Health Canada Santé Canada

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

2002

... working towards the preservation of effective antimicrobials for humans and animals…

Canada

Abbreviations Used Throughout the Report

AMR: Antimicrobial Resistance
AREOS: Antimicrobial Resistant Enteric Organisms
ARO: Antimicrobial Resistant Organism
ATC: Anatomical Therapeutic Chemical
BPW: Buffered peptone water
CCAR: Canadian Committee on Antibiotic Resistance
CDTI: Canadian Disease and Therapeutic Index
CFIA: Canadian Food Inspection Agency
CIDPC: Centre for Infectious Disease Prevention and Control
CIPARS: Canadian Integrated Program for Antimicrobial Resistance Surveillance
CPHLN: Canadian Public Health Laboratory Network
CPS: Compendium of Pharmaceuticals and Specialties
DANMAP: Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DDD: Defined Daily Doses
DPD: Drugs Product Database (Health Canada)
ENDS: Enteric Disease Surveillance
ESCs: Extended-spectrum cephalosporins
FAO: Food and Agriculture Organization
FWZID: Foodborne, Waterborne, and Zoonotic Infections Division Canada
HACCP: Hazard Analysis Critical Control Point
ISO: International Standards Organization
IMS HEALTH: Intercontinental Medical Statistics
LB: Luria-Bertani agar
LFZ: Laboratory for Foodborne Zoonoses
MAC: MacConkey agar
MDR: Multidrug resistant
MICs: Minimum Inhibitory Concentrations
MSRV: Modified Semi-Solid Rappaport Vassiliadis
NARMS: National Antimicrobial Resistance Monitoring System
NCCLS: National Committee on Clinical Laboratory Standards
NESP: National Enteric Surveillance Program
NML: National Microbiology Laboratory
NNDS: National Notifiable Disease Summary program
NSAGI: National Studies on Acute Gastrointestinal Illness
NSCARE: National Steering Committee on Antimicrobial Resistance in Enterics
OIE: Office International des Épizooties
PPHL: Provincial Public Health Laboratory
TSI: Triple Sugar Iron
USDA: United States Department of Agriculture
VDD: Veterinary Drugs Directorate
WHO: World Health Organization

Antimicrobial Abbreviations:

AMC:	Amoxicillin-Clavulanic Acid	GEN:	Gentamicin
		KAN:	Kanamycin
AMK:	Amikacin	NAL:	Nalidixic Acid
AMP:	Ampicillin	SMX:	Sulfamethoxazole
CEP:	Cephalothin	STR:	Streptomycin
CHL:	Chloramphenicol	SXT:	Trimethoprim-Sulfamethoxazole
CIP:	Ciprofloxacin		
CRO:	Ceftriaxone	TCY:	Tetracycline
FOX:	Cefoxitin	TIO:	Ceftiofur
		TIC:	Ticarcillin

Note: Antimicrobial abbreviations are from WHONET 5

About CIPARS

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) has been under development for several years beginning with the launching of several demonstration projects in both the human and agri-food sectors. Information is being collected on antimicrobial use and antimicrobial resistance in enteric pathogens and commensal organisms from the agri-food sectors (farm level, abattoir level and retail level) and enteric organisms isolated from humans. These demonstration projects have been developed in order to test the feasibility of a representative, methodologically unified approach, modeled after international initiatives such as the National Antimicrobial Resistance Monitoring System (NARMS-USA) and the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP-Denmark). These demonstration projects will monitor trends in the development of antimicrobial resistance in enteric pathogens from humans and enteric pathogens and commensal organisms isolated from animal and food sources.

This document is available in alternative formats upon request, and is also available at the Health Canada website: http://www.hc-sc.gc.ca/pphb-dgspsp/cipars-picra/index.html
Aussi disponible en français sur le titre Programme Canadien Intégré de Résistance aux Antimicrobiens 2002. In addition, a document summarizing supportive research is available upon request.

We welcome feedback and suggestions. Please forward your comments and any address changes to: Jennifer_Baker@hc-sc.gc.ca.

ISBN #: H39-1/3-2002E 0-662-35730-2

Table of Contents

Acknowledgements

Editors:
Rebecca Irwin
Kathryn Doré
Richard Reid-Smith

Coordinating Author:
Carolee Bair

Authors:
Danielle Daignault
Kathryn Doré
Lucie Dutil
Rebecca Irwin
David Léger
Elroy Mann
Leah Martin
Cornelius Poppe
André Ravel
Richard Reid-Smith
Carol Tinga
Rafiq Ahmed

External Reviewers:
John Conly
Serge Larivière
Scott McEwen
John Prescott

Data Analysis:
Lucie Dutil
Leah Martin
André Ravel

Translation:
Ethel Perez

The following additional people/committees assisted or provided support to CIPARS 2002:
Lateef Adewoye
Brent Avery
Jennifer Baker
Richard Bean
Louise Beausoleil
Canadian Meat Council
Canadian Poultry & Egg Processors Council
Manon Caron
Marie-Josée Champagne
Ann-Marie Cochrane
Angela Cook
Abigail Crocker
Anne Deckert
Walter Demczuk
Andrea Desruisseau
Lisanne Doré
Manon Fleury
James Flint
Ora Kendall
Kim Klotins
Julie Légaré
Lien Mi Tien
Manisha Mehrotra
Pascal Michel
Anne Muckle
Manuel Navas
Pat Pentney
Dorothy Rhodes
Jiangping Shuai
Erin Fraser
Ole Sorenson
Alfonso Valdivieso
Joyce Van Donkersgoed
Marie Varughese

National, provincial, territorial, university, industry and private laboratories and their collaborators

National Steering Committee for Antimicrobial Resistance Surveillance in Enterics (NSCARE)

National Steering Committee for Monitoring Antimicrobial Use in Agriculture and Veterinary Medicine (interim committee name)

Acknowledgements:
We would like to thank abattoir industry personnel and the Canadian Food Inspection Agency regional directors, inspection managers and onsite staff for their extensive voluntary participation in the CIPARS - Abattoir Component. Without their support the abattoir component could not have been implemented in 2002.

We recognize the US National Antimicrobial Resistance Monitoring System (NARMS) for sharing information and facilitating harmonization with CIPARS.

Additionally we appreciate the effort of the producers participating in research projects, field workers, laboratory technicians and data management staff for their contributions. The careful collection of samples, processing isolates and recording of results are essential to the ongoing success of CIPARS.

Executive Summary

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) was developed as a coordinated suite of demonstration projects in order to test the feasibility of a representative and methodologically unified surveillance system. CIPARS is modeled after initiatives in the United States and Europe for monitoring trends in antimicrobial use and the development of resistance in selected bacterial organisms from human, animal and food sources across Canada. These data are crucial for making regulatory decisions or formulating intervention strategies to contain antimicrobial resistance.

The 2002 CIPARS report provides the most current, valid and representative data. It includes a relevant summary of the 1993-2001 passive surveillance data on *Salmonella* and *Shigella* from human clinical cases, active surveillance data collected from abattoirs across Canada, a summary of the 1999-2002 passive surveillance data on *Salmonella* from animal clinical specimens, and statistics on human antimicrobial use from IMS Health. At the time of this report, data were not yet available from CIPARS active surveillance programs to describe resistance (AMR) in human *Salmonella* isolates or antimicrobial use in animals. Aspects of these will be included in the 2003 CIPARS report.

Health Canada conducted a retrospective analysis of passive laboratory data on *Salmonella* and *Shigella* as an initial step to estimate the burden of AMR among human enteric pathogens. Although the differing laboratory methods for bacterial isolation and testing antimicrobial susceptibility might result in biased estimates, there was an indication that resistance may be increasing among certain strains of *Salmonella*. Reasons for this observation are unknown and may be reflective of individual exposure to antimicrobials, consumption of contaminated food products, or exposure during international travel. To facilitate future analyses, a baseline evaluation of human consumption of antimicrobials has been conducted. In order to standardize reporting of results, data are reported in defined daily doses.

To provide an indirect measure of potential human exposure to antimicrobial resistance arising from consumption of animal-derived products, generic *Escherichia coli* and *Salmonella* were recovered from the intestinal (cecal) contents of healthy animals at slaughter. This sampling was designed to provide estimates of the proportion of bacteria recovered with resistance or decreased susceptibility to the antimicrobials tested. It was not designed to provide estimates of the prevalence of bacterial contamination of meat at slaughter. Abattoir data collected September - December 2002 showed resistance to one or more antimicrobials in 80%, 79% and 31% of generic *E. coli* isolated from chicken, swine and cattle respectively. Forty eight percent of chicken and 45% of swine *Salmonella* isolated from abattoir samples were resistant to one or more antimicrobials. For antimicrobials of greatest importance to human health, no resistance was observed to fluoroquinolones but resistance to ceftiofur was observed in 10% of *E. coli* and 12% of *Salmonella* isolated from healthy chickens at slaughter.

These results, the observed values and the differences between species, will become more interpretable when data have been collected for several years and when concomitant antimicrobial use monitoring data become available. Future CIPARS data will permit analysis of temporal trends of use and resistance, and their correlation among livestock populations. The potential explanations for species differences include differing antimicrobial exposures, animal husbandry practices and species-specific bacterial populations. To shed more light on this complex issue, epidemiologic research is being conducted to identify risk factors for the development and spread of AMR along the food chain.

Section One - Introduction

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) was developed as a coordinated suite of demonstration projects to test the feasibility of a representative and methodologically unified surveillance system. CIPARS, modeled after initiatives in the United States and Europe, was initiated in 2002 with the intention of monitoring trends in antimicrobial use and antimicrobial resistance in selected organisms from human, animal and food sources across Canada. Targeted research projects, including farm and retail studies, have also been launched to support these surveillance initiatives.

Background

Antimicrobial resistance (AMR) is an issue of increasing public concern. In addition to reducing our ability to effectively treat bacterial infections in humans and animals, AMR presents a serious economic challenge. Although the precise financial burden associated with AMR is not known, it is estimated that resistance at least doubles the cost of treating a bacterial infection and adds between $40 and $52 million per year to indirect and direct health care costs in Canada (CCAR, 2002).

Antimicrobial resistance in human medicine is primarily associated with the use of antimicrobials to treat human infections (WHO, 2000; HC 2002). However, significant amounts of antimicrobials are also used in agri-food production, and the contamination of animals and animal products with antimicrobial resistant bacteria has been identified as a source for human infection with resistant organisms (JETACAR 1999; Poppe *et al*, 1998; Wall *et al*, 1994; Molbak *et al*, 1999, Fone and Barker, 1994).

A Call for Action

International public health authorities are urging countries to implement integrated AMR surveillance systems. These systems are needed to implement sound public health interventions and to enhance prudent use practices in human and veterinary medicine. Surveillance is also necessary to support the development of international food safety standards. Multiple committees representing the joint Food and Agriculture Organization (FAO) of the United Nations/World Health Organization (WHO) and the Codex Alimentarius Commission are currently examining the issue of AMR. Food animal producers are under increasing pressure to restrict antimicrobial use to meet domestic and international market demands.

In Canada, the establishment of a national surveillance system to monitor AMR and use in the agri-food and agriculture sectors and the impact of resistance on human health was formally recommend in 1997 at the national consensus conference “Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians” co-convened by Health Canada and the Canadian Infectious Diseases Society. Subsequently, this recommendation received further endorsement from several national external advisory committees to Health Canada; the Enteric Disease Surveillance (ENDS) Steering Committee, the Canadian Committee on Antibiotic Resistance (CCAR), and most recently the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health. This latter committee stated in their 2002 report that “In Canada, as in most countries, the [surveillance] data are fragmentary, often biased, focused on a narrow and variable range of bacterial pathogens, collected in an unsystematic way and not generally compatible between laboratories and/or countries because methods used for testing resistance have not been standardized” (HC, 2002).

Building the System

Health Canada has agreed that a national integrated surveillance system is needed to document the extent and variation in AMR occurrence both geographically and temporally, linked to variations in antimicrobial use and other contributors to AMR. The resulting information, provided in a timely fashion, is vital for the development of appropriate risk management strategies and informed policy decisions.

To guide the development of an integrated national surveillance program, a coordinated effort was needed. The Laboratory for Foodborne Zoonoses (LFZ) and the Foodborne, Waterborne and Zoonotic Infections Division (FWZID) have partnered with the National Microbiology Laboratory (NML) to fulfill this mandate. Together they formed the National Steering Committee on Antimicrobial Resistance in Enterics (NSCARE), which has members from the Canadian Food Inspection Agency (CFIA), and provincial agriculture ministries of Quebec, Ontario and Alberta. Additional input into the development of CIPARS has been received from ENDS, the Canadian Public Health Laboratory Network (CPHLN), and the recently formed National Steering Committee on Antimicrobial Use Monitoring. A CIPARS strategic planning session was conducted in October 2003, which brought together multiple groups to refine the current strategy and plan for future expansion.

The initial work of CIPARS involved implementation of a number of background studies to systematically explore various options for collecting accurate, representative, harmonized national data on the magnitude and distribution of AMR in enteric organisms from animals, food and humans. A similar set of targeted data source assessment studies were conducted for antimicrobial use monitoring purposes in both the human and agri-food sectors.

