

# Scoping a New Zealand Antimicrobial Resistance Surveillance Programme in Food

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## Project Goal and Objectives

The project goal is:

“To examine and summarise a range of the international initiatives in countries with similar agricultural production systems that have been designed and implemented to provide ongoing, permanent, national surveillance systems to monitor antimicrobial resistance trends among selected enteric organisms from animals and animal-derived food sources.”

The objectives are:

- “To review available documentation on an agreed selection of current national antimicrobial resistance surveillance programmes among selected enteric organisms from animals and animal-derived food sources
- To produce a report summarising the findings from the above and comparing and contrasting the schemes examined.”

## Background

The quantity and pattern of antimicrobial use in animals affects occurrence of antimicrobial resistance in bacteria from animals and in animal-derived food and hence human exposure to these resistant bacteria. When pathogens are resistant to essential human antimicrobials the human health consequences include increased treatment failures, increased severity of infections, and infections that would otherwise not have occurred (FAO/OIE/WHO, 2003).

Antimicrobial resistance can be transferred from animals to humans by pathogenic bacteria or transfer of resistance genes carried by commensal bacteria, principally via the food chain. Surveillance of antimicrobial use and antimicrobial resistance is important to identify resistance problems and inform policy to limit emergence and spread of resistance. Monitoring of antimicrobial resistance includes commensal bacteria as well as enteric pathogenic bacteria because in addition to being a potential reservoir of resistance for enteric pathogens through resistance genes transfer, they act as an indicator of selection pressure on bacteria that are rare or difficult to isolate, and may be opportunistic pathogens in some contexts.

Currently there is no surveillance programme of antimicrobial resistance in animal bacteria in New Zealand. Existing information is limited and comes from ad hoc surveys and susceptibility testing of some *Salmonella* and *E. coli* 0157 isolates sent to the Institute of Environmental Science and Research from laboratories involved in slaughterhouse microbiological surveillance. In 1999 the Expert Panel on Antibiotic Resistance and the Antibiotic Resistance Steering Group convened by the Ministry of Agriculture and Forestry recommended that an antimicrobial resistance surveillance programme be set up in food-producing animals (Expert Panel on Antibiotic Resistance, 1999; Antibiotic Resistance Steering Group, 1999). The Steering Group was reconvened by the New Zealand Food Safety Authority (NZFSA) in 2004 and another Expert Panel on Antibiotic Resistance was set up to review and update technical information. Both the

Steering Group and the Expert Panel endorsed the original recommendation. The 2004 Expert Panel proposed a surveillance programme similar to that operating in the United Kingdom using existing or proposed sampling in the food-producing animal industries (Expert Panel on Antibiotic Resistance, 2005).

## **Definition of Antimicrobial Resistance Surveillance**

Surveillance is the ongoing systematic collection, analysis, interpretation and timely dissemination of data critical to the planning, implementation and evaluation of public health practice (CDC, 1986). It provides information for action.

The World Organisation for Animal Health (Office International des Epizooties, OIE) Ad hoc Group of experts on antimicrobial resistance defined antimicrobial resistance surveillance as the continuous investigation of a given bacterial population to detect the occurrence of antimicrobial resistance for control purposes. Monitoring comprises ongoing programmes to detect changes in the prevalence of antimicrobial resistance in a given bacterial population. This definition is derived from the OIE definition of monitoring and surveillance in animal health in the International Animal Health Code (Franklin et al, 2001).

## **Goals and Objectives of Antimicrobial Resistance Surveillance**

The goals (or purpose) of an antimicrobial resistance surveillance programme in animals are to reduce antimicrobial resistance in food-producing animals and the transfer of antimicrobial resistant bacteria from animals to humans. Programme objectives relate to how the data are used for action.

Specific objectives vary in extent among programmes and may include:

- To detect emergence of antimicrobial resistance
- To determine prevalence and spread of antimicrobial resistance
- To determine regional and national trends in the prevalence and spread of antimicrobial resistance
- To assess risk to human health from antimicrobial resistant bacteria from animals and food of animal origin
- To assess risk to animal health from antimicrobial resistance in animal bacterial pathogens
- To provide evidence for policy recommendations for animal and human health
- To detect need for potential interventions
- To evaluate impact of interventions to prevent and/or control antimicrobial resistance
- To guide targeted research
- To investigate any relationship with antimicrobial use
- To investigate any relationship with aspects of agricultural practice

- To contribute to global antimicrobial resistance surveillance.

At a minimum, the objectives include the provision of information about emergence, prevalence, and trends of antimicrobial resistance to guide decision-making.

## **Selection of Antimicrobial Resistance Surveillance Programmes for Review**

In discussion with the NZFSA Project Leader the standards and antimicrobial resistance surveillance programmes of the following organisations and countries were selected for review:

World Health Organisation (WHO)  
World Organisation for Animal Health (OIE)  
European Union  
Denmark  
United Kingdom  
Canada  
United States  
Australia

## **Methods of the Review**

A search of relevant organisational websites was undertaken. Reference lists of reports were also examined. A search of the Medline and PubMed databases using the key words *animal antimicrobial/antibiotic resistance surveillance* revealed no articles that either had not been identified by other means or that added to the material already obtained.

## **International Standards**

### **World Health Organisation (WHO)**

In 1990 the WHO Working Group on Antimicrobial Resistance released *Guidelines for Surveillance and Control of Antimicrobial Resistance* which outlined a methodology for surveillance including bacterial species selection, antimicrobials to be used for susceptibility testing, and standardisation of testing methods and reporting. This was followed by a pilot project on the surveillance of antimicrobial resistance in bacteria from animals and humans, food and the environment.

