiotics, which in turn increases the risk to people from antimicrobial-resistant bacteria developing in the fish and being present on seafood they purchase.[69]

No antimicrobials are specifically registered for commercial fish and aquaculture in Australia but in 2009 the APVMA issued minor-use permits for oxytetracycline by injection for finfish and florfenicol in medicated feed for salmon, trout and barramundi.

Concern about the use of antimicrobials in aquaculture has been evident since the 1999 report. In response to a 2007 request from Food Standards Australia and New Zealand (FSANZ) for advice on the presence of antibiotics in imported seafood, EAGAR stated that:

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[65] Teale, CJ and Moulin, G (2012). *Prudent use guidelines: a review of existing veterinary guidelines.*

[66] Rural and Regional Affairs and Transport Committee Budget Estimates (2012) Question on Notice 272.

[67] Bryce, A (2012) *Rural and Regional Affairs and Transport Committee Estimates*, pp 73.

[68] Rural and Regional Affairs and Transport Committee Budget Estimates (2012) Question on Notice 268.

[69] Barton, MD and Ndi, O (2012). *Can we feel it in our waters? Antimicrobials in aquaculture.*

> *There is a lack of testing in locally farmed seafood for unlicensed antimicrobials. Although no antibiotics are registered for use in aquaculture in Australia, there is evidence for significant off-label use and support for the view that there is a risk of transfer of resistant bacteria to humans from consumption of aquaculture products. (Akinbowale et al.2006). … the NHMRC would encourage FSANZ in future surveys to include both domestic and imported samples and to monitor not only the presence of antibiotic residues but to assess the patterns of resistance in the microbes present.*[70]

A subsequent assessment of the occurrence of resistance to antimicrobials in bacteria from aquaculture species and environments in Australia found resistance to a number of antimicrobials, including ampicillin, amoxicillin, cephalexin and erythromycin, oxytetracycline, tetracycline, nalidixic acid and sulphonamides. Multiple resistance was also observed.[71] These findings indicate that, even though no antibiotics are registered for use in aquaculture, there has been significant off-label use. This has potential implications for human health when fish are eaten and farm run-offs contaminate the environment.[72]

The *Sydney Morning Herald* reported in 2007 that eight tonnes of antibiotics were used in salmon and trout farms in the first three months of 2007. Off-label use is restricted to treatment of a single animal and mass medication is prohibited, yet examples of mass medication have been documented, such as treatment of barramundi with "erythromycin administered in the feed for seven days at … 75mg/kg fish daily".[73]

Concern about the use of antibiotics in aquaculture has recently resulted in the World Organisation for Animal Health (OIE) adopting a prudent use guideline specifically for the use of antimicrobial agents in aquatic animals. This recognises the need for involvement of aquatic animal health professionals in prescribing antibiotics. The Food and Agriculture Organisation of the United Nations (FAO) also reviewed the use of antimicrobials in aquaculture – recommendations of the review included that the responsible use of antibiotics in aquaculture required therapeutic use only, replacing prophylactic use with good husbandry practices.[74]

Monitoring and surveillance of the use of antibiotics in aquaculture in Australia is inadequate. Apart from one study,[75] there is no published information on the extent of antibiotic resistance associated with Australian aquaculture.[76] DAFF conducts an annual survey – the National Residue Survey – but only for residues of antimicrobials, heavy metals and pesticides. Because Australia does not test for antimicrobial resistance in local food products, including aquaculture, it cannot, under World Trade Organization (WTO) rules, test bacteria from imported food products for antimicrobial resistance.[77]

Resistant bacteria in food

In the 1999 report, Recommendation 10 specifically stipulated the need to include the food chain in the overall surveillance system. FSANZ, state and territory governments and the

[70] Letter from NHMRC Professor Warwick Anderson to FSANZ, September 3, 2007 (correspondence pertaining to FOI request).
[71] Akinbowale, OL et al. (2006). *Antimicrobial resistance in bacteria isolated from aquaculture sources in Australia.*
[72] Ndi, OL and Barton, MD (2011). *Incidence of class 1 integron and other antibiotic resistance determinants in Aeromonas spp. from rainbow trout farms in Australia.*
[73] Barton, MD and Ndi, O (2012).
[74] Teale, CJ and Moulin, G (2012).
[75] Akinbowale, OL et al. (2006).
[76] Akinbowale, OL et al. (2007). *Diversity of tetracycline resistance genes in bacteria from aquaculture sources in Australia*.
[77] Barton, MD and Ndi, O (2012).

Australian Quarantine and Inspection Service (AQIS) share responsibility for ensuring that food is safe and that it complies with standards for microbiological contaminants, pesticides and chemical contamination. Australia sets Maximum Residue Limits (MRLs) permitted in food, recommends withholding periods and monitors compliance through the National Residue Survey. Imported foods are inspected by AQIS and the nature of the testing is dependent on a risk assessment by FSANZ. There are two categories of inspection – 'risk' and 'surveillance'. The 'risk'-categorised food has the potential to pose a high or medium risk to public health whereas the 'surveillance' category is generally considered to pose a low risk to public health and safety. Food is automatically categorised as 'surveillance' food unless categorised as 'risk'. Five per cent of all random surveillance foods are referred to AQIS for inspection and 100 per cent of risk-category foods. In 2007 AQIS requested advice on the risk to public health and safety of low residues of antimicrobial compounds on imported seafood. In this letter the point was made that there was no corresponding MRL established in Australia, therefore making them technically non-compliant. In response, FSANZ concluded that the levels detected were all very low and did not raise safety concerns.[78] The Australia Institute subsequently requested that AQIS provide data relevant to surveillance of resistant bacteria on imported foods. In its response it wrote: "Based on the information I have, testing for antibiotic resistant bacteria has not been done under the Imported Food Inspection Scheme."[79]

Since 1999, pilot surveys of antimicrobial resistant bacteria in food have included, in 2007, the DAFF report 'Pilot Surveillance Program for AMR in Bacteria of Animal Origin' and the Food Science Australia report prepared for DOHA, 'Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food'.