Based on the findings of these background studies, it was concluded that, although some data is currently collected via passive surveillance systems and research projects, a new active surveillance program would be needed in order to obtain continuous, methodologically harmonized and nationally representative data on human and agri-food antimicrobial use and bacterial resistance. Active surveillance demonstration projects have now been launched to test the feasibility of a fully integrated national surveillance system. These projects are being developed and implemented in partnership with numerous private and public sector groups*, with Health Canada support and coordination. To enhance the comparability of data domestically and internationally, all laboratories agreed to employ the United States National Antimicrobial Resistance Monitoring System (NARMS) 2002 susceptibility testing methodology, using an automated Sensititre™ System (*TREK Diagnostics*) which tests susceptibility to a panel of 16 antimicrobials using a broth microdilution methodology. LFZ is performing susceptibility testing and primary isolation of bacterial species from animal and food samples, and susceptibility testing for human isolates is being performed by NML. Data sharing agreements have been prepared to facilitate integrated analysis and communication of results.

A number of research and pilot studies have been initiated by Health Canada and/or research partners, in collaboration with public sector and private industry groups, and universities**. The findings of these studies will aid in the development and refinement of the surveillance system (for listing of studies see Summary of Background Studies for CIPARS Development).

CIPARS Current Events

Figure 1 outlines current and future CIPARS activities.

---

* *Public Sector Groups: Canadian Food Inspection Agency, Canadian Public Health Laboratory Network. Private Sector Groups: Intercontinental Medical Statistics Health, Canadian Meat Council, Canadian Poultry and Egg Processors Council, National Renderers Association, Federally Registered Abattoirs.*

** *Public Sector Groups: Ontario Ministry of Agriculture and Food, Alberta Agriculture Food and Rural Development, British Columbia Ministry of Agriculture, Food and Fisheries. Private Sector Groups: Ontario Cattlemen's Association, Centre for Coastal Health, University of Guelph, University of Saskatchewan.*

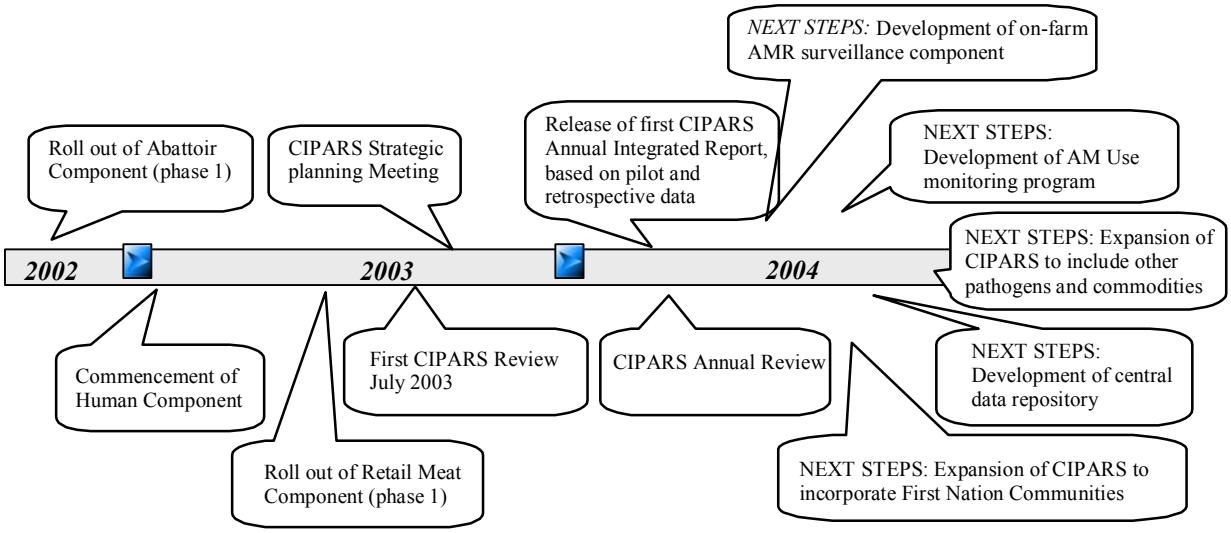


Figure 1. Current and future CIPARS activities

CIPARS 2002 Report Structure

As the CIPARS system components have only recently been initiated, this first annual report is limited to AMR surveillance results from the human and agri-food sectors and nationally representative human antimicrobial use information. Human AMR data for *Salmonella* and *Shigella* were collected retrospectively from five provinces in Canada (Human Antimicrobial Resistance Data Collection and Analysis – Appendix B.1). The agri-food isolates were collected according to a sampling plan designed to provide nationally representative and epidemiologically valid antimicrobial susceptibility data from bacteria isolated from animals entering the food chain (*Abattoir Surveillance* Methods- Appendix B.2). Human antimicrobial use data were collected by IMS Health and assessed by CIPARS with a full understanding of the representativeness and validity of the data (Human Antimicrobial Use Data Collection and Analysis - Appendix B.3).

This report also includes CIPARS future expansion plans, specifically with respect to AMR surveillance and antimicrobial use monitoring in animals. Demographic data, drug classification system, and surveillance methods are included in the appendices.

Section Two - Antimicrobial Resistance

The antimicrobials tested (for both human and agri-food isolates) are classified according to their human health importance using a classification system currently being developed by the Veterinary Drugs Directorate (VDD), Health Canada, within their "Proposed Guidelines for Evaluation of the Microbiological Safety of Veterinary Antimicrobials" (Appendix A.1). This classification system was still being refined when this report was written, thus final classification may differ from that used herein.

Human Antimicrobial Resistance

At the time of this report, data were yet not available from an active AMR surveillance program for human enteric pathogens. However, the following information from recent targeted studies are intended to provide interim data on the extent of AMR in enteric bacteria Canada, as well as context/background for CIPARS, results of which will be published in the 2003 annual report. Details on enteric disease reporting are available in Appendix A.3.

The objectives of the human AMR section are to describe the current reporting structure for enteric diseases, investigate the epidemiology of AMR trends in *Salmonella* and *Shigella* in Canada, and illustrate the strengths and limitations of using routinely generated data for nation-wide AMR surveillance.

Antimicrobial Resistance Trends in *Salmonella* and *Shigella*

Introduction

The Health Canada Foodborne, Waterborne, and Zoonotic Infections Division (FWZID) initiated several studies that support the development of a national AMR surveillance program for enteric pathogens. The following is a summary of a Retrospective Study of AMR among Human *Salmonella* and *Shigella* isolates conducted in five provinces across Canada. The objectives of this study are to describe the current knowledge of AMR in Canada, highlight regional differences in resistance testing, and evaluate the utility of using routinely collected data for AMR surveillance.

In 2002, the provincial public health laboratories in Alberta, Newfoundland and Labrador, Ontario, Prince Edward Island, and Saskatchewan provided FWZID with AMR data for human *Salmonella* and *Shigella* isolates. The study methodology details are described in Appendix B.1. The number of years of data available, the variables included, and the antimicrobial drugs tested in resistance panels varied between and within the provinces (Appendix B.1). Data on phage type was not consistently available; therefore, we omitted this variable from the analysis.

The primary focus was on the most prevalent *Salmonella* serovars and *Shigella* serogroups. Additionally, we describe resistance trends for *Salmonella* Newport because of the emergence in the United States of multidrug resistance in this pathogen (MMWR 2002).

In the final dataset (9171 isolates), 6939 (76%) isolates were *Salmonella* and 2232 (24%) isolates were *Shigella* (Table 1). Overall, the most common *Salmonella* serovars were *S.* Enteritidis, *S.* Typhimurium, and *S.* Heidelberg and the most common *Shigella* serogroups were *S. sonnei* and *S. flexneri.*

Individual Antimicrobial Drug Resistance and Multiple Drug Resistance

Tables 2 and 3 show the percentage of resistant isolates by serovar/serogroup. The percentage of isolates resistant to at least one antimicrobial was higher for *Shigella* than *Salmonella*; this was consistent for all provinces that tested both bacterial species. For *Salmonella*, approximately 54% of isolates were fully susceptible to the range of antimicrobials for which each isolate was tested, in comparison to approximately 23% of *Shigella* isolates. These findings highlight the need to monitor trends in resistance among other enteric microbes, such as *Shigella,* which are not primarily foodborne. This monitoring is especially important because resistance determinants can be exchanged between different enteric bacterial species (Replogle *et al.*, 2000).

In comparison to *Shigella*, we consistently observed a higher percentage of *Salmonella* isolates fully susceptible to all antimicrobials for which the isolates were tested. This finding highlights the need to include non-foodborne bacteria in enteric antimicrobial resistance trend monitoring.

Table 1. Number of human isolates reported and analyzed, by province, 1993-2001

Province	Non-Typhi *Salmonella**		*Salmonella* Typhi		*Shigella*	
	No.	%	No.	%	No.	%
Alberta	1950	29	43	28	1114	50
Newfoundland	75	1	0	0	0	0
Ontario	3895	57	109	71	901	40
Prince Edward Island	102	2	1	1	4	0
Saskatchewan	764	11	0	0	213	10
Totals	**6786**	**100**	**153**	**100**	**2232**	**100**

***Note**: *Includes S. Paratyphi*

Table 2. Antimicrobial resistance among top ten *Salmonella* serovars (human), 1993-2001

Serovar	% resistant to at least one antimicrobial	No. isolates tested	No. isolates by the number of antimicrobials in resistance pattern			
			0	1-4	5-8	9-12
Typhimurium var. Copenhagen	82.7	196	34	120	41	1
Hadar	80.2	383	76	272	34	1
Typhimurium	54.2	2826	1293	327	1188	18
Agona	44.2	129	72	56	1	0
Heidelberg	33.3	874	583	215	72	4
Enteritidis	28.1	788	567	215	6	0
Typhi	22.2	153	119	13	19	2
Infantis	13.5	104	90	14	0	0
Newport	4.8	83	79	3	1	0
Thompson	2.9	206	200	5	1	0
Totals		**5742**	**3113**	**1240**	**1363**	**26**

Note: Isolates were not tested for the same number of antimicrobials. The median number of antimicrobials tested was 14 (range=1-32). Of those isolates resistant to at least five antimicrobials, 98% were tested for 13-32 antimicrobials.

Table 3. Antimicrobial resistance among *Shigella* serogroups, 1993-2001

Serogroup	% resistant to at least one antimicrobial	No. isolates tested	No. isolates by the number of antimicrobials in resistance pattern			
			0	1-4	5-8	9-10
flexneri	93.5	510	33	302	174	1
sonnei	87.8	1607	196	1095	314	2
dysenteriae	79.4	34	7	19	8	0
boydii	75.3	73	18	44	10	1
Totals		**2224**	**254**	**1460**	**506**	**4**

Note: *No serogroup was identified for eight Shigella isolates. Isolates were not tested for the same number of antimicrobials. The median number of antimicrobials tested was 14 (range=1-32). Of those isolates resistant to at least five antimicrobials, 52% were tested for 13-32 antimicrobials.*

Annual Trends in Antimicrobial Resistance

To examine annual trends, we combined the data for 1997-2000 (years available for all provinces). To allow for differences in testing among the provinces (Appendix B.1), we present resistance by antimicrobial class and category of importance to human health, rather than resistance to individual antimicrobials.

Between 1997-2000, *Salmonella* resistance rates were highest for tetracycline, penicillins, chloramphenicol, and nitrofurantoin (Figures 2 and 3). Increases in resistance to tetracycline, penicillins, and chloramphenicol were observed between 1997 and 1999. Between 1999 and 2000, there were apparent increases of 29% and 24% in rates of resistance to aminoglycosides and folate pathway inhibitors, respectively. However, changes in antimicrobial testing may account for these increases. Beginning in 2000, *Salmonella* isolates in these data were tested for resistance to streptomycin and the number of isolates tested for resistance to sulfamethoxazole increased from 33 in 1999 to 741 in 2000. The antimicrobials to which *Salmonella* isolates showed the lowest rates of resistance were quinolones, "other" beta-lactams, and cephalosporins (<5%).

Among *Salmonella* Typhimurium isolates, resistance rates were highest for nitrofurantoin, tetracycline, penicillins, and chloramphenicol (Figures 4 and 5). Between 1999 and 2000, *S.* Typhimurium isolates showed over 40% increases in rates of resistance to folate pathway inhibitors and aminoglycosides. However, as with *Salmonella* isolates overall, changes in the antimicrobials for which these isolates were tested may have contributed to the observed increases.

Shigella isolates showed higher rates of resistance than *Salmonella* isolates (Figure 6 and 7). The highest rates were observed for folate pathway inhibitors, tetracycline, and penicillins. Although the rate of resistance to aminoglycosides increased by 49% between 1999-2000, this can likely be explained by the initiation of testing for streptomycin resistance. Between 1998 and 2000, a decrease of 27% in the rate of resistance to penicillins was observed. Low levels of resistance were seen for nitrofurantoin (0.52%), quinolones (0.84%), and other beta-lactams (1.7%)

Between 1997 and 2000, for *Salmonella* and *Shigella* isolates combined, there were low rates of resistance to ciprofloxacin (0.10%), ceftriaxone (0.17%), and nalidixic acid (1.8%), and high rates of resistance to trimethoprim-sulfamethoxazole (17%) and ampicillin (35%).