In 1997 an expert committee looking at the human health impact of antimicrobial use in food-producing animals stated that surveillance should contribute to detection and prevention of transmission of antimicrobial resistance from animals to humans and to

prudent antimicrobial use in food-producing animals and humans. Antimicrobial resistance surveillance of bacteria from food-producing animals and animal-derived food was then in its infancy. The committee made a number of recommendations relating to surveillance of antimicrobial resistance in bacteria from food-producing animals and animal-derived food.

The recommendations (given in detail below) focused on leadership, national surveillance and coordination, and methodology.

### **WHO Recommendations (WHO, 1997)**

#### *WHO leadership role*

- coordinate international monitoring efforts so data can be compared

#### *National antimicrobial resistance surveillance*

- initial small-scale programmes based on existing resources with gradual expansion
- begin with sentinel studies on isolates already collected in conjunction with other disease control programmes
- include isolates from pigs and poultry

#### *National coordination*

- collaboration of medical, veterinary and agricultural sectors so susceptibility testing is standardised and data can be compared

#### *Methodology*

- important zoonotic foodborne bacteria and key commensal bacteria (*Salmonella*, if feasible *Escherichia coli* and *Campylobacter* spp., others e.g. *Enterococcus* spp. depending on country requirements)
- major food-producing animals including cattle, pigs, and poultry in which the presence or potential transfer of zoonotic bacteria is most likely to be significant
- isolates from healthy and ill livestock, raw meat, and other products e.g. milk, eggs
- use antimicrobials for susceptibility testing that are also used in human medicine and/or known or suspected to select for cross resistance to antimicrobials used in human medicine
- standardised laboratory methods, quality assurance, quantitative data
- timely and comprehensive reporting

Subsequently WHO has had a collaborative approach to antimicrobial resistance involving the United Nations Food and Agriculture Organisation (FAO) and OIE.

Following a World Health Assembly resolution on antimicrobial resistance (1998), the *WHO Global strategy for containment of antimicrobial resistance* was developed (WHO, 2001). This provides a framework of interventions targeting all areas where antimicrobial use occurs and recognises the importance of surveillance. It recommends that surveillance includes antimicrobial use and resistance data and is integrated with the establishment of a national intersectoral task force whose functions include organising data collection.

As part of this strategy, WHO developed with the FAO and OIE global principles or recommendations for antimicrobial use in food-producing animals to protect human health (WHO, 2000). These include programmes to monitor antimicrobial use and

resistance in pathogens and commensals from animals, animal-derived food and humans.

Recommendations from a joint FAO/WHO/OIE expert workshop include:

- establish a national antimicrobial resistance surveillance programme in bacteria in animals and animal-derived food
- use standardised antimicrobial susceptibility testing methods with appropriate quality assurance
- use quantitative susceptibility testing and reporting so results can be compared
- link antimicrobial use data with antimicrobial resistance data, preferably also with human information, and report annually
- at a minimum perform susceptibility testing of non-typhoid *Salmonella* but preferably of a range of bacteria as outlined in the OIE Guidelines (FAO/WHO/OIE, 2003).

The programme's structure should be based on a country's characteristics and capability, and follow OIE guidelines and WHO protocols on isolation, identification and susceptibility testing of common human bacterial pathogens. A further expert workshop examining management options noted the need for improved design and statistical analysis of surveillance programmes (FAO/WHO/OIE, 2004).

Other relevant activities include development of antimicrobial resistance surveillance standards (2001), enhanced surveillance of foodborne disease and antimicrobial resistance of bacteria in food focusing on *Salmonella* (Salm-Surv), and development of an information system that converts susceptibility test results into a common format enabling collaborative national or global surveillance and analyses data (WHONET).

In 2005 a code of practice to minimise and contain antimicrobial resistance was adopted by the FAO/WHO food standards setting body, Codex Alimentarius Commission (CAC). This recommends the establishment of antimicrobial resistance surveillance which is harmonised as much as possible at the international level and with priority given to foodborne bacteria (CAC, 2005).

## **World Organisation for Animal Health (Office International des Epizooties, OIE)**

Following a survey that identified a range of national antimicrobial resistance surveillance programmes in livestock in 16 of 35 member countries, the OIE Regional Commission for Europe in 1998 recommended that member countries implement co-ordinated and harmonised antimicrobial resistance surveillance programmes and the OIE consider establishing an ad hoc expert group to develop guidelines which would take account of scientific work undertaken by WHO and FAO.

In 2000 the OIE set up an expert group on antimicrobial resistance which released guidelines in 2001, including one on the harmonisation of national antimicrobial resistance monitoring and surveillance programmes in animals and animal-derived food. These were adopted by OIE in 2003 and published in the OIE Terrestrial Animal Health

Code (OIE, 2005). OIE guidelines are recognised as international best practice by the World Trade Organisation.

The OIE surveillance and monitoring guideline acknowledges that programmes may be constrained by technical and financial resources and recommends collection of certain standardised data and harmonisation of programmes so that data can be compared internationally. Recommendations for programme design are outlined below.

### **OIE Recommendations (OIE, 2005)**

#### *Animal species/categories for sampling*

- depends on livestock production systems, antimicrobial use patterns, international trading status

#### *Food sampling*

- include food bacterial isolates as raw food of animal origin may be contaminated with resistant bacteria<sup>1</sup>

#### *Sampling strategy*

- depends on programme objectives
- random sampling, stratified by region and animal species category
- continuous sampling to account for seasonal and regional variations
- representative and sufficiently sized sample of the bacterial population of each animal species

The desired level of precision (e.g. 1%, 5%, 10%) in the prevalence estimate that will be obtained from the sample and the degree of confidence (e.g. 90%, 95%) that the estimate would be within this range needs to be determined. Information on the frequency with which bacteria may be isolated and the expected prevalence of resistance in the bacterial population is needed to determine the number of isolates to be tested to get a statistically robust estimate of prevalence.