FSANZ also conducted a risk analysis in 2010 of the importation of NZ apples which may have been treated with streptomycin to control fire blight disease. FSANZ found neglible risk to Australian consumers from potential exposure to antimicrobial-resistant organisms.[80]

The pilot 'Surveillance Program for AMR in Bacteria of Animal Origin', developed by DAFF, was part of its response to the Australian government's 'Strategy for Antimicrobial Resistance Surveillance'. Apart from a national antibiotic resistance survey of broiler chickens in 2000 there had been no surveillance system for AMR in animals at the national level. A pilot surveillance program became the major element of a DAFF action plan for AMR surveillance in food-producing animals. The pilot program was to provide baseline information for the period from November 2003 to July 2004 against which similar future surveillance activities in Australia could be compared. The aim was to assess the prevalence of resistance to important antimicrobials among key indicator organisms found in the guts of food animals and was described as a pilot "because it serves the dual purpose of providing initial prevalence estimates for AMR and defines the feasibility and resource requirements for any future surveillance activity".[81] In its discussion of the significance to human health, the report made the point that the data did show some circumstances in the Australian livestock industry where multiple drug resistance in commensal bacteria was common, and while this did not mostly include resistance to important drug classes of antimicrobials, it said, experience abroad suggested that where multiple drug resistance did occur it could eventually incorporate drugs of critical importance in human medicine.[82]

In addition, the report said,

[78] Letter from FSANZ acting CEO to AQIS, September 17, 2007 (correspondence pertaining to FOI request).
[79] Email from AQIS to TAI, September 6, 2011 (correspondence pertaining to FOI request).
[80] Senate Community Affairs Committee (2012) *Supplementary Budget Estimates*, Question E12-222.
[81] DAFF (2007). *Pilot Surveillance Program for Antimicrobial Resistance in Bacteria of Animal Origin.*
[82] DAFF (2007).

> *A formal evaluation of the pilot program will be undertaken by DAFF, in consultation with the Technical Reference Group and EAGAR, to identify the ongoing needs for a full surveillance program for AMR in animals. The evaluation will also take into consideration surveillance activities underway for AMR in humans and food to ensure shared approaches and integration of the three areas of surveillance.*[83]

It is, however, unclear whether the above-mentioned formal evaluation of the pilot program occurred, whether the DAFF action plan is being implemented or whether similar later surveillance activities in Australia have been undertaken.

It is also of interest to note that in a questions and answers document produced by DAFF regarding the findings of the above pilot, the answer to the question of whether antimicrobial residues states that the JETACAR report found that "it was highly unlikely that the consumption of antibiotic residues in food would lead to the development of resistance".[84]

The actual wording of the report is not quite as unequivocal as this answer suggests.

What JETACAR said was that

> *… dietary consumption of microbiologically active residues of veterinary antibiotics is unlikely to be a major factor in the development of antibiotic resistance in humans, although definitive evidence for or against this position is not currently available.*[85]

It is also interesting to note that there was no discussion of potential allergic reactions to residues on food. This was mentioned in the 1999 report – in particular allergy to penicillin residues for those people hypersensitive to this drug, but also possibly for those allergic to cephalosporins through the use of ceftiofur in animals.[86]

A second pilot survey, the 'Pilot Survey for Antimicrobial Resistant (AMR) Bacteria in Australian Food',[87] was prepared for DOHA in 2008. It looked at the presence of AMR bacteria in raw retail poultry, pork chops, beef mince and iceberg lettuce. It claimed to be the first comprehensive survey of its type in Australia, "intended to provide a baseline to look at trends over time".[88]

The survey found that, "overall resistance to the majority of antibiotics was low by international comparison" and "resistance to 'critically important' antibiotics to human medicine … was non-existent or extremely low in bacteria isolated from raw foods".

The qualification was made however that: "The survey data cannot be used to directly provide information about the development of AMR … however it does provide baseline data suitable for future use in the determination of AMR trends at the Australian retail food level."

There does not appear to have been subsequent comprehensive surveys of AMR in retail foods since this survey.

Between April 2006 and March 2007, a survey of chemicals in imported seafood was undertaken by AQIS. AQIS is responsible for the testing of imported foods but takes advice

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[83] DAFF (2007).
[84] DAFF, *Report of the Department of Agriculture, Fisheries and Forestry: Survey for Antimicrobial Resistance in Bacteria of Animal Origin, Questions and Answers, Question 14..*
[85] JETACAR (1999). pp. 123
[86] Catalyst (2003). *Beef Antibiotics.* 24 July 2003
[87] Barlow, R and Gobius, K (2008). *Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food.*

from FSANZ, the responsible agency for ensuring food safety, regarding the level of testing to be undertaken.

In response to the findings of this survey, the following was written by the Acting Chief Executive of FSANZ to the Executive Director of AQIS:

> *Based on dietary modelling, the FSANZ assessment did not identify any major safety concerns associated with the low levels of antimicrobial residues detected. On these grounds, the residues do not constitute a medium to high risk to public health and safety. … The dietary exposure assessment involved comparing estimated dietary exposures with the established reference health standard for each chemical. Based on this assessment for each chemical and a worst case scenario, the quantities of a particular seafood that would need to be consumed before reaching levels near the reference health standard are generally very large. In the majority of cases, the limit is not reached unless hundreds and sometimes thousands of kilograms of a particular seafood are consumed each day over a lifetime.*[89]

However the EAGAR assessment was far more cautious, specifically mentioning the potential for the presence of antimicrobial compounds to lead to bacterial resistance to those compounds:

