

# Towards a national surveillance program for antimicrobial resistance in animals and animal-derived food

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## Abstract

**One of the major recommendations of the JETACAR report was that a comprehensive national surveillance system be established to measure antimicrobial resistance to cover medical, food-producing and veterinary areas. While there are a number of existing passive surveillance programs on a national, regional and state basis in the medical field, there are few analogous programs in the veterinary area, and none with a particular emphasis on the food chain. The Commonwealth Interdepartmental JETACAR Implementation Group is working with stakeholders to develop this aspect of the national surveillance program based on the Guidelines published by the world organisation for animal health, the Office International des Épizooties. *Commun Dis Intell* 2003;27 Suppl:S111–S116.**

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## Introduction

The Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) made 22 recommendations<sup>1</sup> for an antimicrobial resistance management program that focuses on the use of antimicrobials in both animals and humans. The proposed program covers regulatory controls; monitoring and surveillance; infection prevention strategies; education; and research; communication; and implementation.

A key component of the national program is monitoring and surveillance for antimicrobial resistance—this was addressed in recommendation 10:

*'That a comprehensive surveillance system be established to measure antibiotic-resistance covering all areas of antibiotic use, including medical, food-producing animal and veterinary areas. Where possible, this should use, enhance and extend currently available systems and organisational structures'.*

The Commonwealth Government response to the report in August 2000 largely supported the JETACAR recommendations and supported the development of a national antimicrobial resistance management program.<sup>2</sup> An important component of the Government's response was to institute a review of existing systems of surveillance and monitoring of antimicrobial resistant bacteria in the human and animal health fields. Tenders were advertised in February 2001 and contractors have been working with departmental officers in the Commonwealth as well as holding consultations with industry and State government stakeholders to develop a national antimicrobial surveillance program.

The consultations identified few antimicrobial resistance surveillance programs in the veterinary area that could be readily adapted into a national surveillance program. There is limited passive surveillance of veterinary pathogens via diagnostic submissions, some passive surveillance of zoonotic organisms (*Salmonella*) and some targeted surveillance undertaken by some industries. The main limitations to using existing veterinary data as the basis of a national program are:

- the existing antimicrobial susceptibility test data has not been generated using standardised test methods;

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- most of the available data are for antimicrobial resistance in clinically significant animal pathogens covering therapeutic antimicrobials used in veterinary medicine;
  - there is a lack of data on resistance in commensal bacteria and to those antimicrobials that are used for growth promotant purposes and for some classes of antimicrobials that are not used in food animals in Australia (e.g., fluoroquinolones), but for which resistance is a particular human health concern.

Monitoring and surveillance of antimicrobial resistance derived from the veterinary and agricultural use of antimicrobials will require a new approach. Existing systems are unlikely to meet the animal health and welfare requirements of the animal industries and do not address the public health concerns about resistance that originates from antimicrobial use in animals.

### *International monitoring and surveillance programs*

A number of programs have been instituted in other countries in the past 10 years.

#### **DANMAP (Denmark)<sup>3</sup>**

DANMAP which is a collaborative project between the Danish Veterinary Laboratory, the Danish Veterinary and Food Administration, the Statens Serum Institut and the Danish Medicines Agency commenced in 1995. Annual reports cover antimicrobial resistance in bacteria from humans, food and food animals as well as statistics on the consumption of antimicrobials in humans and animals.

#### **National Antimicrobial Resistance Monitoring System (USA)<sup>4</sup>**

The National Antimicrobial Resistance Monitoring System was established in 1996 as a collaborative project involving the Food and Drug Administration's Center for Veterinary Medicine, US Department of Agriculture and the Centers for Disease Control and Prevention. The program monitors changes in the susceptibilities of human and animal enteric bacteria to a range of antimicrobials. It is designed to address equally the human and the animal components with bacterial isolates collected from human and animal clinical specimens, from healthy farm animals and from raw products derived from food animals.

#### **Swedish Veterinary Antimicrobial Resistance Monitoring (Sweden)<sup>5</sup>**

The Swedish Veterinary Antimicrobial Resistance Monitoring program focuses on both antimicrobial usage statistics as well as on resistance of bacteria of animal origin. To obtain samples representative of the animal population, the number collected at each abattoir is determined in proportion to the number of animals slaughtered at the abattoir each year.