#### *Sample type*

- depends on programme objectives

At the slaughterhouse, sampling of faeces gives antimicrobial resistance prevalence at age of slaughter and of carcasses gives information on slaughter hygiene and level of faecal contamination during slaughtering. Food chain monitoring (e.g. raw and/or processed food) for antimicrobial resistance after slaughter is currently uncommon.

#### *Bacteria*

- include zoonotic e.g. *Salmonella*, *Campylobacter* spp. and commensal bacteria e.g. *Escherichia coli*, *Enterococcus* spp.
- samples are from healthy animals, preferably taken at the slaughterhouse

Prevalence of antimicrobial resistance in animal bacterial pathogens is typically derived from clinical specimens sent to diagnostic laboratories but could also be sought from isolation of potential pathogens from healthy animals.

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

- include all clinically important classes of antimicrobial used in human and veterinary medicine

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<sup>1</sup> The guideline also recommends inclusion of food of plant origin.

### *Standardisation of laboratory methodologies*

- use standardised and internationally recognised laboratory methodologies for identification of bacteria and for antimicrobial susceptibility testing<sup>2</sup>
- laboratories participate in internal and external quality assurance

### *Data recording*

- enter results into a national database
- record results quantitatively as a distribution of minimum inhibitory concentrations (MICs) in milligrams per litre or inhibition zone diameters in millimeters
- report the proportion of resistant isolates based on the distribution of MICs or inhibition zone diameters of the bacterial species

A minimum data set is also identified (Franklin et al, 2001).

### *Central co-ordination*

- a national centre which coordinates the programme and produces an annual report

## **Selected Programmes**

### **European Union**

A key element in relation to the European Union (EU)'s approach to antimicrobial resistance was advice from a committee of independent scientists which recommended actions including harmonised antimicrobial resistance monitoring to reduce overall antimicrobial use in all sectors including animal production (EC, 1999).

Surveillance is one of four key areas included in the European Commission's *Community strategy against Antimicrobial Resistance* (EC, 2001). Member states should establish or strengthen antimicrobial use and resistance surveillance in animals and humans. Priorities in relation to surveillance are to develop surveillance networks at the level of Europe, encourage participation of non-EU countries, and establish and improve antimicrobial use data collection.

Directive 2003/99/EC sets out requirements for surveillance of zoonoses and zoonotic agents including antimicrobial resistant strains. It outlines general and specific antimicrobial resistance surveillance requirements, such as monitoring must include a representative number of *Salmonella* and *Campylobacter* spp. isolates from cattle, pigs and poultry (EC, 2003).

Most EU countries have a programme to monitor resistance but currently there is not a harmonised system that allows comparison of data across countries. This is in contrast to the network of 31 national antimicrobial resistance surveillance systems of seven bacterial isolates from humans with invasive infections, the European Antimicrobial Resistance Surveillance System (EARSS). There is also a surveillance network for

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<sup>2</sup> OIE has developed a guideline (2004) on laboratory methodologies for bacterial antimicrobial susceptibility testing.

*Salmonella* and verocytotoxin-producing *E. coli* (VTEC) human infections and antimicrobial resistance (Enter-Net). Antimicrobial use data collection is at different stages of development among countries.

Since 1998 the European Association of Feed Additives Manufacturers (FEFANA) has operated an antimicrobial resistance surveillance programme in most EU countries of *Enterococcus faecium* in pigs and poultry at slaughter. Inclusion of *Salmonella*, *Campylobacter* spp. and *E. coli* is under consideration (Defra, 2004).

## Denmark

The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP) covers surveillance of antimicrobial resistance in bacteria from food, livestock, humans and the environment. It is a fully integrated surveillance programme including antimicrobial use and antimicrobial resistance in animals, food and humans.

The following details of the programme's development and design are available from the most recently published annual report (Emborg et al, 2005).

DANMAP was set up in 1995 jointly by the Ministry of Food, Agriculture and Fisheries and Ministry of Health and was the first programme to establish continuous antimicrobial resistance monitoring. It is run by the Danish Institute for Food and Veterinary Research (DFVF), Statens Serum Institut and Danish Veterinary and Food Administration, and funded jointly by the Ministry of Family and Consumer Affairs (MFCA) and Ministry of the Interior and Health (MIH).

The programme is designed to detect changes in antimicrobial resistance in food-producing animals at the national level. It is not able to detect emergence of resistance occurring only at a low level.

Antimicrobial susceptibility testing is carried out of *Campylobacter* spp. from pigs, broilers and cattle, *Enterococcus* spp.<sup>3</sup> from pigs (faeces) and broilers (cloacal swab), and *E. coli* from pigs, broilers and cattle at slaughter.

*Salmonella* from pigs, poultry (broilers and layers) and cattle are also monitored. The majority of isolates from pigs and poultry are from sub-clinical infection and the majority of isolates from cattle are from clinical cases.

Stratified random sampling is carried out at slaughter with the number of samples for each slaughterhouse determined in proportion to the number of animals slaughtered annually. Each sample represents one herd or flock. Samples are collected once a month (weekly for broilers) by meat inspection staff or company personnel and sent to DFVF. The broiler, cattle and pig slaughterhouses in the surveillance programme account for 95%, 90% and 95% respectively of total production of these animal species.

The programme also monitors susceptibility in *E. coli* from cattle, poultry and pigs and *Staphylococcus hyicus* from pigs among clinical specimens.