> *EAGAR noted that the presence of antimicrobial compounds was of concern for all sources of farmed seafood, including domestically produced product. EAGAR expressed concerns particularly about the presence of fluoroquinolone (flumequine, ciprofloxacin and enrofloxacin) residues, which were found predominantly in prawns. EAGAR considers that any development of resistance to fluoroquinolones would constitute a high risk to their efficacy in clinical medicine. … Transfer of quinolone and flouroquinolone resistance genes between bacteria is being described with increasing frequency. … There is obviously a risk of either potentially pathogenic human bacteria that are quinolone or flouroquinolone resistant contaminating the seafood, or of resistance being transferred from non-pathogenic bacteria to pathogenic bacteria in the environment and in those handling the raw seafood.*[90]

EAGAR encouraged FSANZ to, in future surveys, "include both domestic and imported samples and to monitor not only the presence of antibiotic residues but to assess the patterns of resistance in the microbes present".[91]

Regarding the advice from EAGAR, FSANZ stated in a letter to the Executive Director of AQIS that

> *In summary, FSANZ concludes that the levels of antimicrobial compounds detected in the AQIS survey of a range of imported seafood are all very low and do not raise safety concerns. Acknowledging the concerns expressed by EAGAR in relation to the potential for developing antimicrobial resistance through chemical residues in seafood, the preferred risk management approach would be to enhance collaboration between the relevant authorities, to optimise effective enforcement measures and ensure ongoing protection of consumer health.*[92]

It is unclear whether this preferred risk management approach has been implemented or even what it means. It also unclear whether EAGAR's advice was actioned in any meaningful

[89] Stockwell, D (2007), letter to Stephen Hunter, Australian Quarantine and Inspection Service.
[90] Letter from NHMRC Professor Warwick Anderson to FSANZ, September 3, 2007 (correspondence pertaining to FOI request).
[91] Letter from NHMRC Professor Warwick Anderson to FSANZ.
[92] Letter from FSANZ to AQIS, September 17, 2007 (correspondence pertaining to FOI request).

way and whether this proposed enhanced “collaboration between the relevant authorities, to optimise effective enforcement measures and ensure ongoing protection of consumer health” has resulted in the meaningful outcomes necessary for protection of public health in Australia.

In a recent interview, FSANZ Chief Scientist Paul Brent said he did not consider superbugs spreading via the food chain to be a serious risk and that: “There's a small amount of it that may be contributed by food, but the main contributor is doctors overprescribing antibiotics."[93]

Given the above statements of concern from EAGAR and the lack of comprehensive monitoring and surveillance of resistant bacteria in domestic and imported food products, it is unclear what evidence Paul Brent relied upon to inform this statement. His statement stands in stark contrast to the concerns raised by infectious disease doctors such as Dr Peter Collignon and Dr Lindsay Grayson. Dr Grayson has recently suggested that resistant bacteria in animals may be responsible for people from Victorian rural communities being hospitalised with multi-resistant infections more usually seen in people who had been travelling overseas.[94] It is suspected that there may be multiple sources for the introduction of the superbug known as 244, with imported food also implicated.

There has also been evidence of the presence of banned antibiotics in imported seafood, and medical doctors have expressed concern about inadequate testing.

Australian medical experts have raised the alarm over a rising number of Asian fish imports containing banned antibiotics, with a recent consignment of fish from Vietnam being stopped by biosecurity officials because they contained enrofloxin, an antibiotic banned in Australia. Last year, three loads of Vietnamese fish similarly failed tests for banned antibiotics. Prof John Turnidge expressed concern about the potential for such contamination to lead to resistance to antibiotics and criticised the federal government’s low levels of testing.[95]

As previously mentioned, under WTO rules Australia cannot require testing for resistance in imported food products because it does not carry out resistance surveillance in local animal isolates.[96]

The testing for antibiotic-resistant bacteria in food is an important part of monitoring AMR as well as for ensuring food safety. The above description of the various pilot programs and the response from FSANZ indicates that, despite the 1999 report and concerns expressed by the WHO, there is a rather ad hoc approach to decisions about testing for resistant bacteria and a failure to follow up initial surveys. It is concerning that under WTO rules, Australia cannot require regular testing of imported foods because of its failure to do the same with local foods. A comprehensive surveillance program for Australian animals and foods is necessary not only because it would ensure there is a strong evidence base for any domestic regulatory changes but also because it would allow Australia to apply the same standard to imported foods, with testing in the exporting country as well as in Australia.

International comparisons

It is interesting to compare the approach of Australian regulators to those in Denmark. The Danish Integrated Antimicrobial resistance Monitoring and Research Program (DANMAP) was established by the Danish Ministry of Health in 1995. DANMAP reports annually on the

[93] Duxfield, F (2012).
[94] Duxfield, F (2012).
[95] Fyfe, M and Millar, R (2012). *Alarm at antibiotics in fish imports.*
[96] Barton, MD and Ndi, O (2012).

occurrence of antimicrobial resistance in zoonotic, indicator and pathogenic bacteria from animals, food and humans in Denmark. Its objectives are:[97]

- to monitor the consumption of antimicrobial agents for food animals and humans
- to monitor the occurrence of antimicrobial resistance in bacteria isolated from food animals, food of animal origin and humans
- to study associations between antimicrobial consumption and antimicrobial resistance
- to identify routes of transmission and areas for further research studies

Samples are taken from veterinary practices, abattoirs, regional food control laboratories and hospitals and general practice.

The evidence gathered through this comprehensive surveillance has allowed appropriate action to be taken to reduce use of antimicrobials in Denmark. In 1995 Denmark banned the use of avoparcin, and five years later banned all antimicrobial growth promoters for animal feed additives in 2000. The EU Council decided in 2002 that all use of antimicrobial growth promoters cease, starting in 2006.