#### **RESABO (France)<sup>6</sup>**

RESABO is a network of regional veterinary laboratories in France. The program is managed by a central reference laboratory (CNEVA, Lyon). Features of the program include standardised methods for all laboratories, collation and reporting of data on resistance and undertaking specific studies on mechanisms for resistance.

The appropriate aspects of these programs, together with the international standard developed by the world organisation for animal health, the Office International des Épidémiologies (OIE), could form the basis for the design of an Australian program.

## *The international standard*

The OIE is the international standards setting organisation recognised by the World Trade Organization for the elaboration of international standards, guidelines and recommendations on matters of animal health and zoonoses relevant for trade in animals and animal products. The OIE has produced a number of guideline documents<sup>7</sup> outlining a comprehensive strategy that can form the blueprint for member countries to manage antimicrobial resistance arising from the agricultural and veterinary use of antimicrobials. The guidelines cover:

- risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin;
- prudent and responsible use of antimicrobial agents in veterinary medicine;
- monitoring the quantities of antimicrobials used in animal husbandry;
- standardisation and harmonisation of laboratory methodologies used for the detection and quantification of antimicrobial resistance; and
- harmonisation of national antimicrobial resistance monitoring and surveillance programs in animals and animal derived food.

## *Application of the OIE Guideline on monitoring and surveillance to Australia*

The OIE Guideline was developed by an ad hoc group of experts on antimicrobial resistance of the OIE. The objective is to allow the generation and consolidation of comparable results on a national level and to compare the situations on a national, regional and international level. National systems should be able to detect the emergence of resistance and to determine the prevalence of resistant bacteria. The resulting data can then be used in the assessment of risks to public health and form the basis of risk management policy. Specific factors identified for harmonisation include antimicrobial usage patterns, animal species, food commodities, bacterial species, antimicrobials to be tested, laboratory methods, and data reporting.

### **Risk assessment**

A comprehensive risk assessment should take account of agricultural production systems, animal husbandry and antimicrobial usage patterns in Australia. This, together with the subsequent issues discussed in this paper, will be used in the development of a surveillance program for antimicrobial resistance of food-animal origin.

### **Antimicrobial usage patterns**

Acquired antimicrobial resistance arises from the selection pressure exerted on bacteria by antimicrobials in their immediate environment. The types of antimicrobials used and the extent, quantities and patterns of their use should be taken into account in designing a surveillance program. Mechanisms to collect these data objectively are needed.

### **Animals to be sampled**

A risk assessment should take account of the relative importance of the various categories of livestock in potentially contributing to antimicrobial resistance. A key consideration will be knowledge of antimicrobial use patterns in the various livestock industry sectors. Categories of livestock that should be considered for sampling include cattle and calves, slaughter pigs, broiler chickens, layer hens, and farmed aquatic animals.

## Food to be sampled

Contaminated food is the principal route of transmission of antimicrobial resistance from animals to humans, either by pathogens or by transfer of resistance genes carried by commensal bacteria. The earlier in the processing chain that samples can be taken, the more likely it is that susceptibility test results can be associated with on-farm management issues.

## Sampling strategies

Once the objectives of any program are decided, an early decision is whether reliance can be made on existing passive surveillance programs (usually based on data from veterinary diagnostic submissions), whether existing programs need to be modified or whether a new active surveillance program should be undertaken to meet the objectives.

The sampling strategy should ensure the representativeness of the population of interest. Options for sampling<sup>8</sup> are simple random, random systematic, stratified random collection (e.g., by age group or production system) or purposive sampling (targeted at specific groups e.g., cull dairy cows) with random sampling within each group. If the sampling strategy is robust then use of statistically based sample sizes will allow a more accurate estimate of the prevalence of antimicrobial resistance in the population of interest.

Some knowledge of the expected prevalence of resistance will allow decisions to be made on the number of samples that will be required to give the desired level of precision of the prevalence estimate. For example, if the expected prevalence in a large population were 10 per cent, then the number of samples required to give a statistically valid estimate of the prevalence with 5 per cent precision and 95 per cent level of confidence would be 138 samples.

## Sample specimens to be collected

Ideally samples should be taken on-farm. While this may be an option for individual sick animals, the most practical point of sampling is at the abattoir or processing plant where animals from a number of properties can be sampled over a relatively short period of time. In these circumstances, the best specimen for investigating resistance is faeces (10–50 gm) in livestock and whole caeca in poultry. If the interest is surveillance of resistance in the food chain after slaughter, then tissue or swab samples should be taken from the carcass or food product.