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<sup>3</sup> In 2004 *Enterococcus* spp from cattle were not included.

DFVF is the national reference laboratory for *Salmonella* in animals and receives all isolates for typing. One isolate per serotype per farm is selected for DANMAP. Isolates from clinical specimens are selected by a pseudo-random process (no details given) among isolates from specimens sent to DFVF from the laboratory of the Federation of Danish Pig Producers and Slaughterhouses.

DANMAP includes samples of meat and imported meat from wholesale and retail outlets. No details of this component of the programme were found.

Methods are standardised for the examination of samples from animals for bacterial species and susceptibility testing of isolates and performance testing is carried out to assess comparability of the antimicrobial susceptibility testing of the participating laboratories.

Results from slaughterhouse samples for bacteria and of susceptibility testing are stored in a central database. Susceptibility data are stored as continuous values (MICs) and categorised as susceptible or resistant as defined by relevant microbiological breakpoints. Each isolate is identified by bacterial species, possibly subtype, date and place of sampling, animal species, and information on herd or flock of origin.

Results are reported as the distribution of MICs and percentage resistant with 95% confidence intervals to clinically important antimicrobials among certain bacterial serotypes from certain animal species.

An annual report on antimicrobial resistance in bacteria from animals, food and humans is produced.

The programme has enabled the effect of changes in use of different antimicrobials on prevalence of resistance of *E. faecium* from food-producing animals at slaughter and from retail meat to be determined (Monnet et al, 2000).

## United Kingdom

The following details of the UK programme's development and design are available from the Department for Environment, Food and Rural Affairs' (Defra) website.

Since 1970 Defra has funded the monitoring of *Salmonella* isolates from animals and their environment and, since 1998, clinical isolates of veterinary pathogens and some commensals e.g. *E. coli* for antimicrobial resistance.

Defra has funded surveys (since 2002) of antimicrobial susceptibility of *E. coli* including VTEC, *Salmonella*, *Campylobacter* spp., and *Enterococcus* spp. from caecal samples from cattle, sheep and pigs at the time of slaughter. Poultry will be included from 2006.

The Department of Health released a cross-Government strategy and action plan on antimicrobial resistance in 2000 in response to recommendations in the House of Lords Science and Technology Select Committee's report on antimicrobial resistance. Surveillance is a key element of the plan. Defra subsequently released a specific

strategy for surveillance of antimicrobial resistance in animals in England and Wales (Defra, 2004).

The proposed programme includes surveillance of antimicrobial resistance in bacteria from healthy and ill animals and antimicrobial use, and addresses a number of recommendations from the Department of Health's (now Food Standards Authority) Advisory Committee on the Microbiological Safety of Food report on antimicrobial resistance in relation to food safety (1999). The initial focus is on food-producing animals although samples collected for other purposes from non-food-producing animals will be included.

The intent is to harmonise veterinary and medical antimicrobial susceptibility testing and reporting procedures so that the system is integrated and there is data comparability with other EU countries.

Bacteria that will be considered for inclusion are *E. coli*, *Salmonella*, *Campylobacter jejuni*, *Campylobacter coli*, VTEC and *Yersinia* spp. in cattle, pigs, poultry and sheep, and *E. faecium* in pigs and poultry as well as certain animal pathogens e.g. *Streptococcus* spp. The sample source has not been identified.

Defra has set up an Antimicrobial Resistance Coordination Group (DARC) to advise on the sampling strategy and priority antimicrobials, and monitor the results. The strategy will be evaluated by Defra.

Similar action plans have been developed for Scotland and Northern Ireland.

## Canada

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is modeled on DANMAP and the US National Antimicrobial Resistance Monitoring System (NARMS). It is harmonised with NARMS.

The following details of the programme's development and design are available from the most recently published annual report (PHAC, 2005).

CIPARS was set up in 2002 in response to recommendations of the Health Canada (HC) Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health (2002). Initially based on sampling of healthy animals at slaughter and animal clinical isolates, a retail meat component and human clinical isolates were added in 2003 and a farm component in 2004. The intent is to also integrate human and animal antimicrobial use data into the programme. Animal antimicrobial use data have not been included in annual reports published to date but will be in subsequent reports.

The programme monitors *E. coli* and *Salmonella* from pigs and broilers and *E. coli* from cattle (excluding calves slaughtered for veal) at slaughter. Inclusion of *Salmonella* from cattle was discontinued due to low prevalence. Caecal sampling is carried out as the caecal contents most closely represent the farm environment.

Federally inspected slaughterhouses are selected randomly with selection probability being proportional to annual slaughter volume. However participation is voluntary. At the end of 2003 there were 55 slaughterhouses in the programme.

Sampling of each animal species is random. The number of samples is proportional to each slaughterhouse's annual slaughter volume among all the participating slaughterhouses. Sampling is continuous throughout the year. The expected number of isolates is set at 150 per bacterial species for each animal species per year across Canada. The number of samples is determined by the expected prevalence of the bacterial species in caecal contents. There is a trade off between statistical precision and affordability.

To minimise costs the annual number of samples to be collected is divided by five (10 for pigs) resulting in collection periods distributed evenly over the year. For a sampling week the five samples are collected by industry personnel under guidance of the Canadian Food Inspection Agency (CFIA) Veterinarian-in-Charge at the slaughterhouse's convenience within 12-36 hours from animals from different lots. The sampling protocol is modified to accommodate various plant line configurations.