Prior to an effective control program being introduced, pig production in Denmark was responsible for about 80 per cent of use of antimicrobials. To reduce the use of flouroquinolones and cephalosporins, new guidelines for pig production were introduced in 2005. These guidelines were found not to be effective, so in 2010 they were supplemented by the 'yellow card' system, which meant farmers and veterinarians promoting a high consumption of antimicrobials were issued with a yellow card and subsequently required to develop a plan to reduce use. This system has successfully and significantly reduced the use of antimicrobials in pig production. In June 2010, the Danish Meat Association voluntarily discontinued use of cephalosporins in pig production for two years, resulting in a 50 per cent reduction from 2009 to 2010.

The report also describes the Swedish 'Feedingstuffs Act', which came into force in 1986 and banned the use of antibiotic growth promotants. This ban resulted in animal consumption of antibiotics dropping by 50 per cent. There were no major problems for calves, fattening pigs, turkeys or laying hens, but problems did arise for meat chickens and weaner pigs.

Role of industry

There is concern around the world about the lack of research into new antibiotics. In 2011, scientists from the Infectious Diseases Society of America (IDSA) called for the Congress and relevant US federal agencies to give clear guidance on design and implementation of necessary research on antibiotics.[98]

Pharmaceutical companies are focusing on drugs that are more profitable, such as those used for chronic diseases such as diabetes. In 1990, there were nearly 20 pharmaceutical companies actively researching and developing antibiotics. In 1991, 50 per cent of pharmaceutical companies ended or decreased funding for antibiotic research, and today there are just two.[99]

Recommendation 18 of the 1999 report, which concerns further research, noted that there was "no centrally coordinated antibiotic research facility and that little attention has been focused on clinical and veterinary problems of antibiotic resistance or on possible solutions". This situation does not appear to have changed.

[97] DANMAP, *About DANMAP,* (website).
[98] Infectious Disease Society of America (2012) *Statement of the Infectious Diseases Society of America presented at the Interagency Task Force on Antimicrobial Resistance (ITFAR) Meeting.*
[99] Blanchard, K (2011). *Battling superbugs no longer possible without new antibiotics.*

It is also evident that industry is not always cooperative when attempts are made by regulators to limit the use of the drugs they sell. There has been resistance from the pharmaceutical industry, trade organisations and nations when countries have attempted to ban the use of drugs for public health reasons. For example an EU ban on use of hormone growth promotants was challenged by the US, Canada, and Australia as a third party, through the WTO.[100] The multinational company Pfizer responded with legal action when the Danish government moved to ban virginiamycin and threatened to extend its lawsuit to the rest of the EU, as did pharmaceutical company, Alpharma.[101]

In Australia in 2005, Phibro Animal Health challenged the decision of the APVMA to change regulations regarding the use of virginiamycin by applying for a review of the decision in the Administrative Appeals Tribunal (AAT) – Pfizer Animal Health had sold its interests in products containing virginiamycin to Phibro in 2001. The APVMA had reviewed the future registration of virginiamycin as a result of concerns about the potential to impact on the use of antibiotics in human medicine and in response to JETACAR.

The review focused on "whether continued use of the products would be likely to have an effect that is harmful to human beings, whether the products are effective for the purposes claimed and whether the labels contain adequate instructions."

In Feb 2003 virginiamycin was placed in the S4 (prescription only) category as a result of concerns raised through the review. It was also decided that certain variations to labelling should also occur – that is, label restraint statements which prohibited the use of a product in specific ways.[102]

The APVMA decision was to vary the then recently approved labels for the containers of three particular products – Eskalin Feed Premix for Cattle, Eskalin Wettable Powder Spray-On Feed Premix and Eskalin 500 Feed Premix. The changes included not labelling the products as growth promotants and limiting the period over which they could be administered. Reasons given for this decision were that the APVMA was not satisfied that the labels of the products contained adequate instructions.[103]

The Australia Institute submitted a FOI request to the APVMA seeking information regarding the proceedings of the application by Phibro to the AAT. Phibro Animal Health's arguments included that the APVMA "was wrong in fact and in law" in deciding that without the additional labelling restraints "the APVMA could not be satisfied that the continued use of the three products in question would not be 'likely' to have an effect that is harmful to human beings within the meaning of s.34(1)(a)(ii) of the Agvet Code".[104]

The position of the APVMA was supported by both DOHA and EAGAR; however EAGAR was either unable or unwilling to provide expert witnesses to the proceedings and the APVMA legal advice included the following:

> *Despite many requests for EAGAR to actively assist the APVMA in the conduct of the case, by providing EAGAR members to give evidence for the APVMA, the EAGAR*

[100] JETACAR (199) pp. 76.
[101] Vos, E (2004). *Antibiotics, the Precautionary Principle and the Court of First Instance. Cases T-13/99 Pfizer Animal Health SA v Council of the European Union and T-70/99 Alpharma Inc v Council of the European Union.*
[102] APVMA (2004). *Findings of the reconsideration of the registration of products containing Virginiamycin and their labels.*
[103] Letter to Peter Doyle, Managing Director Phibro Animal Health from APVMA, November 16 2004 (correspondence pertaining to FOI request).
[104] Phibro Animal Health Pty Ltd Administrative Appeals Tribunal Application for Review of Decision - Reasons for application, received March 2005 (document obtained under FOI)

> *has not yet done so. In my opinion, unless EAGAR provides willing and active support to the APVMA in the conduct of this matter, including by providing an EAGAR Board member to give evidence, the APVMA will lose the case. If EAGAR does not actively assist in this way, in the very near future, it will be necessary for the APVMA to settle the proceeding on the best terms it can.*[105]

Dr Peter Collignon offered to be an expert witness as a clinician and previous member of the EAGAR Committee, but for reasons unknown this offer was not taken up.[106]

Mediation was subsequently pursued and a member of EAGAR was included in the negotiation. A compromise was reached and labels were varied so as to require the products to be prescribed by veterinarians in accordance with the Australian Veterinary Association's "Code of Practice for Prescription and Use of Products which contain Antimicrobial Agents"[107] rather than the preferred label restraint statements.