For all *Salmonella* serotypes and *Shigella* serogroups, a relatively low percentage of isolates resistant to Category I antimicrobials (very high human health importance) (<4%) was observed. *Salmonella* isolates demonstrated an increasing temporal trend for resistance to Category II antimicrobials (high human health importance). Rates of resistance to Category II antimicrobials among *Shigella* isolates fluctuated from a high of 88% in 1998, to 74% in 2000.

Overall, antimicrobial resistance rates in *Shigella* and *Salmonella* for drugs of very high human health importance (Category I) remained quite low over time (<4%). However, rates of resistance to drugs of very high and high human health importance (Category I and II drugs) appear to be increasing among *Salmonella* isolates.

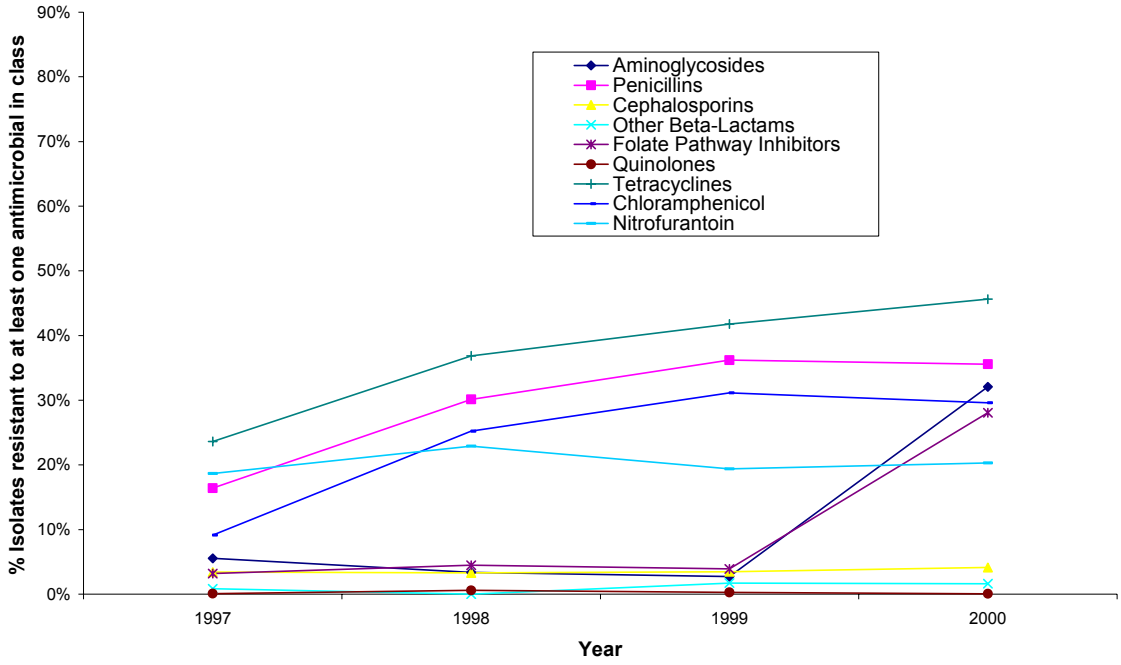


Figure 2. Antimicrobial resistance among human *Salmonella* isolates from five Canadian provinces, by antimicrobial class, 1997-2000

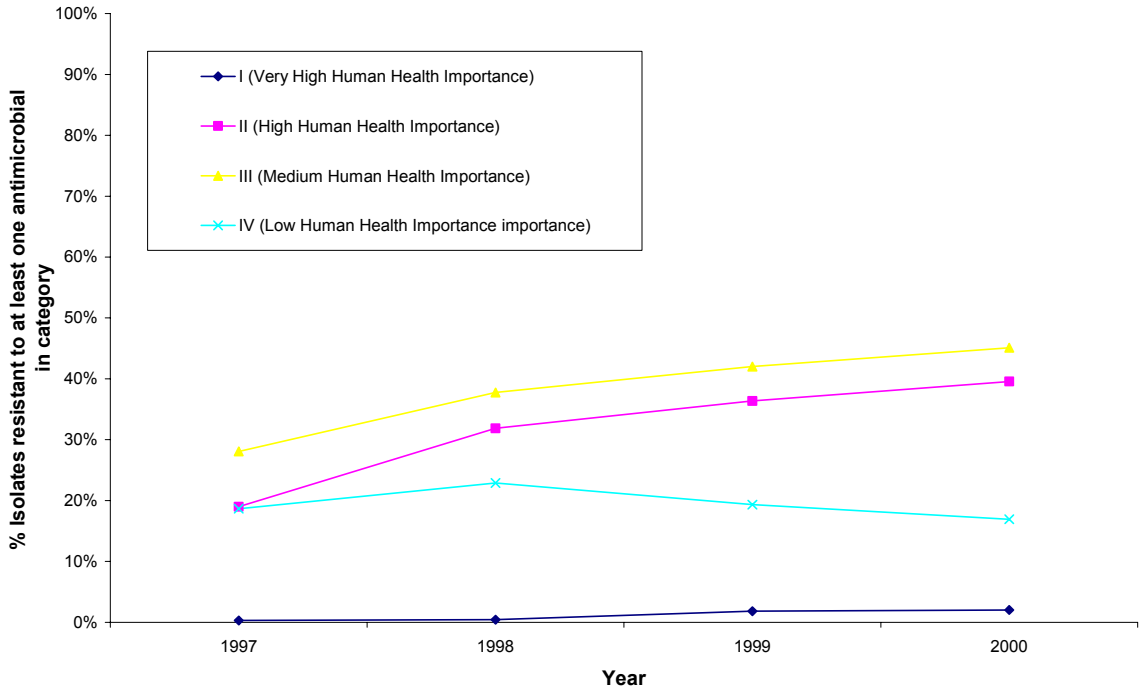


Figure 3. Antimicrobial resistance among human *Salmonella* isolates from five Canadian provinces, categorized by importance to human health, 1997-2000

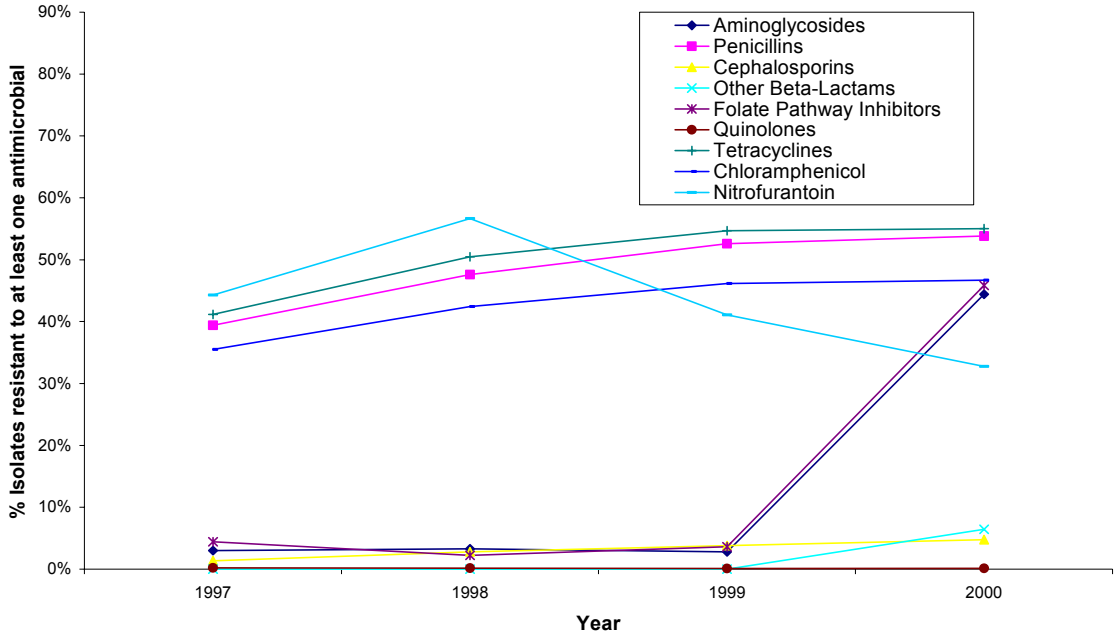


Figure 4. Antimicrobial resistance among human *Salmonella* Typhimurium isolates from five Canadian provinces, by antimicrobial class, 1997-2000

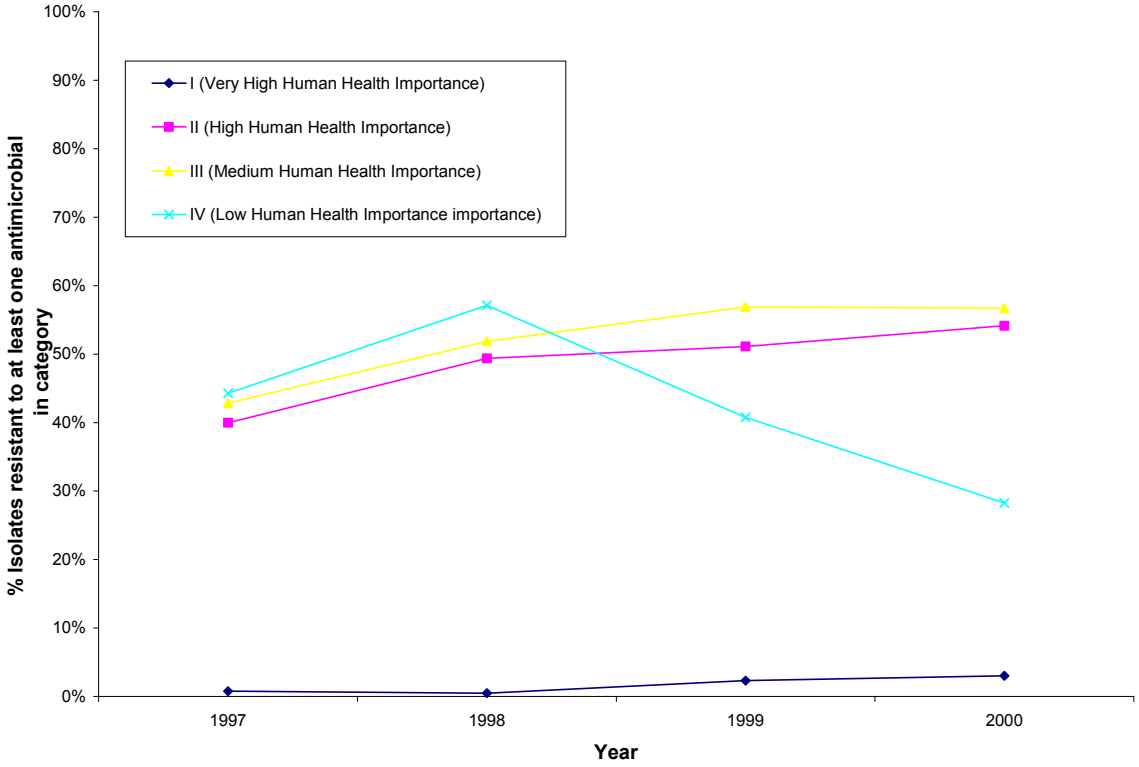


Figure 5. Antimicrobial resistance among human *Salmonella* Typhimurium isolates from five Canadian provinces, categorized by importance to human health, 1997-2000

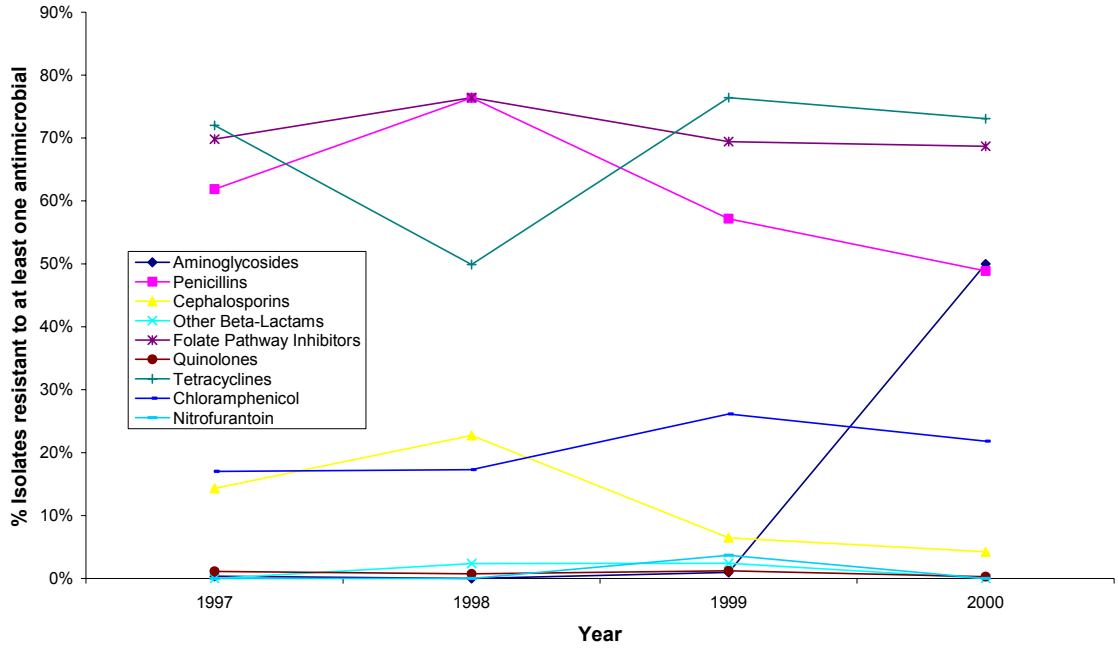


Figure 6. Antimicrobial resistance among human *Shigella* isolates from five Canadian provinces by antimicrobial class, 1997-2000