CIPARS also includes a retail raw meat component which monitors *E. coli* from ground beef, pork, and chicken and *Enterococcus* spp., *Salmonella* and *Campylobacter* spp. from chicken in two provinces. Isolation of *Salmonella* and *Campylobacter* spp. from ground beef and pork was initially included but was discontinued due to the low recovery rate. Continuous weekly sampling is carried out from randomly selected census areas weighted by population. One or two areas per province are sampled by field workers on each sampling day. There is one sampling day per week. Four stores (generally three chain and one independent) are selected by store type per area. One sample of each meat type is collected from each store (i.e. total of 12 samples, three per store). The sampling protocol is based on estimated prevalence to give 100 isolates per meat type per province and allows for 20% lost or damaged samples. The data are not representative from each province, food-producing animal and bacterial species.

There is intent to extend retail surveillance to other provinces, add other bacterial species (not specified) and farmed food-producing species (not specified).

As well as active surveillance of healthy animals and animal-derived food, CIPARS includes passive surveillance of antimicrobial resistance in *Salmonella* from human and animal (cattle, pigs, chickens, turkeys) clinical specimens from laboratories. All provincial public health laboratories send human isolates to the National Microbiology Laboratory. Isolate submission protocols vary among provinces according to population with only a subsample, except for two serotypes, submitted from the four most populated provinces. All animal isolates are submitted from veterinary diagnostic laboratories to the Public Health Agency of Canada (PHAC) Laboratory for Foodborne Zoonoses' (LFZ) *Salmonella* typing laboratory which is an OIE reference laboratory and member of the WHO Salm-Surv network.

Faecal sampling from broilers, pigs and feedlot cattle for *E. coli*, *Enterococcus* spp., *Salmonella* and *Campylobacter* spp. at farm-level began in 2004. This uses sentinel farms and includes antimicrobial use monitoring to get estimates of group and individual animal antimicrobial use. There is no published data yet on the farm component.

Laboratory methods for isolation of the various bacterial species and antimicrobial susceptibility testing are standardised and samples from the slaughterhouse and retail components are sent to the LFZ laboratories.

Data analysis is carried out by LFZ and the percentage of resistant isolates based on the distribution of MICs is reported.

The programme is funded by the PHAC, Health Canada (Health Products and Food Branch), and CFIA. There is in-kind support from the meat processing industry and provincial public health laboratories.

Advice is provided to CIPARS by the National Steering Committee for Antimicrobial Resistance Surveillance in Enterics (NSCARE).

## United States

The National Antimicrobial Resistance Monitoring System – Enteric Bacteria (NARMS) was established in 1996 following the recommendation of a Food and Drug Administration (FDA) advisory committee set up to advise on approval of fluoroquinolones for use in poultry.

In 1999 the US General Accounting Office (GAO) recommended that the Department of Health and Human Services (DHHS) and Department of Agriculture (USDA) work together to develop and implement a plan for the safe use of antimicrobials in agriculture (GAO, 1999) and a Federal Interagency Task Force on Antimicrobial Resistance was set up. This resulted in an action plan on antimicrobial resistance (2001) developed by the Task Force.

The following details of NARMS' development and design are available from the most recently published annual report (NARMS, 2003).

NARMS started with non-typhoid *Salmonella* and expanded to include *Campylobacter* spp. (1998), *E. coli* and *Enterococcus* spp. (2000), and retail meat surveillance. Geographic coverage has also increased. It is integrated with antimicrobial resistance surveillance in humans but not antimicrobial use. It involves the FDA Center for Veterinary Medicine (CVM), Centers for Disease Control and Prevention (CDC) of the DHHS and USDA.

Depending on the bacteria, all or a random sample of human isolates from state (all) and local public health laboratories are sent to CDC for *Salmonella*, *Campylobacter* spp., *E. coli*, *Enterococcus* spp. and *Shigella*. *Listeria monocytogenes* and *Vibrio* were originally included but dropped after pilot studies showed a low prevalence of resistance (GAO, 2004).

The animal component of NARMS comprises healthy farm animals, animal clinical specimens, animals at slaughter, and ground products at processing plants. All federally inspected slaughterhouses and processing facilities have been included since 2000.

Cattle, pigs and broilers are sampled at slaughter and ground chicken, turkey and beef are sampled at the processing plant for *Salmonella*. Samples include carcass swabs, carcass rinsates, and ground product. Sampling for *Salmonella* is for regulatory compliance (Hazard Analysis and Critical Control Point Compliance Testing Programme) and is not designed statistically to estimate national prevalence.

The USDA's Food Safety and Inspection Service (FSIS) inspection personnel collect a daily sample until the sample set is completed. The number of samples per set is determined by whether sampling is of a carcass or raw ground product. Sampling is ongoing at six to 12 month intervals with further sampling if a facility does not comply with the *Salmonella* standard. The programme therefore includes selection bias as facilities that do not meet the *Salmonella* performance standard are overrepresented.

Randomly selected chilled cattle and pig carcasses are swabbed at three different sites after 12 hours of cooling. A sample set is 82 samples for young cattle, 58 samples for mature cattle and 55 samples for pigs.

Fifty-one samples comprise a broiler carcass set. Broilers are randomly sampled after immersion chilling. The whole bird carcass is rinsed with water and 30 mls of the rinsate is sent for analysis.

Fifty-three samples of 25 grams after final grinding are taken for raw ground chicken, turkey and beef products.

Following *Salmonella* testing the FSIS laboratories send the chicken carcass rinsate samples to USDA's Bacterial Epidemiology and Antimicrobial Resistance Research Unit for culture, isolation and susceptibility testing of *Campylobacter* spp., *E. coli* and *Enterococcus* spp. However the recovery rate of *Campylobacter* spp. is considered to be affected by the time taken for transport.