[105]Renwick, J (2005). *Virginiamyacin – Administrative Appeals Tribunal Proceedings: Summary of Opinion.*
[106] Interview with author, September 4 2012.
[107] Agreement Pursuant to Section 42C of the Administrative Appeals Tribunal Act 1975 between Phibro Animal Health Pty Ltd and Australian Pesticides and Veterinary Medicines Authority.

In the Mediation Position Paper, the APVMA stated that it considered the regulatory decision being challenged

> *… establishes a prudent use regime for virginiamycin. It considers it can be satisfied of its legislative obligations if a veterinary surgeon can only prescribe virginiamycin for therapeutic purposes in accordance with the re-treatment intervals on the label. It is for this reason the APVMA placed the re-treatment interval as a mandatory instruction, known as a 'restraint label', on the label. If it were an advisory instruction a veterinarian would be legally able to prescribe virginiamycin for any purpose and for any duration. Its use would be unregulated and the danger to human health due to the emergence of antibiotic resistance would be unchecked.*[108]

And of the proposed compromise the APVMA as respondent said:

> *While not resiling from its review findings, The Respondent has proposed to the Applicant that a code of practice for the prescription and use of products that contain virginiamycin be developed by the Australian Veterinary Association (AVA). The Respondent has provided to the Applicant a document entitled Elements Which the APVMA Believes Should Be Encompassed in an AVA Code of Practice for Prescription and Use of Products which Contain Virginiamycin.*[109]

Earlier advice made the point that

> *… it is plain that Phibro propose to leave no stone unturned in examining scientific issues in this matter. This development confirms that, if the matter cannot be resolved by agreement, there will be a long and no doubt hard-fought case to be determined by the Tribunal. … the advantage of mediation is that if settlement is possible, very considerable legal expenses will be saved in this matter, and if it is not possible, there will be an opportunity for both parties to refine their thinking about the real issues in dispute.*[110]

Also of interest is that in the legal opinion provided it was also noted that the European Union had banned virginiamycin as an in-feed growth promotant in 1998 and, though challenged, this decision was upheld. It was noted that, unlike in Australia, the EU courts apply the "precautionary principle", permitting decisions to prevent risks to human health.

> *… even if there is scientific uncertainty as to their existence or extent. … That is, if the risk although nevertheless not fully demonstrated by conclusive scientific evidence, appears to be adequately backed up by the available scientific data at the time the decision was taken, the precautionary principle will protect a banning decision: see Pfizer decision paras 138-146.*[111]

It was further explained that the APVMA does not apply the precautionary principle test and consideration was given to the relevant test as described in the *Agricultural and Veterinary Chemicals Code Act 1994* (Cth).

[108] Phibro animal Health Pty Ltd and APVMA ats AAT Proceedings V2004/1317&V2005/185 Mediation Position Paper of the Respondent Para 20, 4 December 2007 (document obtained under FOI)
[109] Phibro Animal Health Pty Ltd and APVMA AAT Proceedings V2004/1317&V2005/185 Mediation Position Paper of the Respondent, 4 December 2007 (document obtained under FOI)
[110] APVMA ats Phibro Animal Health Pty Ltd Memorandum Dr James Renwick para. 3, 17 November 2005 (document obtained under FOI)
[111] APVMA ats Phibro Animal Health Pty Ltd Opinion Dr James Renwick para. 25-26, November 2005 (document obtained under FOI)

The process described in the box above highlights a number of issues, including the capacity of government agencies to defend decisions they have made in the public interest when they are faced with legal challenges by extremely well resourced multinational pharmaceutical companies. It also raises questions about the capacity and resourcing of advisory committees relied upon by government departments to provide necessary legal support as expert witnesses and the implications of not applying the precautionary principle where human health is at risk.

While in principle there is no problem seeking a mediated settlement, there is indeed a problem if mediation is sought only because the legal proceedings are too expensive or resource-intensive for the government agency charged with protecting the public interest. The failure of Australian governments to create a comprehensive and national system of surveillance and monitoring of the use of antimicrobials and incidence of AMR – and the consequential gaps in data – weakens the position of policy makers and regulators further.

It is also important to note that antimicrobial supply data is provided to the APVMA on a voluntary basis only. In response to The Australia Institute's FOI request for access to data collected since the original and only publicly available report, it was stated:

> *The data collected by the APVMA has been supplied on a completely voluntary basis by the product registrants. On 4 Feb 2003, APVMA published a Gazette Notice entitled 'Code of Practice on Collection of Animal Antimicrobial Supply Data for Submission to the National Registration for Agricultural and Veterinary Chemicals'. The purpose of the Gazette Notice was to provide guidance to product registrants about the data collection process. The Gazette Notice relevantly provides that… the aim of this Code is to enable the submission of antimicrobial supply data from registrants on a voluntary basis . These aims are balanced by the need to maintain privacy of commercially confidential information.*

It may be the case that voluntary provision of information from pharmaceutical companies, albeit with Commercial in Confidence limitations, does result in an accurate and reliable base of data on which to assess risk and develop public policy. It is not however clear that an evaluation has occurred to support this premise. Once again it may well exist but if so it is not easily discovered.

Engagement of communities in decisions related to the use of antimicrobials

Both the WHO and the 1999 JETACAR report stress the need for community engagement if there is to be societal change in attitudes towards and use of antibiotics.

The JETACAR report stressed the importance of communication, describing it as "an interactive exchange of information and opinions between regulators and stakeholders including the general public"[112] and noting that such communication

> *… should include explanation of the overall hazard that has been identified and characterised and the process for assessment of the risks for individual antibiotics on a case by case basis … communication of hazard and risk to all concerned parties, especially the public, must therefore be a continuous process.*[113]

Effective community engagement requires that information and evidence gathered is made available in an accessible form. Without access to such public sector information, meaningful

[112] JETACAR (1999). p xxxiii.
[113] JETACAR (1999). p xxxiii.

input from the broader community is less likely. The importance of the right to information was acknowledged by the Australian Parliament in 2010 through the creation of the Office of the Australian Information Commissioner (OAIC) and through reform of the *Freedom of Information Act*.