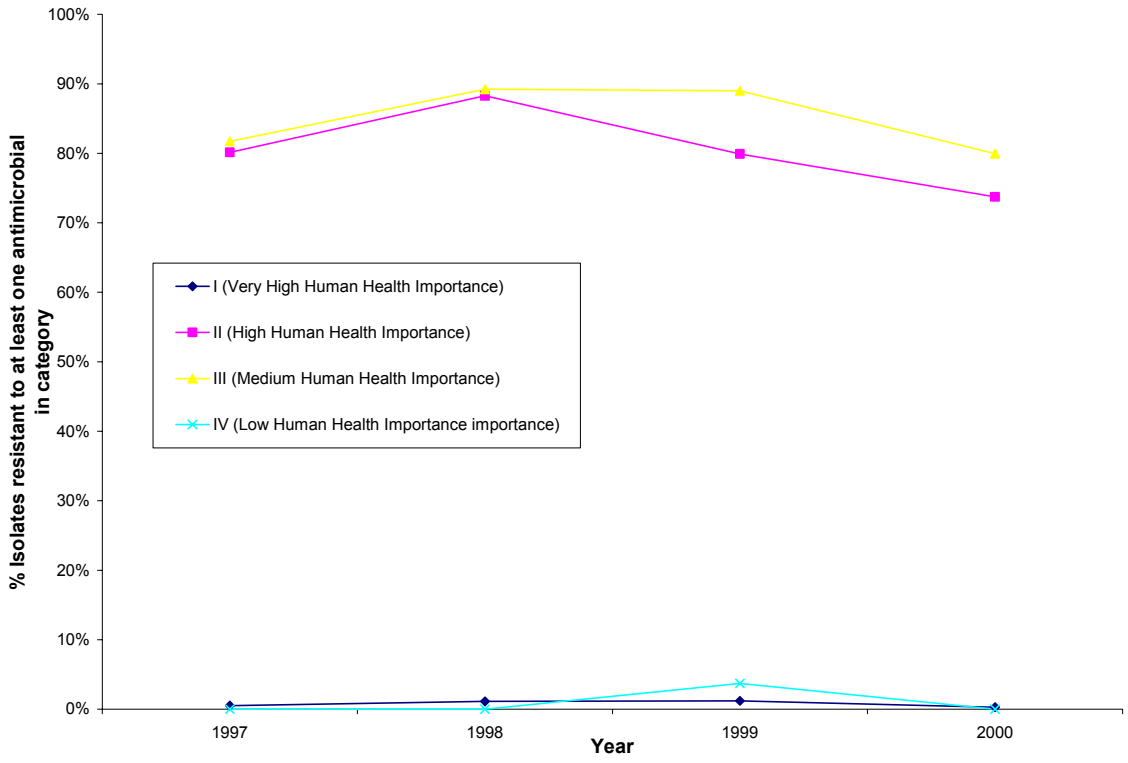


Figure 7. Antimicrobial resistance among human *Shigella* isolates from five Canadian provinces, categorized by importance to human health, 1997-2000

Salmonella *Newport*

Between 1997 and 2001, the five participating provinces conducted AMR testing on 83 *Salmonella* Newport isolates: 35 (42%) in Ontario, 22 (27%) in Alberta, 19 (23%) in Saskatchewan, five (6.0%) in Prince Edward Island and two (2.4%) in Newfoundland and Labrador. This represents 16% of the 355 isolates reported by NML/NESP for these years [CCDR 2003].

Ontario was the only province that observed resistance among *S*. Newport isolates. Four isolates (11%) were resistant to at least one antimicrobial, having the following four resistance patterns: TCY, SXT, TCY SXT, and AMP CHL TCY TIC SXT. The difference between Ontario and the other provinces may be associated with the emergence of multidrug resistant *S*. Newport in the United States. For example, in April 2002, an *S*. Newport outbreak occurred in the United States involving five states (New York, Michigan, Pennsylvania, Ohio, and Connecticut); four of these states border Ontario (CDC, 2002). This closer proximity of Ontario to the affected states may explain why Ontario observed resistant *S*. Newport.

Data Limitations

This study included the five provinces that collected AMR data and were interested in participating. These provinces represent approximately 53% of the Canadian population. The provinces differed in the information they collected, which limited inter-provincial comparability of the data. Furthermore, our ability to investigate temporal trends for resistance to individual antimicrobials was limited because the antimicrobials tested varied within the provinces from year-to-year and from isolate-to-isolate.

The presence of resistance in *Salmonella* Newport in Ontario may herald a growing public health issue for Canada. An active surveillance system is required to assist in the detection of emerging drug resistant pathogens, such as *S.* Newport (carrying novel resistance patterns) and monitoring the spread of bacteria and AMR patterns of public health concern across the country.

Antimicrobial Resistance in the Agri-food Sector

CIPARS relies primarily on *Active Surveillance* to monitor the occurrence of AMR in the agri-food sector. *Active Surveillance* includes two components: *Abattoir Surveillance* which collects AMR data from animals at the point of entry into the food chain, and *Retail Surveillance* which targets AMR present in animal-derived food purchased by consumers (Ravel, 2001). The *Abattoir Surveillance* began in September 2002, and involves voluntary participation of slaughterhouses (n=51). Currently, this surveillance project collects cecal samples from cattle, swine and broiler chickens, and is investigating AMR in generic *E. coli* and *Salmonella.* The *Retail Surveillance* was launched in the summer of 2003 and results will be available in the 2003 report.

CIPARS also relies on isolates obtained through the *Passive Surveillance* of *Salmonella* in animals. These isolates are clinical *Salmonella* isolates submitted to the *Salmonella* Typing Laboratory of LFZ. This laboratory is an ISO 17025 accredited laboratory and an Office Internationale des Epizooties (OIE) Reference Laboratory for salmonellosis. It receives isolates from several veterinary diagnostic laboratories across Canada. *Passive Surveillance* also provided information on pork (meat) derived from healthy swine. Please see Appendix B.2 for further details on methodology for *Active* (*Abattoir*) and *Passive Surveillance.*

The objectives of the agri-food AMR section of this year's report were to: present the individual antimicrobial drug resistance, multiple drug resistance and AMR patterns for generic *E. coli* and *Salmonella* for the sampled commodities, and to describe trends across bacterial species and across commodity groups.

The data in this section are presented in Parts I and II, representing the *Abattoir* and *Passive Surveillance* respectively. Part III provides a discussion and synthesis of the key findings.

Part I – Active Surveillance of Healthy Animals and Passive Surveillance of Food of Animal Origin

Beef Cattle – Generic *E. coli* Isolates

(*Abattoir Surveillance* n=78 isolates)

For 2002, bovine *E. coli* isolates were all from feedlot cattle.

Individual Antimicrobial Drug Resistance: All *E. coli* isolates were fully susceptible to: ceftiofur, ceftriaxone, ciprofloxacin, nalidixic acid, amikacin, amoxicillin-clavulanic acid, cefoxitin, gentamicin, kanamycin, and trimethoprim-sulfamethoxazole (Figure 8 and Appendix Table A.4.1). Resistance to ampicillin, cephalothin, and chloramphenicol was less than 3%). The highest levels of resistance were to tetracycline (27%), streptomycin (12%), and sulfamethoxazole (9%).

Multiple Drug Resistance: Sixty-nine percent of the isolates were susceptible to all 16 antimicrobials tested (Figure 9). Resistance to more than three antimicrobials was present in 1% of isolates (1 isolate).

AMR Patterns: Eight different resistance patterns were identified within the 24 resistant *E. coli* isolates (Appendix Table A.4.2).

Results from the first year of *Abattoir Surveillance* showed that 69% of *E. coli* isolated from bovine cecal samples were susceptible to all antimicrobials tested. All isolates were susceptible to antimicrobials of greatest human health importance (ceftiofur, ceftriaxone, ciprofloxacin). With the exception of tetracycline (27%), resistance to the other antimicrobials tested was null or below 12%.

Beef Cattle - *Salmonella* Isolates

(*Abattoir Surveillance* n=1 isolate)

Only one *Salmonella* isolate was recovered from beef cattle through the *Abattoir Surveillance*.

This isolate was *S*. London and it was resistant to tetracycline only.

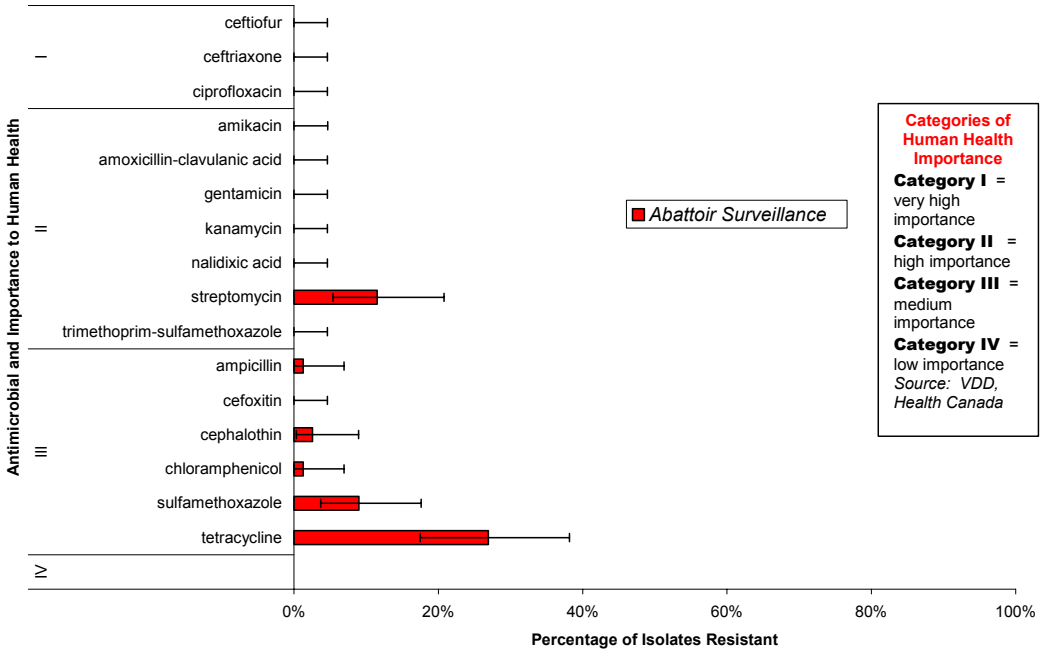


Figure 8. Individual antimicrobial drug resistance in **bovine *E. coli*** isolates, including 95% confidence intervals; *Abattoir Surveillance,* n=78 isolates

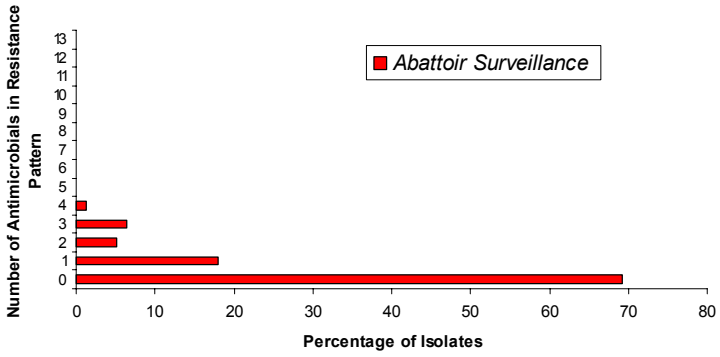


Figure 9. Multiple drug resistance in **bovine *E. coli*** isolates; *Abattoir Surveillance,* n=78 isolates

Swine – Generic *E. coli* Isolates

(*Abattoir Surveillance* n=38 isolates)

Individual Antimicrobial Drug Resistance: All *E. coli* isolates were fully susceptible to ceftiofur, ceftriaxone, ciprofloxacin, nalidixic acid, amikacin, amoxicillin-clavulanic acid, and cefoxitin (Figure 10 and Appendix Table A.4.1). The highest levels of resistance were to tetracycline (79%), streptomycin (45%), sulfamethoxazole (37%), and ampicillin (29%). Resistance levels to cephalothin, chloramphenicol, gentamicin, kanamycin, and trimethoprim-sulfamethoxazole ranged from three to 13%.

Multiple Drug Resistance: Twenty-one percent of *E. coli* isolates were susceptible to all antimicrobials tested, 16% were resistant to only one (tetracycline), 60% were resistant to two to five antimicrobials and none were resistant to more than 7 (Figure 11).

AMR Patterns: Sixteen different resistance patterns were identified among the 30 resistant *E. coli* isolates, and all included resistance to tetracycline (Appendix Table A.4.3). The two most common resistance patterns were: streptomycin-tetracycline (7 isolates), and tetracycline alone (6 isolates).