Healthy farm animals are monitored by the USDA's National Animal Health Monitoring System (NAHMS). NAHMS involves a random sample of livestock and poultry operations although participation is voluntary. There is a five year rotation between surveys of each commodity. Each survey has a statistical representation of greater than 95% of on-farm animal production in the US for that particular time period. Management information e.g. antimicrobial use is also collected. Animal isolates and on-farm faecal samples from NAHMS are also sent to the Antimicrobial Resistance Research Unit.

Animal clinical specimens are from 12 veterinary diagnostic laboratories and a random sample of the National Veterinary Services Laboratory's isolates excluding isolates from states where sentinel diagnostic laboratories are located.

Since 2002 the programme has included a retail component based on a pilot study in one state the preceding year. Retail raw meat samples (ground beef, ground turkey, pork chops, chicken breasts) are collected from grocery shops in the 10 states (initially six) which participate in CDC's FoodNet programme.<sup>4</sup> The same catchment area as FoodNet is used as far as possible. Since 2005 there has been stratified random sampling. Two samples of each meat type per store are collected from five primary and,

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<sup>4</sup> FoodNet is active surveillance of the monthly number of laboratory confirmed cases of these pathogens for defined regions within each of the participating states.

if necessary, three backup stores per month (40 meats per month) for *E. coli*, *Salmonella*, *Campylobacter* spp. and *Enterococcus* spp. Only four sites test for *E. coli* and *Enterococcus* spp. due to the large number of isolates. Isolates are sent from FoodNet laboratories to the CVM Office of Research Laboratory for antimicrobial susceptibility testing.

Since 2002 NARMS has also included a pilot study of animal feed ingredients collected at rendering plants.

Standardised laboratory methods are used in the animal, retail and human components of NARMS. Antimicrobials for susceptibility testing are selected annually based on clinical importance. Laboratories participate in internal and external programmes (e.g. WHO - *Salmonella*) to monitor the quality assurance of susceptibility testing. The percentage of resistant isolates based on the distribution of MICs is reported.

An annual report is prepared by each participating agency who are working towards a similar format so data can be directly compared. The goal is to eventually have integrated reporting. There is an annual NARMS meeting to present the data. Lack of available data on the quantity of antimicrobial use in specific food-producing animals and humans hinders data interpretation.

In 2004 GAO recommended the DHSS and USDA develop and implement a plan to collect animal antimicrobial use data. Some on-farm use data are available through NAHMS but these are limited as the surveys are periodic and only for certain species. Available sales data are not differentiated by animal species and data for some classes are merged (GAO, 2004).

NARMS collaborates with antimicrobial resistance monitoring systems in other countries, including Canada, Denmark, France, the Netherlands, Norway, Sweden and Mexico so information can be shared on the global dissemination of antimicrobial resistant foodborne pathogens. It supports international foodborne disease surveillance e.g. Salm-Surv and other national surveillance programmes. It has proposed setting up an international collaborative group on enteric bacteria antimicrobial resistance surveillance.

The programme is being reviewed by the FDA Science Board (external advisory board) in the 2006 fiscal year. In 2005 a two day meeting was held with external experts to find out their opinions on key elements of NARMS and to discuss future directions to contribute to this review. Issues raised included the need for a nationally representative sample and programme design, including sample size estimates, to be based on meeting its objectives (NARMS, 2005).

It is funded by the FDA through interagency agreements with USDA and CDC, though USDA (particularly the Animal and Plant Health Inspection Service and FSIS) and CDC also provide in-kind support.

The range of animal species and sources makes data from animal isolates more difficult to interpret compared to the human clinical isolate data (IFT, 2006).

The Collaboration in Animal Health, Food Safety and Epidemiology established by USDA in 2003 also focuses on antimicrobial resistance in animals. This programme involves quarterly collection of 40 faecal and 60 blood samples from pigs at 40 farms (as

at May 2004) from four states for *E. coli*, *Salmonella*, *Campylobacter* spp. and *Enterococcus* spp. It includes some on-farm antimicrobial use data. Depending on funding, it is intended that other species and samples at slaughter will be included, and epidemiological studies, field investigations, and risk analyses will be carried out.

## Australia

In 1997 the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) was set up to assess the scientific evidence linking the use of antimicrobials in food-producing animals and the emergence of antimicrobial resistance. The Australian Government supported the conclusions and recommendations of the JETACAR report (1999) and cited monitoring and surveillance as one of five key areas of a national antimicrobial resistance management programme (Commonwealth Department of Health and Aged Care, 2000). Subsequently the Commonwealth established:

- 1) the Commonwealth Interdepartmental JETACAR Implementation Group to manage the Australian Government's implementation plans for JETACAR's recommendations; and
- 2) the Expert Advisory Group on Antimicrobial Resistance (EAGAR), an advisory committee of the National Health and Medical Research Council, to provide independent advice on antimicrobial resistance including integration and interpretation of surveillance information to national, state and territory governments and regulatory authorities.

A national surveillance strategy, *Strategy for Antimicrobial Resistance (AMR) Surveillance in Australia* was released in 2003 in response to JETACAR's recommendation for antimicrobial resistance surveillance. The intent is for an integrated surveillance system which includes antimicrobial resistance in humans, animals and animal-derived food, and antimicrobial use in humans and animals. Factors identified for consideration in the development of the national surveillance programme were based on the OIE guideline (Webber and Valois, 2003).

The following information is available from the Australian Department of Health and Ageing (DoHA) and Department of Agriculture, Fisheries and Forestry (DAFF) websites.

Establishment of a central coordinating unit located at the DoHA is proposed to collate, analyse and report national antimicrobial resistance surveillance data.