The OAIC Strategic Plan defines the purpose of the Office as being "to promote information rights and the strategic management of government information". The vision is "an Australia where government information is managed as a national resource". The plan also sets out that: "The economic and social value of public sector information can be enhanced by publication and information sharing. This requires that information can easily be discovered and used by the community and other stakeholders."[114]

While meaningful community engagement has not been evident since the 1999 report, recent reforms to information law and the establishment of the OAIC may support a more transparent and accountable process of community engagement in future. The functions of the OAIC are underpinned by the notion that government-held information is a national resource. The first of the OAIC Principles on Public Sector Information is "Open access to information – a default position" and the second is "Engaging the community".[115]

The National Strategy for the Quality Use of Medicines (QUM) also highlights education as an essential part of improving community understanding of how medicines should be used. The first principle underlying the strategy is the primacy of consumers: "The National Strategy recognises both the central role consumers play in attaining QUM and the wisdom of their experience. Consumers must be involved in all aspects of the National Strategy."

There have been various consumer campaigns, such as the National Medicines Week campaigns. NPS MedicineWise have run campaigns such as Common Colds need Common sense and the current community awareness campaign[116] – 'Become an antibiotic resistance fighter' – which includes an integrated educational and awareness campaign to encourage people to change the behaviours which contribute to antibiotic resistance. Such a campaign was implemented in Sweden and between 1993 and 1997 antibiotic prescribing was reduced by 22 per cent. A 2010 study showed that 78 per cent of the Swedish population is willing to abstain from antibiotics.

In writing this paper it has become clear that it is not possible to obtain a comprehensive picture of what has actually been done regarding management of the threat of AMR in Australia since the 1999 report. There has been no obvious or effective effort by DOHA or any other agency to keep the community informed of progress in implementation of the recommendations of the 1999 report, or any subsequent strategy. As already mentioned, a JETACAR website was launched by the NHMRC in March 2001. The aim of this website was "to keep stakeholders informed", but this website no longer exists and it is unclear when or why it was taken down.

While information received under FOI has assisted to some extent in trying to understand what has happened since the 1999 report, there would need to be many more FOI requests and consequent negotiations with the agencies from whom the information was sought to get a more complete picture. If government departments took their responsibility to keep the public informed seriously, such an approach would not be necessary.

[114] Office of the Australian Information Commissioner (OAIC) (2011) *Information policy: Principles on open public sector information.*
[115] OAIC (2011).
[116] Binns, P and Stowasser, D. (2012).

A survey regarding community understanding of AMR was undertaken by The Australia Institute in 2011 and the results indicated a fairly wide understanding (84 per cent of respondents) that overuse of antibiotics can lead to bacteria becoming resistant. Fewer respondents (60 per cent) knew that antibiotics are routinely added to food for some kinds of animals grown for human consumption, and fewer again (49 per cent) knew that residue from antibiotics can be present in or on some kinds of fresh food at the time of purchase. Of those respondents who were aware of the use of antibiotics for food animals, 93 per cent thought food products should be labelled to inform consumers of the routine use of antibiotics in animal food. Such community sentiment should be taken seriously. It is important to many people that they have good information about the food products they purchase.

Conclusion – where to from here?

Initially there appeared to be strong commitment to implementing the recommendations of the 1999 report – however, most initiatives failed to result in any comprehensive systematic response to the issue. Unless there is a careful examination of what actually went wrong post JETACAR, we cannot assume that in 2022 we will not again be looking at another largely wasted decade. Committees, taskforces and groups were set up but disbanded, pilots programs failed to be anything other than pilot programs, undertakings were not carried out.

The process was and is characterised by a lack of leadership and a lack of effective action or accountability. It raises questions not only about the political process and public administration, but also about the barriers to progress created by the federated nature of Australia, the role of industry and the resourcing and capacity of regulators to protect public health and the environment. This paper has only scratched the surface, but has provided evidence to suggest there have been serious failures of public administration, and that it is necessary to devise a much more accountable and transparent system of management of AMR in Australia.

Most of the underlying factors listed by the WHO as drivers of AMR[117] are evident in Australia, including that there is inadequate national commitment to a comprehensive and coordinated response; ill-defined accountability and insufficient engagement of communities; weak or absent surveillance and monitoring systems; potentially inappropriate and irrational use of medicines, including in animal husbandry; a need for improvement in infection prevention and control practices, as well as insufficient research and development on new products.

For Australia, a developed country, this is a significant failure not only in terms of protecting public health domestically but also in the global fight against AMR.

A number of groups including NPS MedicineWise, the Australasian Society for Infectious Diseases and the Australian Society for Antimicrobials have noted the lack of a comprehensive and coordinated approach to antimicrobial drug resistance in Australia and have proposed the establishment of a national antimicrobial resistance management body to implement national surveillance, coordinate education and stewardship programs, implement infection prevention and control policies, support research and advise regulatory bodies. It is argued that antimicrobials should be regulated differently from all other drugs and that a single body should be responsible for management of their use across agriculture, production of food animals and in human medicine. The example of the control of quinolone prescribing in Australia is used to support the argument for regulation as a tool to reduce inappropriate use of antimicrobials and resultant AMR.[118]

[117] WHO (2012a).
[118] Cheng, AC et al. (2012).

Recommendation 21 of the 1999 report addressed the need for such a body, stressing the importance of independence, appropriate secure funding and accountability and transparency measures.