Results from the first year of *Abattoir Surveillance* showed that 21% of *E. coli* isolated from porcine cecal samples were susceptible to all antimicrobials tested. All isolates were susceptible to antimicrobials of greatest importance to human health (ceftiofur, ceftriaxone, ciprofloxacin). Seventy-nine percent of the isolates expressed resistance to tetracycline. Resistance to ampicillin, sulfamethoxazole, or streptomycin was between 29 and 45%. Multiple drug resistance was common (60%), and generally involved two to five antimicrobials; primarily including tetracycline, streptomycin and sulfamethoxazole.

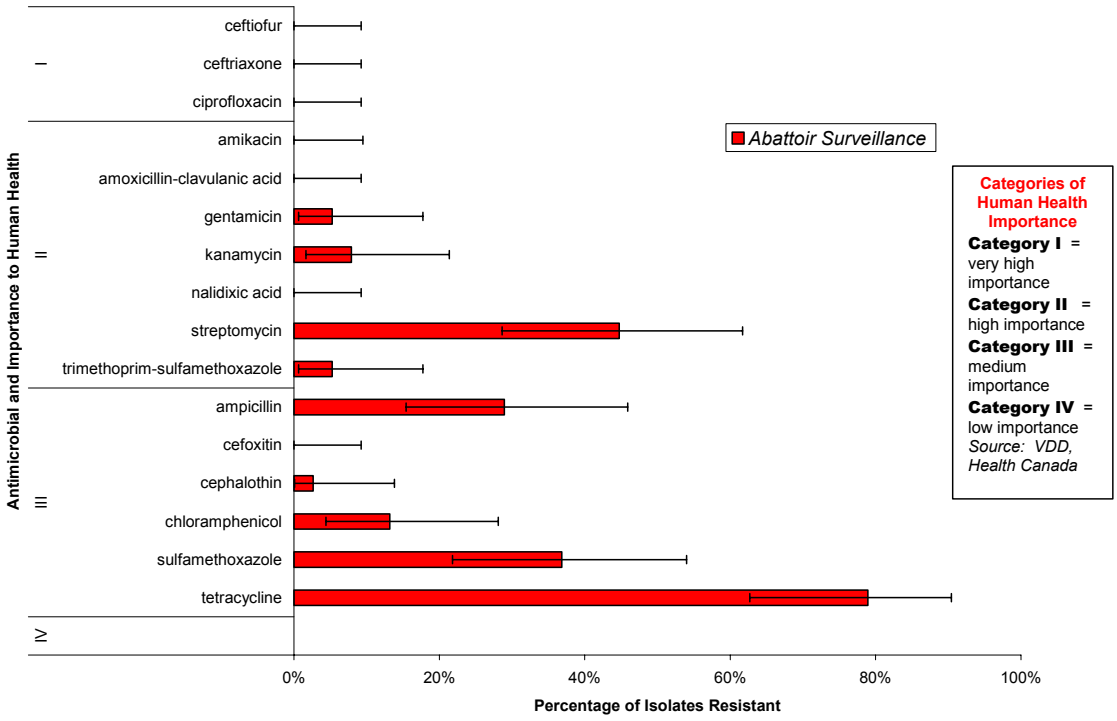


Figure 10. Individual antimicrobial drug resistance in **porcine *E. coli*** isolates, including 95% confidence intervals; *Abattoir Surveillance,* n=38 isolates

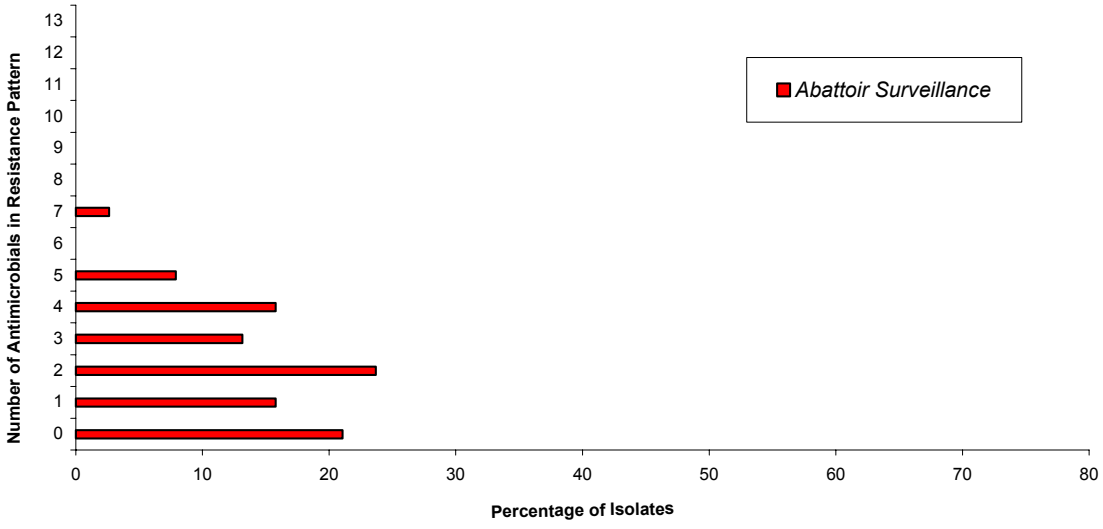


Figure 11. Multiple drug resistance in **porcine *E. coli*** isolates; *Abattoir Surveillance* n=38 isolates

Swine - *Salmonella* Isolates

(*Abattoir Surveillance* n=101; *Passive Surveillance* Pork n=33)

Individual Antimicrobial Drug Resistance: The *Salmonella* isolates from porcine cecal samples obtained through *Abattoir Surveillance* were susceptible to ceftiofur, ceftriaxone, ciprofloxacin, nalidixic acid, and amikacin (Figure 12 and Table A.4.4). The highest levels of resistance were to kanamycin (13%), chloramphenicol (16%), ampicillin (21%), sulfamethoxazole (32%), streptomycin (34%), and tetracycline (38%). Ceftiofur resistance was detected in one meat isolate obtained through *Passive Surveillance*.

Multiple Drug Resistance: Among the isolates from *Abattoir Surveillance*, 55% were susceptible to all antimicrobials tested (Figure 13). Resistance to five antimicrobials was the most frequent multiple drug resistance. Seventy percent of the meat isolates from *Passive Surveillance* were susceptible to all antimicrobials tested.

AMR Patterns: Seventeen different AMR patterns were identified among the 45 resistant porcine *Salmonella* isolates from the *Abattoir Surveillance* (Appendix Table A.4.5). Three patterns were more frequent than others: the ACSSuT pattern (15 isolates with or without resistance to other antimicrobials), joint resistance to streptomycin, sulfamethoxazole and tetracycline (15 isolates with or without resistance to other antimicrobials, excluding those with the ACSSuT pattern) and resistance to tetracycline alone (6 isolates). The ACSSuT pattern was also the most frequent pattern identified among meat samples.

Serovars And Resistance: From the *Abattoir Surveillance,* 27 different serovars were found; the five most frequent being Typhimurium var Copenhagen, Derby, Typhimurium, Heidelberg, and Infantis (Table 4 and Appendix Table A.4.5). Resistance to five or more antimicrobials was found for *S.* Typhimurium, Typhimurium var Copenhagen, Heidelberg and Mbandaka. One isolate of *S.* derby recovered from a pork meat sample expressed resistance to 8 antimicrobials. *S.* Typhimurium and Typhimurium var Copenhagen, and especially those with phage 104, were associated with AMR patterns involving a larger number of antimicrobials.

Results from the first year of *Abattoir Surveillance* showed that 55% of *Salmonella* isolated from porcine cecal samples were susceptible to all antimicrobials tested. All *Abattoir* isolates were susceptible to antimicrobials of greatest importance to human health (ceftiofur, ceftriaxone, and ciprofloxacin). Resistance to tetracycline, streptomycin or sulfamethoxazole was between 32% and 38%. Seventy percent of all meat (pork) isolates obtained through *Passive Surveillance* were susceptible to all antimicrobials tested. Ceftiofur resistance was detected in one meat (pork) sample (3% of *Passive Surveillance* pork isolates). Resistance patterns in porcine *Salmonella* were clearly linked to serovars and phagetype.

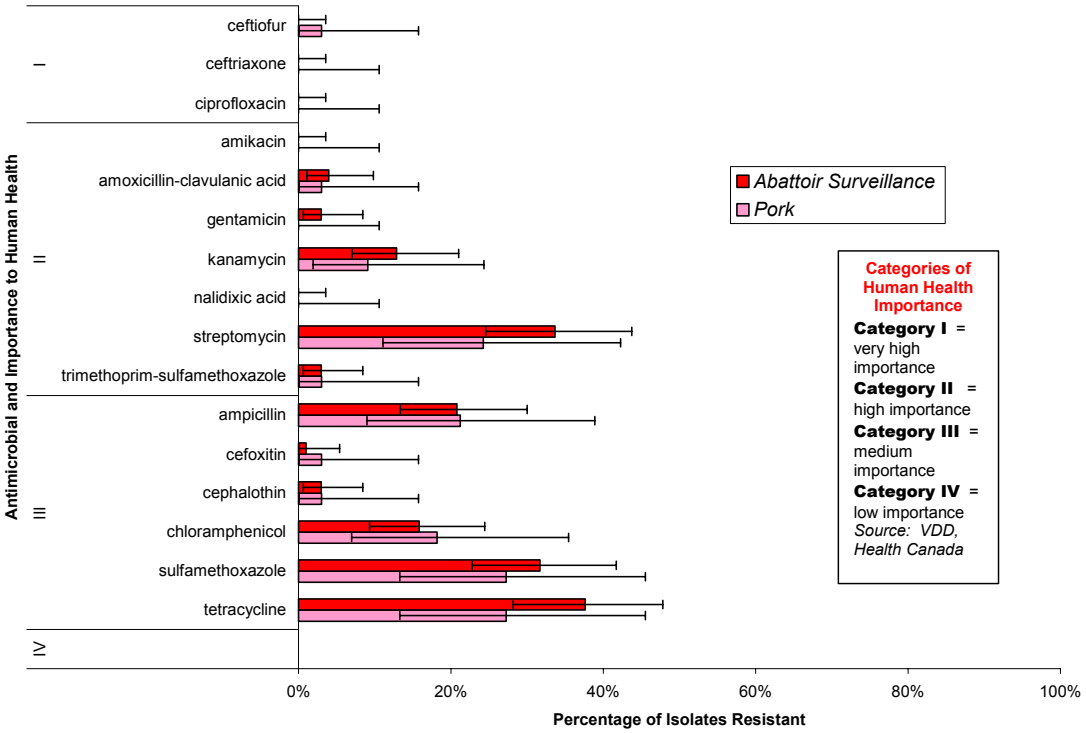


Figure 12. Individual antimicrobial drug resistance in **porcine *Salmonella*** isolates, including 95% confidence intervals; *Abattoir Surveillance* (n=101); pork (n=33)

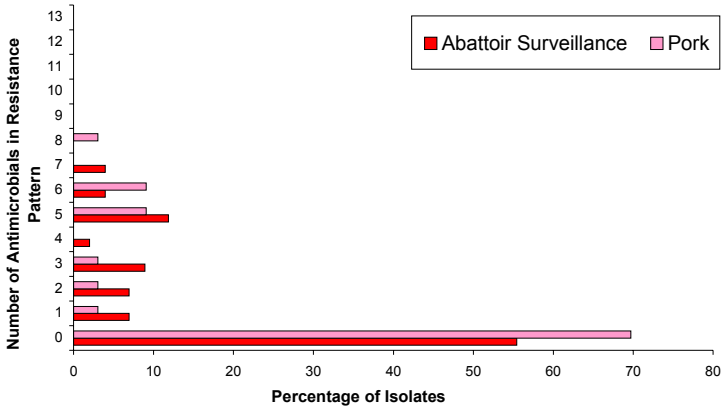


Figure 13. Multiple drug resistance in **porcine *Salmonella*** isolates; *Abattoir Surveillance* (n=101), pork (n=33)

Table 4. *Salmonella* serovars from **swine** (*Abattoir Surveillance*) and **pork** *(Passive Surveillance)*

Serovar	%n (n)	No. Isolates by the number of antimicrobials in resistance pattern			
Abattoir Surveillance **(n=101)**		**0**	**1-4**	**5-8**	**9-13**
Typhimurium var Copenhagen	19.8 (20)	4	3	13	0
Derby	13.9 (14)	1	13	0	0
Typhimurium	8.9 (9)	5	0	4	0
Heidelberg	6.9 (7)	3	3	1	0
Infantis	5.9 (6)	6	0	0	0
Brandenburg	5 (5)	5	0	0	0
Muenchen	5 (5)	5	0	0	0
Mbandaka	4 (4)	1	1	2	0
Senftenberg	4 (4)	3	1	0	0
Ohio	3 (3)	3	0	0	0
Other Serovars	23.8 (24)	20	4	0	0
Totals		**56**	**25**	**20**	**0**
Passive Surveillance **Pork (n=33)**					
Typhimurium	33.3 (11)	3	2	6	0
Infantis	30.3 (10)	10	0	0	0
Salmonella spp.	21.2 (7)	7	0	0	0
Derby	6.1 (2)	0	1	1	0
Cerro	3 (1)	1	0	0	0
London	3 (1)	1	0	0	0
Muenchen	3 (1)	1	0	0	0
Totals		**23**	**3**	**7**	**0**

Broiler Chicken – Generic *E. coli* Isolates

(*Abattoir Surveillance* n=40)

Individual Antimicrobial Drug Resistance: All *E. coli* isolates were susceptible to ceftriaxone, ciprofloxacin, nalidixic acid, and amikacin (Figure 14 and Appendix Table A.4.1). Ceftiofur resistance was detected in 10% of the isolates. The highest levels of resistance were to: tetracycline (65%), streptomycin (52%), sulfamethoxazole (45%), ampicillin (32%), kanamycin (25%), cephalothin (22%), and gentamicin (20%).