DAFF developed an action plan for antimicrobial resistance surveillance in animals which led to the setting up of a pilot surveillance programme from November 2003 (until July 2004). The programme comprised caecal samples from cattle (feedlot, grass-fed and dairy), pigs, and broilers for *E. coli* and *Enterococcus* spp. and from broilers for *Campylobacter* spp. Samples were collected from slaughterhouses in four states. This sampling was in addition to that carried out for existing microbiological surveillance in slaughterhouses.

Ten beef and seven pig slaughter facilities were chosen based on levels of throughput and geographical spread. Poultry processing plants were representative of the major companies from each of the states to account for differences in antimicrobial use

between companies and between states. The sampling strategy aimed for no more than one isolate per farm or representative group of livestock. The total number of samples was 200 each for cattle and pigs and 300 for poultry. The target number of bacterial isolates based on an expected prevalence of resistance of less than 10% is 138 samples per animal species/bacterium combination (95% confidence and 5% precision). Equal numbers of samples were collected every two to three months to take account of summer and winter feeding patterns and seasonal variations. Antimicrobials identified as being of greatest public health importance were used in susceptibility testing.

The pilot programme was funded by DAFF. There is no publicly available report on the outcomes of the pilot and whether the programme's design has been modified as a result.

Antimicrobial resistance among *Salmonella* is monitored through the passive surveillance programmes of the Australian *Salmonella* Reference Centre and National Enteric Pathogens Surveillance Scheme which includes isolates from ill and healthy animals, domestic and imported food.

A Technical Reference Group advises on implementation of DAFF's action plan and interprets surveillance data prior to discussion with stakeholders and forwarding to EAGAR. The Group has recommended future surveillance should include bobby calves, companion animals and farmed fish.

## Comparison of Programmes

Antimicrobial resistance surveillance programmes are based largely on zoonotic and commensal bacteria from food-producing animals. Some programmes include retail food of animal origin and animal pathogens. Most programmes are (or intend to be) integrated with antimicrobial resistance among human enteric pathogens. Inclusion of antimicrobial use in humans and animals is also a feature. Table 1 summarises the main features of the programmes that were examined.

Of the five national programmes that were examined, only DANMAP and NARMS have been operating more than five years. With the exception of NARMS, programmes have not been piggy-backed onto pre-existing microbiological monitoring systems. Although NARMS is based on slaughterhouse regulatory compliance monitoring this is supplemented by components, such as on-farm monitoring, designed for specific purposes including antimicrobial resistance monitoring. The programmes are funded by

**Table 1: Comparison of national antimicrobial resistance surveillance programmes against the WHO/OIE guidelines**

	WHO/OIE	Denmark DANMAP	UK <sup>#</sup>	Canada CIPARS	US NARMS	Australia <sup>#</sup>
Food animals	Y	Y	Y	Y	Y	Y
Animal-derived food	Y	Y	N	Y	Y	Y - intent
Animal clinical isolates	Y	Y	Y	Y	Y	Y
Other	feed (OIE)	environment	N	farm	farm, feed ingredients	N
Antimicrobial use	Y	Y	Y	Y	N	Y - intent
Human isolates	Y	Y	Y	Y	Y	Y
Bacteria	S, C, E, Ec	S, C, E, Ec	Not decided- S,C, Ef, Ec, Y	S, Ec (also C, E at farm)	S, C, E, Ec	S, C, E, Ec
Animal species	Pg, Po, Ca	Pg, Po, Ca	Pg, Po, Ca, Sh	Pg, Po, Ca	Pg, Po, Ca	Pg, Po, Ca
Sampling:						
slaughterhouse	Y	Y	Not decided	Y	Y – incl processing plants	Y
type	faeces, caecal (Po), carcass swab	faeces, cloacal swab	?	caecal	carcass swab, rinsate, ground product	caecal
continuous	Y	Y	?	Y	N	2-3 monthly
random	Y	Y	?	Y	N	?Y
sufficient size	Y	Y	?	Y	?Y	Y
Priority antimicrobials	Y	Y	Y	Y	Y	Y
Standardised laboratory methods	Y	Y	Y	Y	Y	?Y
Quality assurance	Y	Y	Y	Y	Y	?Y
Quantitative data	Y	Y	Y	Y	Y	?Y
Central database	Y	Y	?	?Y	N	?
Reporting	annual	annual (integrated)	?	annual (integrated)	annual (not yet integrated)	?
Central coordination	Y	Y	Y	Y	Y	Y
Funding	?	MFCA, MIH	?Defra	PHAC, HC, CFIA	FDA, USDA, CDC	DAFF, DHA

# under development

NS not specified

S *Salmonella*, C *Campylobacter* spp., E *Enterococcus* spp., Ef *E. faecium*, Ec *E. coli*, Y *Yersinia*  
Pg pigs, Po poultry, Ca cattle, Sh sheep

government with mention of in-kind support from industry in the case of DANMAP and CIPARS.

DANMAP is considered to be the most functional antimicrobial resistance surveillance system in contributing to public health surveillance and policy (NARMS, 2005). DANMAP is the only programme that gives temporal relationships between antimicrobial use and resistance although CIPARS has started to collect on-farm use data. It collects the most comprehensive use data (quantities in different species by age group and administration method) of all the programmes. CIPARS is driven out of the PHAC so is more focused on human health outcomes than the other programmes.

Central intersectoral co-ordination and independent scientific oversight are also common features of national programmes.

## Evaluation of Antimicrobial Resistance Surveillance Programmes

The CDC recommends periodic evaluation of surveillance programmes to ascertain how well a programme meets its purpose and objectives (CDC, 1988; CDC, 2001). This involves assessment of the programme's attributes (outlined below).