The need for such a cross-sectoral coordinated approach was made very evident in a recent ABC radio program,[119] when Professor Chris Baggoley, Chief Medical Officer for the Australian government, was asked about the need for testing of foods for superbugs. He was apparently unaware that such testing was not regularly undertaken and when asked why he responded that it was "not within my purview". This fact was further outlined in Estimates when, after a series of questions about overall coordination of management of AMR by Senator Richard Di Natale, Ms Halton, Secretary of the Department of Health and Ageing conceded that

> *The points you make about relationships across agriculture et cetera are absolutely well made. Following on from this, I am happy to undertake to write to my colleagues in agriculture.*[120]

Ms Halton also mentioned the Food Regulation Standing Committee and committed to write to it to make the point that work was going on in DOHA, adding that "we will make sure that there is high-level liaison, and at the next Estimates we will be able to tell you what has been going on".

It is disturbing that such high-level liaison was only prompted by the questions of a Senator and not part of an organised and strategic response to AMR or, indeed, as a response to the 1999 report recommendations or the concerns of the WHO. It appears DOHA has not accepted responsibility for overall coordination of the management of AMR, despite it being a clear and present threat to public health in Australia and around the world. It also appears that no other agency has taken on this role, despite the ongoing calls for an integrated approach.

As explained above, the government has recently announced the establishment of a new AMR advisory committee, the AMRSC. This new subcommittee will provide a voice on AMR directly to the Australian Health Ministers Advisory Council (AHMAC) via the Australian Health Protection Principal Committee (AHPPC). The terms of reference and membership were endorsed by AHMAC at a meeting in August 2012. It is funded by ACSQHC until 30 June 2013 after which time the arrangement will be reviewed.[121]

While establishment of such an advisory committee may indicate that the government is aware and concerned about the serious public health threat posed by AMR in Australia, it is not a particularly reassuring initiative in itself. While the advice of such an expert committee is likely to be very important in informing the development of evidence-based public policy on reducing AMR, history tells us that the establishment of such a committee will not necessarily, in itself, result in the desired outcomes. As explained earlier in this paper a similar advisory committee, EAGAR, was established in 2001 as a result of the recommendations of the 1999 report. Despite its best intentions and expertise it was unable to counter the lack of political and public sector leadership. According to Prof Mary Burton, School of Pharmacy and Medical Sciences, University of South Australia:

[119] Duxfield, F (2012).
[120] Halton, J (2012) *Community Affairs Legislation Committee,* pp. 88.
[121] Wright, P (2012)

> *EAGAR worked hard to drive the implementation of the recommendations (although it was not EAGAR's brief to do so) but was discontinued after two NHMRC triennial cycles. Now there is no Australian focus on antibiotic resistance and the issue has dropped off the political agenda.*[122]

Development of an effective AMR reduction management plan will require ongoing expertise and monitoring of both problems and solutions. For this reason it is important that any administrative structure established to manage AMR is given legislative status, so that there is at least some measure of protection from the vagaries of political and public service changes. While there may be new solutions and strategies developed, the JETACAR recommendations form a solid start for an effective plan – as does the WHO's 'Global Strategy for Containment of Antimicrobial Resistance', released in 2001.

The terms of reference of any agency established to reduce AMR should be broad and reflect the complex nature of AMR and the number of agencies and interests involved. It should also be empowered to consider and recommend budget, legislative and structural change where necessary. Ongoing and independent oversight should be part of any AMR strategy, with evaluative mechanisms included at the earliest possible stage of planning. Such measures are essential to ensure accountability and transparency. Clearly history does not indicate that internal government processes will deliver the necessary outcomes or accountability.

In addition, the importance of leadership from governments cannot be understated. According to the WHO, awareness at the political level is essential but often lacking. Political commitment is stressed as "an indispensable prerequisite" for action.[123]

Successful development and implementation of a comprehensive strategy and action plan to reduce AMR requires there be

- strong political awareness, leadership and will
- transparent and accountable public sector practice
- one government department and minister with overall responsibility for reducing AMR
- a single management body with its own legislative base which reports regularly and directly to the parliament – the body should also be empowered to self-initiate reports where necessary *and would itself be reviewed at a minimum every three years by an independent expert individual or body*
- a long-term view and commitment with appropriate and ongoing resourcing
- a coordinated cross-sectoral approach including both political, public, community and private interests.

The costs and consequences of not acting immediately to reduce AMR will be felt not only in the health sector but will also have repercussions on trade and travel, as a result of the cross-border spread of resistant infections.[124]

Given the pressing nature of the problem and the catastrophic impact of antimicrobial resistance, effective action must be taken urgently.

[122] *APVMA Science Fellows Symposium, 19 April 2010*
[123] WHO (2012b).
[124] WHO (2012b).

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Appendix A

Establishment of the Antimicrobial Resistance Subcommittee

During 2011 two Colloquia on the issue of antimicrobial resistance (AMR) were hosted by the Australian Commission on Safety and Quality in Health Care (ACSQHC). Since the last Colloquium in November, it has been possible to take advantage of a restructuring of the Australian Health Ministers Advisory Council (AHMAC) committees. AHMAC endorsed the establishment of a new subcommittee, to be known as the AMR Subcommittee (AMRSC) in April 2012 to support an integrative approach to the national strategy on AMR in Australia. As a result, the work of the Colloquia will now be subsumed into the subcommittee. A preliminary meeting of AMRSC took place on 11 April 2012 and the first formal meeting of the subcommittee took place on 20 July 2012.

The AMRSC will report directly to the Australian Health Protection Principal Committee (AHPPC). AHPPC is attended by Chief Health Officers from each of the jurisdictions, as well as the Chairs of the Public Health Laboratory Network, Communicable Disease NetworkAustralia, Environmental Health Subcommittee, National Health Emergency Management Subcommittee, and Blood Borne Virus and Sexually Transmissible Infections Subcommittee. This new subcommittee will provide a voice on AMR directly to AHMAC via AHPPC.