## Bacteria to be tested

The bacteria of interest are listed in Table 1 and can be divided into three groups.

**Table 1. Bacteria for potential inclusion in a surveillance program**

Target animals	Pathogens	Zoonotics	Commensals
Cattle	<i>Pasteurella</i> spp. <i>Haemophilus somnus</i> <i>Staphylococcus aureus</i> <i>Streptococcus agalactiae/uberis</i>	<i>Salmonella</i> spp.	<i>Escherichia coli</i> <i>Enterococcus faecium/faecalis</i>
Pigs	<i>Actinobacillus pleuropneumoniae</i> <i>Brachyspira</i> <i>Streptococcus suis</i>	<i>Salmonella</i> spp.	<i>Escherichia coli</i> <i>Enterococcus faecium/faecalis</i>
Poultry	<i>Escherichia coli</i>	<i>Campylobacter</i> <i>Salmonella</i> spp.	<i>Escherichia coli</i> <i>Enterococcus faecium/faecalis</i>
Fish	<i>Vibrio</i> spp. <i>Aeromonas</i> spp.		

## *Animal pathogens*

Monitoring of resistance in animal pathogens will allow early detection of the emergence of resistance that could be of animal (and human) health concern. The results can be used by veterinarians to make informed prescribing decisions and in developing prudent use guidelines.

## *Zoonotic bacteria*

Samples for isolation of *Salmonella* can either be taken at the abattoir, or isolates originating from other sources can be obtained from national laboratories such as the National Enteric Pathogens Surveillance Scheme and the Australian Salmonella Reference Centre. Isolates should be identified and serotyped according to international methods. *Campylobacter* isolates should be identified to species level.

## *Commensal/indicator bacteria*

*Escherichia coli* and enterococci are regarded as commensal bacteria common to all animals and man. They constitute a reservoir of resistance genes that are capable of transmission to pathogens or to other commensals. It is particularly important that the various enterococcus species are correctly identified, as there are differences in innate resistance to some antimicrobials among the different species.

### **Antimicrobials to be used in susceptibility testing**

It would be cost-prohibitive to monitor all clinically important antimicrobials used in animals and humans. Table 2 contains a list of antimicrobial groups that could be considered for inclusion in a national surveillance program. Priority should be given to monitoring those antimicrobials identified in the risk assessment as having the greatest public or animal health concern in Australia.

**Table 2. Antimicrobials that may be included in an antimicrobial resistance surveillance program**

<b>Antimicrobial class</b>	<b>Animal pathogens Gram -ve</b>	<b>Animal pathogens Gram +ve</b>	<b><i>Salmonella/ Escherichia coli</i></b>	<b><i>Campylobacter</i></b>	<b><i>Enterococcus</i></b>
Aminoglycosides	+	+	+		+
Amphenicols	+	+	+		
Beta-lactams	+	+	+	+	+
Cephalosporins	+		+		
Glycopeptides		+			+
Lincosamides		+			
Macrolides		+		+	+
Quinolones	+	+	+	+	+
Streptogramins					+
Sulfonamides	+		+		
Tetracyclines	+	+	+	+	+

## Standardised testing methods and quality control

A wide variety of antimicrobial sensitivity test (AST) methods are used around the world. The most commonly used methods are disk diffusion, broth dilution and agar dilution. Regardless of the AST method used, all aspects of the method must be rigorously standardised to ensure accurate and reproducible results. Appropriate reference organisms should be included in every AST run as a quality control measure to ensure the accuracy of the test results. Where a number of laboratories are involved in a testing program, it is advisable that the same method is used in all laboratories and that the performance of laboratories is monitored through regular participation in a proficiency testing program.

## Data collation and reporting

In choosing an AST method, it is preferable that the result can be recorded quantitatively (minimum inhibitory concentration in mg/Litre or inhibition zones in millimetres) rather than qualitatively as 'resistant' or 'susceptible'. This will allow the early detection of emerging resistance and trends to be followed. Consideration needs to be given to having the raw data sent to a central point for entry into a national database to facilitate evaluation of the data in response to various questions and for the generation of regular reports for the information of national regulatory agencies and the public.

## Conclusion

This paper has provided some background and made recommendations for factors to be considered in the development of an antimicrobial resistance surveillance program for Australia. It may be necessary to develop the program in an incremental way based on priorities established through a risk assessment that considers animal husbandry conditions in Australia and their associated antimicrobial use patterns.

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