### Attributes of Surveillance Programmes (CDC, 2001) applied to Antimicrobial Resistance

#### *Simplicity*

- structure; ease of operation

#### *Flexibility*

- adapt to changing demands with minimal extra time or resources

#### *Data quality*

- completeness; validity

#### *Acceptability*

- willingness of others to participate

#### *Sensitivity*

- proportion of antimicrobial resistance detected; ability to detect changes over time

#### *Predictive value positive*

- proportion of reported antimicrobial resistance that is antimicrobial resistance

*Representativeness*

- accurate description of antimicrobial resistance in time, place and food-producing animal species/animal-derived food

*Timeliness*

- availability of information for prevention and control measures; identification of trends, outbreaks, or effect of interventions

*Stability*

- reliability (ability to collect, manage and provide data successfully) and availability (ability to be operational when required)

Simplicity relates closely to timeliness and acceptability and affects the resources required to run the programme. Acceptability and representativeness are related to data quality.

No information about the evaluation of programmes such as recommended by the CDC (1988; 2001) was found with the possible exception of NARMS. However of the six programmes that were examined, three (EU, UK, Australia) may be considered to be in an early developmental stage and four (CIPARS, EU, UK, Australia) have been operating less than five years. NARMS is currently being reviewed by the FDA Science Board but no information about the review's terms of reference was found. In 2005 there was a stakeholders' meeting to contribute to the review which brought up attributes such as representativeness (NARMS, 2005).

Antimicrobial resistance surveillance programmes differ with respect to scope, objectives and methodology therefore individual attributes may vary in importance among them. From the information available the author has made some judgements about attributes of the well-established programmes (Table 2). The EU, UK and Australian programmes have been excluded as they are in a relatively early stage of development.

The information available suggests that most programmes have made trade-offs and weighed the expected benefits against the costs of various components. The attributes of a surveillance programme together influence its usefulness and cost. An antimicrobial resistance surveillance programme in food-producing animals is useful if it contributes to prevention and control of animal antimicrobial resistance, including enhanced understanding of its impact on public health. It is difficult to assess the usefulness of the individual programmes as effects on policy decision-making are not necessarily fully evident from published documents. It is also unclear what interventions have occurred as a result of surveillance data as opposed to political decisions. NARMS and in particular DANMAP have enabled assessment of the effects of measures but these programmes have been operating for over 10 years. Some programmes appear to be using surveillance data to make decisions about refinement of the programme e.g. certain bacterial species have been dropped, and to influence actions such as collection of antimicrobial use data.

**Table 2: Assessment of the Attributes of the CIPARS, NARMS and DANMAP**

Attribute	
Simplicity	Multiple reporting levels and integration of related systems mean programmes are reasonably complex
Flexibility	Adaptation to additional data sources over time and use of standard data formats suggests flexibility
Data quality	Data assumed to be valid given standardised laboratory and reporting methods but level of completeness from various data sources is not known
Acceptability	Assumed to have reasonably high acceptability based on time they have been operating and their ability to expand over time
Sensitivity	Not possible to judge the sensitivity of data or each data source. However as long as sensitivity does not change greatly over time, a programme that does not have high sensitivity is still useful in monitoring trends
Predictive value positive	Likely to be reasonably high given standardised laboratory methods and laboratory quality assurance
Representativeness	Varies among programme components depending on programme objectives. Animal component of NARMS is less representative than animal component of DANMAP and CIPARS. Trade-offs have been made presumably on the basis of resources
Timeliness	Not possible to judge timeliness of information for immediate opposed to long term control. Publication of annual reports varies from six months to about two years after year end. NARMS also holds a meeting to present results
Stability	Assumed to be reasonably stable based on time they have been operating

## Conclusion

National antimicrobial resistance surveillance systems for enteric bacteria from food-producing animals and animal-derived food are at various stages of development and implementation in different countries.

Although the earlier in the food chain that samples are collected, the more likely that the results can be assessed in relation to on-farm antimicrobial use and management, most programmes collect samples at the slaughterhouse. This appears to be the most practical and cost-effective collection point and animals from a number of farms can be sampled over a relatively short period.

Programmes tend to monitor for antimicrobial resistance among *Salmonella*, *Campylobacter* spp., *E. coli*, and *Enterococcus* spp. Cattle, pigs and broilers are the most commonly monitored animals.

Antimicrobial use monitoring needs to be included to aid interpretation of antimicrobial resistance data. To evaluate the consequences of animal antimicrobial use and monitor the effectiveness of interventions designed to reduce antimicrobial resistance in bacteria

from food-producing animals, laboratory methods and reporting must be standardised to allow data comparison with human antimicrobial resistance surveillance.

The well-established programmes (DANMAP, NARMS and CIPARS) have improved national understanding of the prevalence of animal antimicrobial resistance, but apart from DANMAP, have not been able to date to link animal antimicrobial resistance to animal antimicrobial use and human antimicrobial resistance. This appears to be due largely to problems with antimicrobial use data and/or integration with human antimicrobial resistance surveillance systems. Although difficult to select among these three programmes, DANMAP and/or NARMS which both have over 10 years experience and international relationships, are probably the most useful programmes for the NZFSA to consider further, if it decides to implement antimicrobial resistance surveillance of enteric bacteria from food-producing animals and animal-derived food in New Zealand. The possible advantages of NARMS are, although it is less representative, the programme is currently being formally reviewed and appears to have stronger international relationships. On the other hand, DANMAP has made a greater contribution to policy and Denmark's administrative system is more akin to New Zealand's than the federal and state system of the US.

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