Multiple Drug Resistance: Twenty percent of the *E. coli* isolates were susceptible to all antimicrobials tested and 12% were resistant to only one antimicrobial (Figure 15 and Appendix Table A.4.6). Pentaresistance (22%) and resistance to two antimicrobials (18%) were most frequently observed multiple drug resistances.

AMR Patterns: Twenty-four resistance patterns were identified with no predominant pattern (Appendix Table A.4.6). However, joint resistance to sulfamethoxazole, streptomycin and tetracycline plus other antimicrobials was found in 13 isolates. The most resistant *E. coli* isolate showed resistance to ACSSuT, plus ampicillin, cephalothin, cefoxitin, ceftiofur gentamicin, and trimethoprim-sulfamethoxazole.

Results from the first year of *Abattoir Surveillance* showed that 20% of *E. coli* isolated from broiler chicken cecal samples were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 10% of isolates. Resistance to ceftiofur was always associated with resistance to amoxicillin-clavulanic acid and cefoxitin. Multiple drug resistance was present (68% of isolates) with a wide range of different patterns, usually involving resistance to at least tetracycline, streptomycin and sulfamethoxazole.

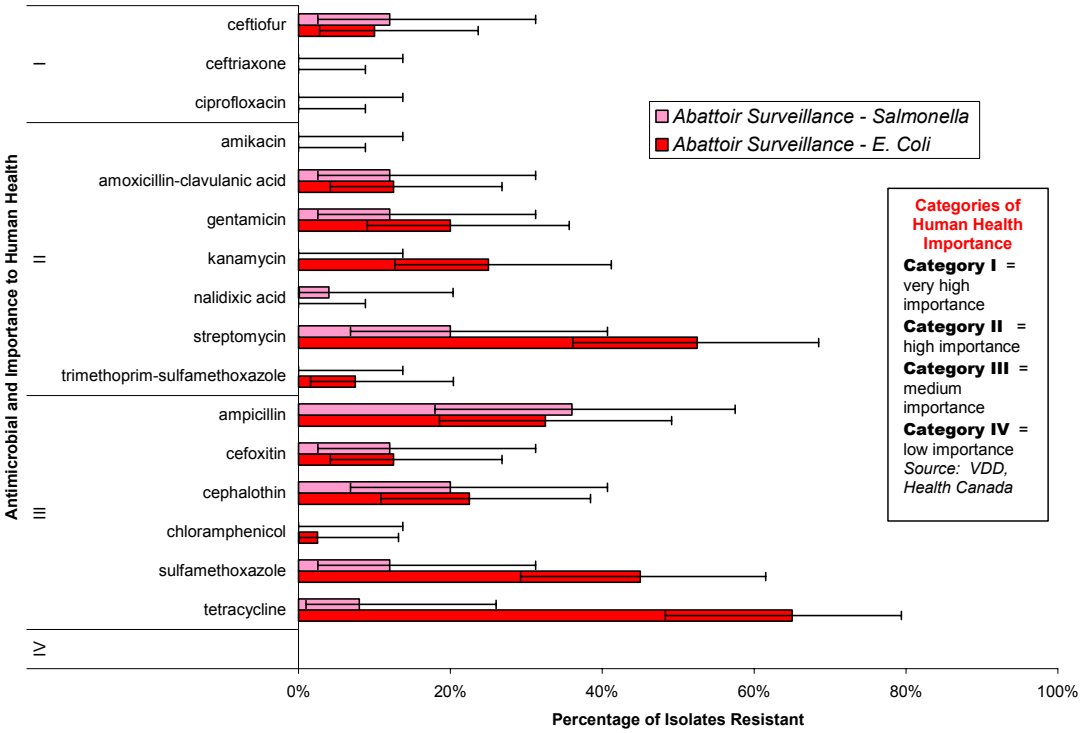


Figure 14. Individual antimicrobial drug resistance in ***Salmonella*** (n=25) and ***E. coli*** (n=40) isolates from **broiler chickens**, including 95% confidence intervals; *Abattoir Surveillance*

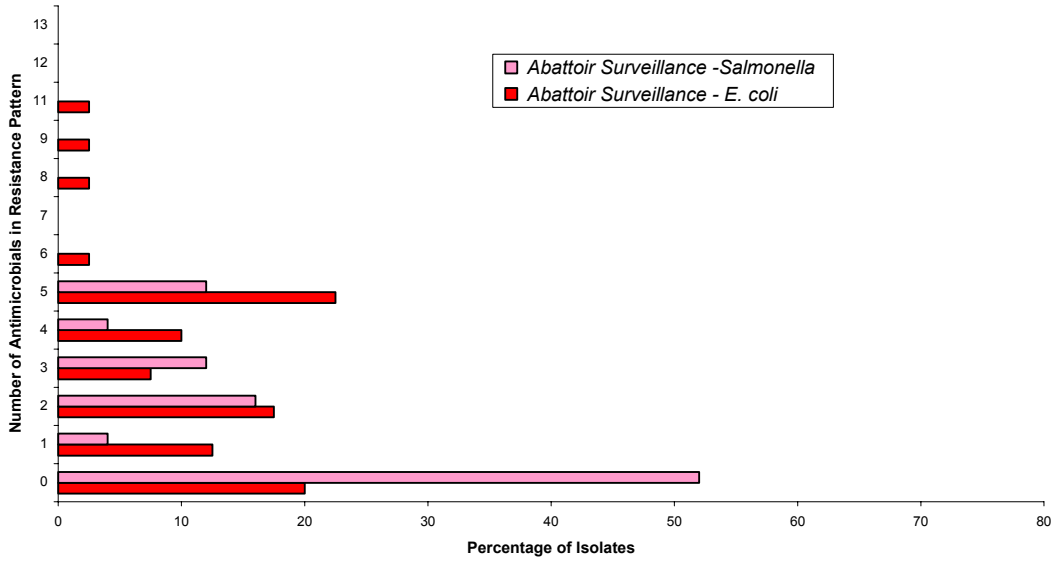


Figure 15. Multiple drug resistance in ***Salmonella*** (n=25) and ***E. coli*** (n=40) isolates from **broiler chickens**; *Abattoir Surveillance*

Broiler Chicken - *Salmonella* Isolates

(*Abattoir Surveillance* n=25)

Individual Antimicrobial Drug Resistance: All isolates from the *Abattoir Surveillance* were susceptible to ceftriaxone, ciprofloxacin, amikacin, chloramphenicol, kanamycin, and trimethoprim-sulfamethoxazole (Figure 14 and Appendix Table A.4.4). Twelve percent of the isolates were resistant to ceftiofur, and resistance to nalidixic acid was occasional (4%). The highest level of resistance was to ampicillin (36%), followed by cephalothin (20%) and streptomycin (20%).

Multiple Drug Resistance: Approximately one half of *Salmonella* isolates were susceptible to all antimicrobials tested (Figure 15).

AMR Patterns: The 12 resistant *Salmonella* isolates showed 8 different resistance patterns, with no predominant pattern types (Appendix Table A.4.6).

Serovars and Resistance: *S.* Heidelberg was the most frequent serovar (68%), followed by *S.* Kentucky (16%). Only 41% of the *S.* Heidelberg isolates susceptible to all antimicrobials versus 100% of the *S.* Kentucky (Table 5). Most AMR patterns (*S.* Heidelberg) included resistance to amoxicillin-clavulanic acid, cephalothin, cefoxitin, ceftiofur and ampicillin (Appendix Table A.4.7).

Results from the first year of *Abattoir Surveillance* showed that 52% of *Salmonella* isolated from broiler chicken cecal samples were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 12% of isolates. Resistance to ceftiofur was always associated with resistance to ampicillin, amoxicillin-clavulanic acid, cephalothin, and cefoxitin. Among resistant isolates, multiple drug resistance was present (92%) with a wide range of different patterns involving up to five antimicrobials.

Table 5. *Salmonella* serovars from **broiler chicken**; *Abattoir Surveillance* (n=25)

Serovar	% n (n)	No. isolates by the number of antimicrobials in resistance pattern			
		0	1-4	5-8	9-13
Heidelberg	68 (17)	7	7	3	0
Kentucky	16 (4)	4	0	0	0
Bradford	4 (1)	1	0	0	0
Hadar	4 (1)	0	1	0	0
Thompson	4 (1)	1	0	0	0
I:6.8:-:enx	4 (1)	0	1	0	0
Totals		**13**	**9**	**3**	**0**

Part II – Diseased Animals – *Passive Surveillance* of *Salmonella* from Clinical Isolates

Salmonella isolates from the *Passive Surveillance* database originated mainly from veterinary diagnostic submissions. Most samples were likely obtained from diseased animals, which may or may not have received antimicrobials prior to the sample collection.

Sample submissions also may have followed therapeutic failure (or therapy failure). These possibilities could artificially increase the apparent levels of resistance among diseased animals. For these reasons, clinical isolates are a good source of data for the detection of AMR

to new compounds or the identification of new multiple drug resistance patterns, but are not ideal for assessing the magnitude of the AMR problem.

Isolates included in the 2002 *Passive Surveillance* were collected from 1999 to 2002, and processed in 2001 and 2002 (Appendix Table A.4.8). The numbers of isolates processed in 2001 and 2002 were 869 and 727 respectively. All years were merged into one dataset because annual variations could represent a change in the source of submission, rather than a true temporal change. Different susceptibility testing ranges were used in 2001 and 2002 for several of the antimicrobials tested (Appendix B.2).

Cattle - Clinical *Salmonella* Isolates

(*Passive Surveillance* n=478)

Note: *The proportions of samples from 'Dairy animals', 'Veal', 'Beef cattle' and 'Feedlot' subjects amongst the Bovine Salmonella isolates from the Passive Surveillance were unknown.*

Individual Antimicrobial Drug Resistance: All bovine clinical *Salmonella* isolates were susceptible to ceftriaxone, ciprofloxacin, nalidixic acid and amikacin (Figure 16). Resistance to ceftiofur was observed in 8% of the isolates. The highest levels of resistance (between 50 and 60%) were observed for ampicillin, streptomycin, sulfamethoxazole and tetracycline.

Multiple Drug Resistance: Thirty-six percent of the isolates were susceptible to all 16 antimicrobials tested (Figure 17). However, 48% were resistant to five to 8 antimicrobials and 8% were resistant to 9 or more antimicrobials. The maximum number of antimicrobials where resistance was detected on the same isolate was 13 (n=1 isolate).

AMR Patterns: Twenty percent of isolates expressed the ACSSuT pattern (Appendix Table A.4.10), 18% expressed the AKSSUT pattern, while 14% expressed the ACKSSuT pattern. These patterns were found alone or in combination with resistance to other antimicrobials. Bovine clinical isolates were rarely (0.6%) resistant to only one antimicrobial.

Serovars and Resistance: *S.* Typhimurium and *S.* Typhimurium var Copenhagen represented more than half of the isolates (Table 6). These two serovars were also the most resistant, frequently showing resistance to five or more antimicrobials. Twelve isolates of *S.* Newport also expressed resistance to multiple drugs, the number of antimicrobials in the resistant patterns being between 9 and 11. The patterns ACSSuT, ACKSSuT and AKSSuT and resistance to amoxicillin-clavulanic acid, cefoxitin, ceftiofur and cephalothin were linked with the aforementioned serovars (Appendix Table A.4.11).

Results from *Passive Surveillance* showed that 36% of all bovine clinical *Salmonella* isolates were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 8% of the bovine clinical isolates. Forty-eight percent of isolates were resistant to between five and 8 antimicrobials and 8% were resistant to 9 or more antimicrobials. The serovars *S.* Typhimurium and *S.* Newport often expressed resistance to multiple antimicrobials.