AMRSC brings together agencies that are currently driving national AMR activities. AMRSC will not only provide a basis to promote information exchange, coordination and co-operation at a national level, it will also provide a platform for Australia to benefit from, and contribute to, international discussions on AMR.

The role of the AMRSC is to:

- Advise the AHPPC on matters relating to AMR.
- Provide expert advice and assistance on issues relating to AMR.
- Recommend action on national priorities for AMR.

AMRSC's purpose is the development of a national strategy to minimise AMR. This includes coordination of national activities such as:

- a comprehensive national AMR and usage surveillance system
- education and stewardship programs
- infection prevention and control guidelines
- research into AMR and its prevention
- a review of the current regulatory system applying to antimicrobials, and
- community and consumer campaigns.

Membership of AMRSC includes nominations from the following organisations:

- Australian Commission on Safety and Quality in Health Care
- National Health and Medical Research Council
- National Prescribing Service
- Australasian Society for Infectious Disease
- Australian Society for Antimicrobials
- AustralasianCollegefor Infection Prevention and Control
- Communicable Disease NetworkAustralia
- Public Health Laboratory Network
- Therapeutic Goods Administration
- Pharmaceutical Benefits Advisory Committee

- Department of Health and Ageing
- Department of Agriculture, Fisheries and Forestry
- Australian Pesticides and Veterinary Medicines Authority

As its first initiative AMRSC will oversee the production of a scoping study and development of a business case for national surveillance of AMR and antimicrobial usage. Dr Ramon Shaban, Director (Griffith Graduate Infection Control Program, Griffith Health Institute Research Centre for Clinical and Community Practice Innovation) and Associate Professor Keryn Christiansen (former Head of the Department of Microbiology and Infectious Diseases at Royal, PathWest Laboratory Medicine, Perth Hospital in Western Australia) will join Dr Marilyn Cruickshank (AMRSC Chair and Healthcare Associated Infection Program Manager ACSQHC) as co-authors of the report.

Consultation with key stakeholder organisations and individuals will commence in September 2012. This will be followed by a public consultation of the draft report December 2012-February 2013.

Appendix B

Committees established after the 1999 Report

2000 Commonwealth Interdepartmental JETACAR Implementation Group (CIJIG)

CIJIG was established in November 2000. The CIJIG was composed of technical experts and senior representatives from relevant areas within the Department of Health and Ageing (DOHA) and was jointly chaired by DOHA and the Department of Agriculture, Fisheries and Forestry. The respective Chairs of the Australian Health Ministers' Conference (AHMC), the Primary Industries Standing Committee (PISC) formerly the Standing Committee on Agriculture and Resource Management (SCARM) and the Expert Advisory Group on Antimicrobial Resistance (EAGAR) were also invited to attend CIJIG meetings.

Outcomes.

- In May 2001 CIJIG held a National Summit on Antibiotic Resistance.
- A Progress Report on Implementation of the JETACAR recommendations was produced in about 2001/2002. For reasons unknown, this report was rescinded in 2008 by the Department of Health and Ageing. (Rescinded publications no longer represent a Department's position on the matters covered.)
- A second progress Report was released in March 2003. This report has not been rescinded.

This appears to be the last Progress Report produced and the CIJIG was disbanded at some point not long after this report.

2001 Expert Advisory Group on Antibiotic Resistance (EAGAR)

The EAGAR was set up in 2001 and was tasked with providing advice to Commonwealth, State and Territory and Commonwealth Statutory organisations. It was to work closely with the CIJIG to develop and implement the national antibiotic resistance management program. It was to report through the CIJIG to the Ministers, and advise on policy and guidelines. During 2001, EAGAR developed and commenced the use of a protocol to assess the risk of antibiotic resistance developing in new and existing antibiotics. EAGAR was discontinued after two NHMRC triennial cycles and according to Prof Mary Barton School of Pharmacy and Medical Sciences University of South Australia.

"EAGAR worked hard to drive the implementation of the recommendations (although it was not EAGAR's brief to do so) but was discontinued after two NHMRC triennial cycles. Now there is no Australian focus on antibiotic resistance and the issue has dropped off the political agenda"[125]

2000 The Australian Health Minister's Conference AHMC JETACAR Taskforce.

This taskforce was appointed by AHMC in 2000 to assist formal consultation with the States and Territories and to monitor implementation. This Taskforce consisted of State and Territory representatives and was appointed by the Australian Health Ministers' Conference (AHMC) to monitor the implementation process and report progress to the Minister for Health and Ageing. The group also assisted Commonwealth Interdepartmental JETACAR Implementation Group (CIJIG) by providing advice in specific areas of expertise. It was

[125] Barton, M. (2010) "Antibiotic Resistance in Australian Animals in 2010-What lies ahead*?'APVMA Science Fellows Symposium, 19 April 2010*

tasked with facilitating implementation of The Report's recommendations in cooperation with the Commonwealth and monitoring progress towards implementation and to report to the Australian Health Ministers' Conference by July 2001. According to the Department of Health Ageing website on JETACAR, The "AHMC has completed its work and was disbanded in 2002".

It is not clear why it was thought the work of monitoring progress towards implementation of the recommendations of The Report would have been completed by 2002, and that therefore there would be no need for the Taskforce after that time. Given the magnitude and complexity of the task it would seem reasonable to assume an ongoing need for such a body and that the responsibility to "consult with the Commonwealth and other key stakeholders in preparation of a progress report" would also be ongoing, as proper scrutiny and accountability would require there be more than the one progress report which was produced in 2003. (There had been a previous progress report about 2001/2002 but for some reason it was rescinded in 2008.)

Other Committees set up include

- The then Agriculture and Resource Management Council of Australia and New Zealand (ARMCANZ) JETACAR Taskforce to monitor the JETACAR implementation from the animal industry perspective.
- Primary Industries Standing Committee (PISC) JETACAR Taskforce.