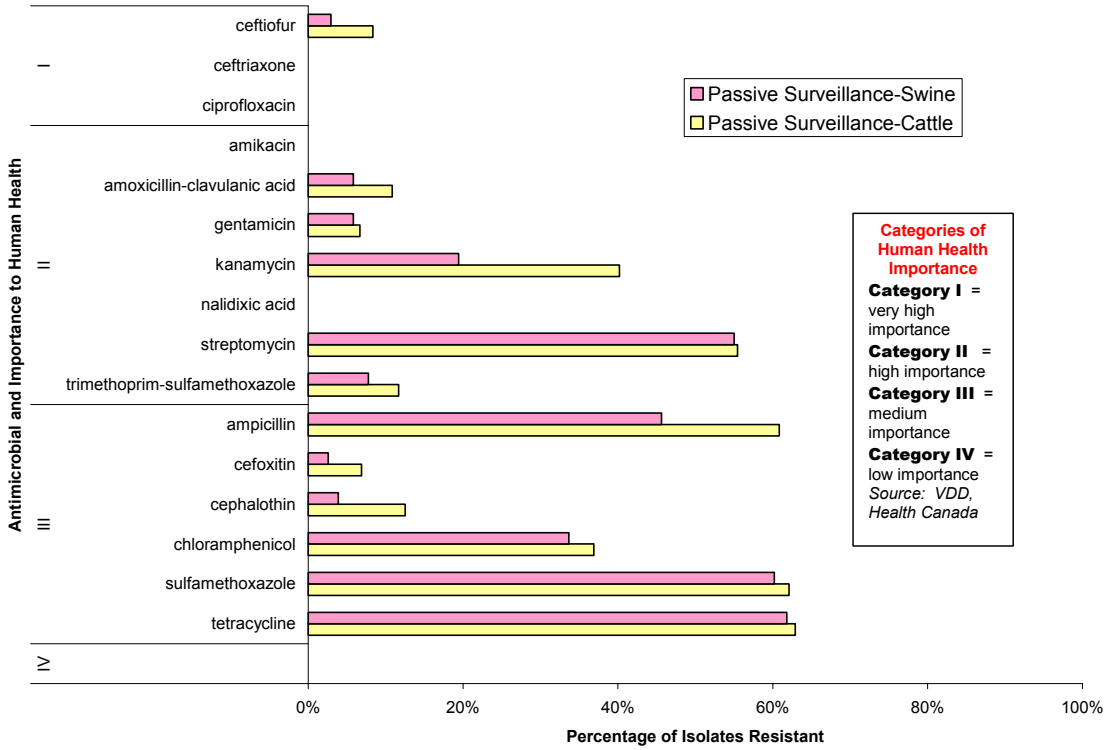


Figure 16. Individual antimicrobial drug resistance in ***Salmonella*** from **bovine** (n=478) and **porcine** (n=309) clinical isolates; *Passive Surveillance*

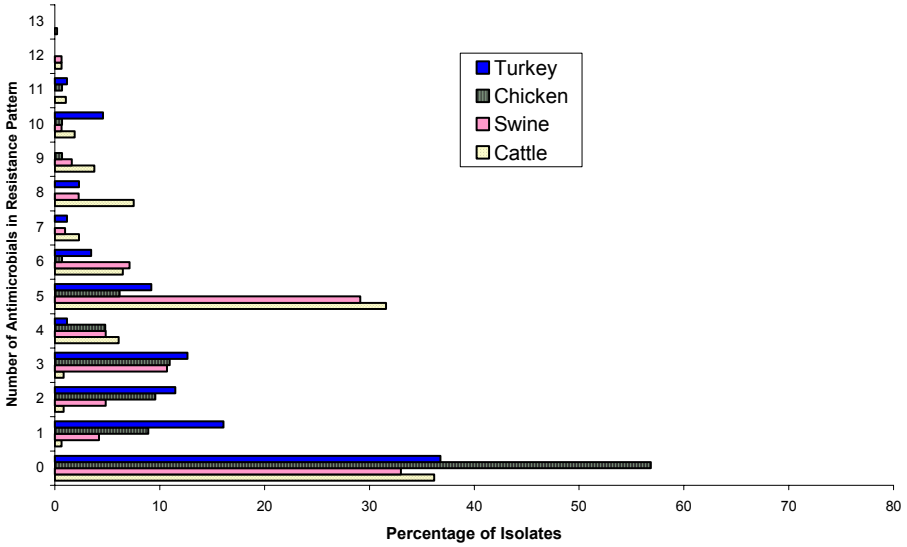


Figure 17. Multiple drug resistance in ***Salmonella*** isolates from **cattle** (n=478), **swine** (n=309), **chicken** (n=146) and **turkey** (n=87); *Passive Surveillance*

Table 6. *Salmonella* serovars from **cattle** (clinical isolates); *Passive Surveillance* (n=478)

Serovar	%n (n)	No. isolates by the number of antimicrobials in resistance pattern			
		0	1-4	5-8	9-13
Typhimurium	33.5 (160)	25	2	121	12
Typhimurium var Copenhagen	27.4 (131)	3	27	95	6
Kentucky	9 (43)	42	1	0	0
Muenster	6.5 (31)	30	0	1	0
Cerro	3.3 (16)	16	0	0	0
Salmonella spp.	3.3 (16)	8	1	4	3
Newport	2.5 (12)	0	0	0	12
Heidelberg	2.3 (11)	6	3	1	1
Stanley	1.5 (7)	2	1	4	0
Dublin	0.8 (4)	2	2	0	0
Other serovars	9.4 (47)	39	3	3	2
Totals		**173**	**40**	**229**	**36**

Swine - Clinical *Salmonella* Isolates

(*Passive Surveillance* n=309)

Individual Antimicrobial Drug Resistance: All isolates were susceptible to amikacin, ceftriaxone, ciprofloxacin and nalidixic acid (Figure 16). Resistance to ceftiofur was detected in 3% of the isolates (Appendix Table A.4.12). Resistance levels were highest (more than 50%) to tetracycline, streptomycin and sulfamethoxazole.

Multiple Drug Resistance: Thirty-three percent of the isolates were susceptible to all 16 antimicrobials tested (Figure 17). The maximum number of antimicrobials where resistance was detected on the same isolate was 12 (n=2 isolates).

AMR Patterns: The ACSSuT pattern was expressed by 24% of the isolates, while ACKSSuT and AKSSuT were expressed by approximately 8% of the isolates. These patterns were found alone, or in combination with resistance to other antimicrobials (Appendix Table A.4.12).

Serovars and Resistance: The most frequent serovars were *S.* Typhimurium and *S.* Typhimurium var Copenhagen (Table 7). *S.* Typhimurium, Agona, Infantis and Ohio had AMR patterns involving more then 8 antimicrobials. *S. T*yphimurium var Copenhagen and *S.* Derby, and other less frequent serovars, also expressed multiple drug resistance, involving a large variety of antimicrobials (Appendix Table A.4.13).

Results from *Passive Surveillance* showed that 33% of all porcine clinical *Salmonella* isolates were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 3% of the porcine clinical isolates. Thirty-nine percent of isolates were resistant to between five and 8 antimicrobials and 3% were resistant to 9 or more antimicrobials. *Salmonella* Typhimurium and *S.* Typhimurium var Copenhagen were the most frequent serovars, and together with *S.* Agona, Infantis, Ohio and Derby, they represented the most resistant porcine clinical serovars.

Table 7. *Salmonella* serovars from **swine** (clinical isolates); *Passive Surveillance* (n=309)

Serovar	%n (n)	No. isolates by the number of antimicrobials in resistance pattern			
		0	1-4	5-8	9-13
Typhimurium	41.1 (127)	29	17	76	5
Typhimurium var Copenhagen	21 (65)	15	16	34	0
Derby	9.1 (28)	7	19	2	0
Salmonella spp.	4.2 (13)	7	1	5	0
Agona	3.2 (10)	3	6	0	1
Heidelberg	2.6 (8)	2	6	0	0
Mbandaka	1.9 (6)	5	1	0	0
Brandenburg	1.6 (5)	5	0	0	0
Infantis	1.6 (5)	4	0	0	1
Krefeld	1.6 (5)	3	0	2	0
Other serovars	12.0 (37)	22	10	3	2
Totals		**102**	**76**	**122**	**9**

Chicken - Clinical *Salmonella* Isolates

(*Passive Surveillance* n=146)

Note: *Chicken isolates from Passive Surveillance may include layer hens in addition to broilers. The current metadata does not permit further distinction.*

Individual Antimicrobial Drug Resistance: All isolates were susceptible to amikacin, ceftriaxone, ciprofloxacin, nalidixic acid and trimethoprim-sulfamethoxazole (Figure 18). Resistance to ceftiofur was observed in 3% of the isolates. The highest levels of resistance were to ampicillin, streptomycin, sulfamethoxazole and tetracycline (20% to 30%).

Multiple Drug Resistance: Fifty-seven percent of the isolates were susceptible to all 16 antimicrobials tested (Figure 17).

AMR Patterns: The most frequent AMR patterns were streptomycin-tetracycline and tetracycline alone, which were both observed in 6% of the isolates (Appendix Table A.4.15).

Serovars and Resistance: *S.* Heidelberg was the most frequent serovar, followed by *S.* Typhimurium and *S.* Enteritidis (Table 8). Serovar Heidelberg was the most frequently resistant, and most of these isolates were resistant to less than five antimicrobials. One Heidelberg isolate did express the ACKSSuT pattern, in addition to resistance to amoxicillin-clavulanic acid, cefoxitin, ceftiofur, cephalothin, and gentamicin. All *S.* Enteritidis isolates were susceptible to the full panel of 16 antimicrobials. The AKSSuT was only observed in two non-typable *S.* Typhimurium isolates and two *S.* Typhimurium var. Copenhagen phagetype 208 (Appendix Table A.4.16). The ACSSuT pattern was observed in two *S.* Typhimurium var. Copenhagen DT104, one *S.* Typhimurium DT104 and one *Salmonella* sp. DT302.

Results from *Passive Surveillance* showed that 56% of all clinical *Salmonella* isolates from chicken were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 3% of the clinical isolates from chicken.

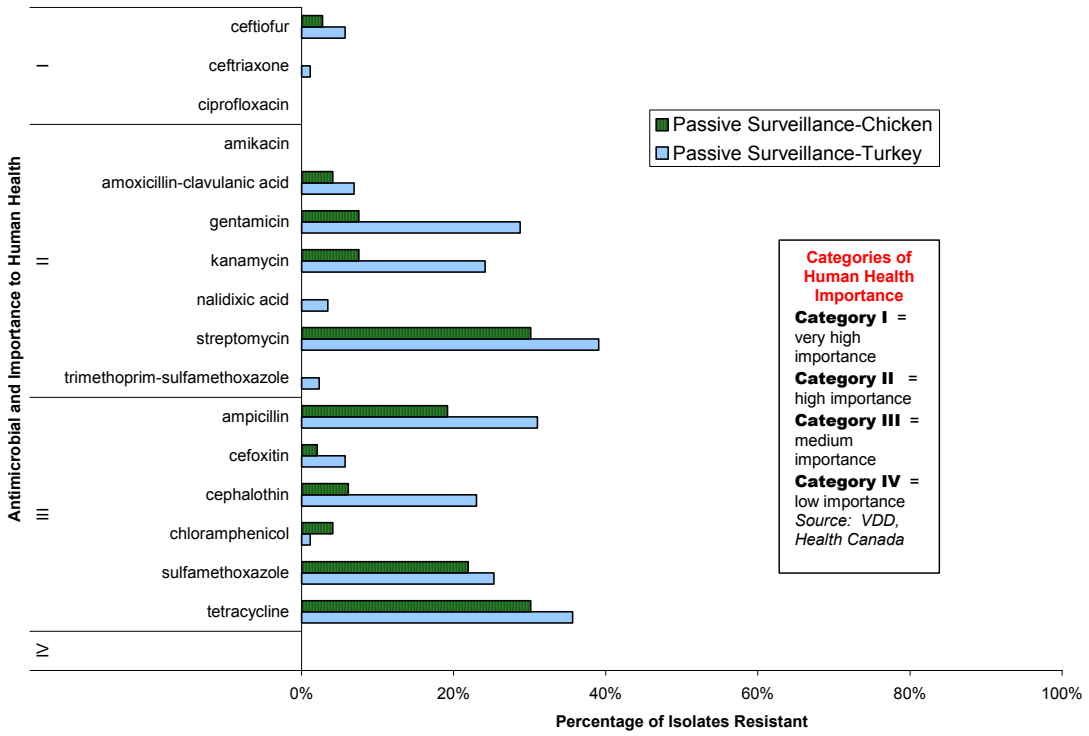


Figure 18. Individual antimicrobial resistance in clinical ***Salmonella*** isolates from **chicken** (n=146) and **turkey** (n=87); *Passive Surveillance*

Table 8. *Salmonella* serovars from **chicken** (clinical isolates); *Passive Surveillance* (n=146)

Serovar	%n (n)	No. isolates by the number of antimicrobials in resistance pattern			
		0	**1-4**	**5-8**	**9-13**
Heidelberg	43.8 (64)	39	22	1	2
Typhimurium	14.4 (21)	16	2	3	0
Enteritidis	8.2 (12)	12	0	0	0
Hadar	6.2 (9)	1	7	1	0
Salmonella spp.	6.2 (9)	4	4	1	0
Putten	4.1 (6)	0	6	0	0
Schwarzengrund	4.1 (6)	0	6	0	0
Typhimurium var Copenhagen	3.4 (5)	0	1	4	0
Senftenberg	2.7 (4)	4	0	0	0
Kentucky	2.1 (3)	2	1	0	0
Other serovars	4.9 (7)	5	1	0	1
Totals		**83**	**50**	**10**	**3**

Additional Information from Passive Surveillance

Turkey - Clinical *Salmonella* Isolates

(*Passive Surveillance* n=87)

Individual Antimicrobial Drug Resistance: All isolates were susceptible to amikacin and ciprofloxacin (Figure 18 and Appendix Table A.4.14). Six percent of isolates expressed resistance to ceftiofur, and 3.4% to nalidixic acid. One isolate (1.1%) was resistant to ceftriaxone, which was the only case of resistance to this antimicrobial identified in all the data from animal and/or meat sources. The highest levels of resistance (between 20 and 40%) were observed to streptomycin, tetracycline, ampicillin, sulfamethoxazole, cephalothin, gentamicin and kanamycin.

Multiple Drug Resistance: Thirty-seven percent of isolates were susceptible to all 16 antimicrobials (Figure 17). A slightly larger proportion (41%) was resistant to between one and four antimicrobials, while 16% were resistant to five to 8 antimicrobials.

AMR Patterns: The AKSSuT pattern was frequently observed (11%) (Appendix Table A.4.17). It was always associated with other AMR to other drugs, such as resistance to several cephalosporins and to gentamicin

Serovars and Resistance: *S.* Heidelberg and *S.* Senftenberg were the most frequent serovars (Table 9). Fifty percent of these serovars were resistant to at least one antimicrobial. However, isolates resistant to AKSSuT and additionally to amoxicillin-clavulanic acid, cefoxitin, ceftiofur, cephalothin and gentamicin, including one isolate which was also resistant to ceftriaxone, were all *S.* Bredeney serovars (Appendix Table A.4.17). The AKSSuT pattern was detected in *S.* Heidelberg, *S.* Muenster, *S.* Montevideo and *S.* Typhimurium DT194 isolates. *S.* Heidelberg DT32 was the only serovar expressing the ACSSuT pattern.

Results from *Passive Surveillance* showed that 37% of all clinical *Salmonella* isolates from turkey were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 6%, and one isolate (1%) was resistant to ceftriaxone. *S.* Heidelberg and *S.* Senftenberg were the most frequent serovars among clinical turkey isolates. S. Bredeney was the serovar with the highest number of antimicrobials within a resistance pattern and included resistance to ceftriaxone (1 isolate).

Table 9. *Salmonella* serovars from **turkey** (clinical isolates); *Passive Surveillance* (n=87)

Serovar	%n (n)	No. isolates by the number of antimicrobials in resistance pattern			
		0	1-4	5-8	9-13
Heidelberg	36.8 (32)	15	14	3	0
Senftenberg	23 (20)	4	12	4	0
Bredeney	6.9 (6)	0	0	1	5
Muenster	6.9 (6)	4	1	1	0
Agona	2.3 (2)	1	1	0	0
Hadar	2.3 (2)	0	2	0	0
Montevideo	2.3 (2)	0	0	2	0
Newport	2.3 (2)	2	0	0	0
Saintpaul	2.3 (2)	1	1	0	0
Schwarzengrund	2.3 (2)	0	2	0	0
Typhimurium	2.3 (2)	0	1	1	0
Other serovars	10.3 (9)	5	2	2	0
Totals		**32**	**36**	**14**	**5**

Feed and Rendered Ingredients - *Salmonella* isolates

(*Passive Surveillance* n=65)

Individual Antimicrobial Drug Resistance: All isolates were susceptible to ceftriaxone, ciprofloxacin, nalidixic acid, amikacin, gentamicin and kanamycin (Figure 19). Three percent of isolates expressed resistance to ceftiofur. Resistance to streptomycin and tetracycline were found in more than 10% of the isolates. Resistance to amoxicillin-clavulanic acid, ampicillin, cefoxitin, cephalothin, chloramphenicol, sulfamethoxazole and trimethoprim-sulfamethoxazole were also observed in one to five percent of the isolates.

Multiple Drug Resistance: Eighty-eight percent of the isolates were susceptible to all 16 antimicrobials tested.

AMR Pattern: The AMR patterns observed were: streptomycin and tetracycline (n=4); streptomycin (n=1); streptomycin, sulfamethoxazole and tetracycline (n=1); ACSSuT, amoxicillin-clavulanic acid, cefoxitin, ceftiofur and cephalothin (n=1); and ACSSuT, amoxicillin-clavulanic acid, cefoxitin, ceftiofur, cephalothin and trimethoprim-sulfamethoxazole (n=1).

Serovars and resistance: There was no clear predominance of any one serovar among the *Passive Surveillance* isolates (Table 10 and Appendix Table A.4.18). Resistance to 10 antimicrobials was observed in the *S.* Newport isolate and resistance to 9 antimicrobials was observed in the *S.* Typhimurium DT108 isolate.

Results from *Passive Surveillance* showed that 87% of all *Salmonella* isolates from feed and rendered ingredients were susceptible to all antimicrobials tested. Of the antimicrobials of greatest importance to human health, ceftiofur resistance was detected in 3% of the isolates.

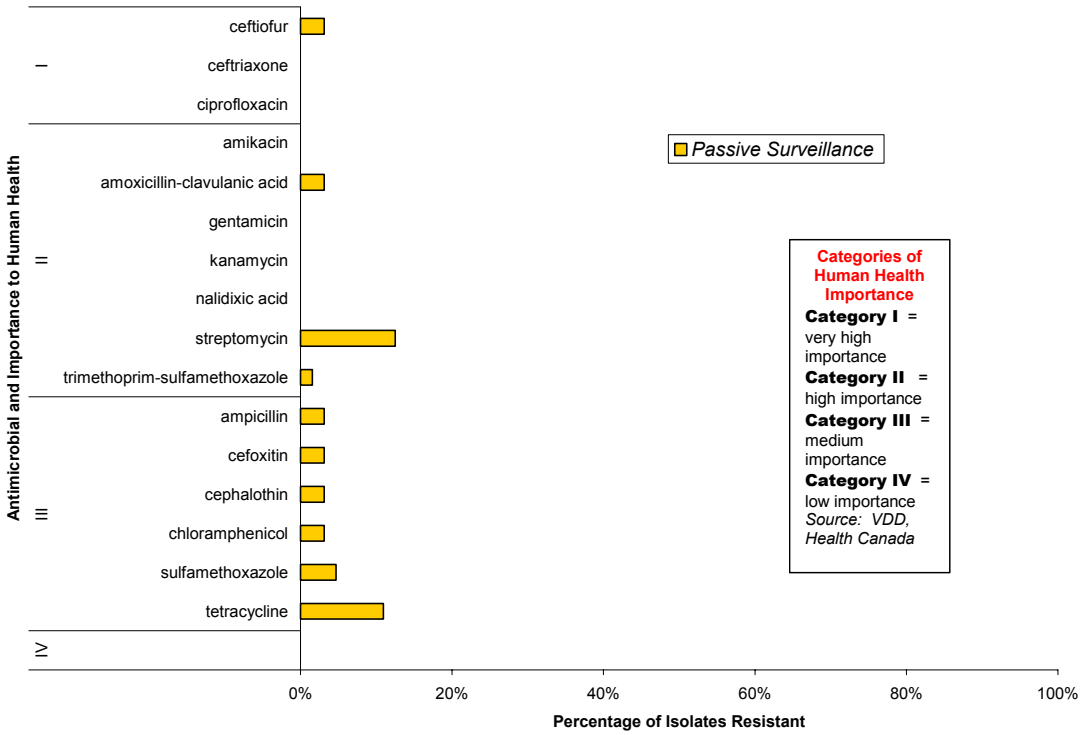


Figure 19. Individual antimicrobial resistance in *Salmonella* from **feed and rendered ingredients**; *Passive Surveillance* (n=65)

Table 10. *Salmonella* serovars from **feed and rendered ingredients**; *Passive Surveillance* (n=65)

Serovar	%n (n)	No. isolates by the number of antimicrobials in resistance Pattern			
		0	1-4	5-8	9-13
Salmonella spp.	15.6 (10)	10	0	0	0
Tennessee	9.4 (6)	5	1	0	0
Cubana	6.3 (4)	4	0	0	0
Mbandaka	6.3 (4)	1	3	0	0
Montevideo	6.3 (4)	4	0	0	0
Orion var 15+	6.3 (4)	4	0	0	0
Senftenberg	6.3 (4)	4	0	0	0
Brandenburg	4.7 (3)	3	0	0	0
Livingstone	4.7 (3)	3	0	0	0
Oranienburg	4.7 (3)	3	0	0	0
Other serovars	30.0 (20)	16	2	0	2
Totals		**57**	**6**	**0**	**2**

Part III: Discussion of Agri-Food Antimicrobial Resistance Results

The agri-food AMR results are summarized in Tables 11 and 12.

Table 11. Summary of agri-food antimicrobial resistance surveillance findings

	Cattle			Swine				Chicken			Turkey	Feed and Rendered Ingredients
	E. coli	*Salmonella* Active	*Salmonella* Passive-clinical	*E. coli*	*Salmonella* Active	*Salmonella* Passive-pork	*Salmonella* Passive-clinical	*E. coli*	*Salmonella* Active	*Salmonella* Passive-clinical	*Salmonella* Passive-clinical	*Salmonella* Passive
number of isolates tested	78	1	478	38	101	33	309	40	25	146	87	65
% of isolates susceptible to all antimicrobials tested	69%	0 %*	36%	21%	55%	70%	33%	20%	52%	57%	37%	88%
% of isolates resistant to 5 or more antimicrobials	0%	0 %*	55%	11%	20%	21%	42%	33%	12%	9%	22%	4%
% of isolates resistant to Category I antimicrobials	0%	0 %*	8% (ceftiofur)	0%	0%	3% (ceftiofur)	3% (ceftiofur)	10% (ceftiofur)	12% (ceftiofur)	3% (ceftiofur)	10% (ceftiofur, ceftriaxone)	3% (ceftiofur)

***Note**: * there was only one isolate tested*

Table 12. Antimicrobial resistance and most frequent *Salmonella* serovars

Species	Most Frequent[1] Serovars expressing no resistance (n)	Most Frequent Serovars expressing resistance to 1 to 4 antimicrobials (n)	Most Frequent Serovars expressing resistance to 5 to 8 antimicrobials (n)	Most Frequent Serovars expressing resistance to 9 to 13 antimicrobials (n)
Abattoir surveillance				
Cattle		London (1)		
Swine	Infantis (6) Brandenburg (5) Muenchen (5) Typhimurium (5) Typhimurium var Copenhagen (4) Heidelberg (3) Ohio (3) Senftenberg (3)	Derby (13) Heidelberg (3) Typhimurium var Copenhagen (3) Hadar (2)	Typhimurium var Copenhagen (13) Typhimurium (4) Mbandaka (2) Heidelberg (1)	
Chicken	Heidelberg (7) Kentucky (4) Bradford (1) Thompson (1)	Heidelberg (7) Hadar (1)	Heidelberg (3)	
***Passive surveillance* – Meat**				
Pork	Infantis (10) *Salmonella* spp. (7) Typhimurium (3)	Typhimurium (2) Derby (1)	Typhimurium (6) Derby (1)	
***Passive surveillance* – Clinical isolates**				
Cattle	Kentucky (42) Muenster (30) Typhimurium (25) Cerro (16) *Salmonella* spp. (8)	Typhimurium var Copenhagen (29) Heidelberg (3) Dublin (2) Typhimurium (2)	Typhimurium (121) Typhimurium var Copenhagen (95)	Newport (12) Typhimurium (12) Typhimurium var Copenhagen (6) *Salmonella* spp. (3)
Swine	Typhimurium (29) Typhimurium var Copenhagen (15) Derby (7) *Salmonella* spp. (7) Brandenburg (5) Mbandaka (5)	Derby (19) Typhimurium (17) Typhimurium var Copenhagen (16) Agona (6) Heidelberg (6)	Typhimurium (76) Typhimurium var Copenhagen (34)	Typhimurium (5) Ohio (2) Agona (1) Infantis (1)
Chicken	Heidelberg (39) Typhimurium (16) Enteritidis (12) *Salmonella* spp. (4) Senftenberg (4)	Heidelberg (22) Hadar (7) Putten (6) Schwarzengrund (6) *Salmonella* spp. (4)	Typhimurium var Copenhagen (4) Typhimurium (3) Hadar (1) Heidelberg (1) *Salmonella* spp. (1)	Heidelberg (2) Bredeney (1)
Turkey	Heidelberg (15) Muenster (4) Senftenberg (4) Newport (2) *Salmonella* spp. (2)	Heidelberg (14) Senftenberg (12) Hadar (2) Schwarzengrund (2)	Senftenberg (4) Heidelberg (3) Montevideo (2) Anatum (1) Bredeney (1) Muenster (1) Tennessee (1) Typhimurium (1)	Bredeney (5)
***Passive surveillance* – Feed and Rendered Ingredients**				
	Salmonella spp. (10) Tennessee (5) Cubana (4) Montevideo (4) Orion var 15+ (4) Senftenberg (4) Brandenburg (3) Livingstone (3) Oranienburg (3)	Mbandaka (3) Derby (1) Hadar (1) Tennessee (1)		Newport (1) Typhimurium (1)

Note: *1= Most frequent Serovars were those representing 5% or more of the isolates from each category*

Number of isolates tested: The sampling plan for the *Abattoir Surveillance* was designed to yield, on an annual basis, 150 isolates of each targeted bacterial species, within each tested commodity. As the *Abattoir Surveillance* only commenced in September 2002, the number of isolates recovered in 2002 was less than the annual target. The precision of some estimates was low to moderate as shown by the large confidence intervals in the figures, and this may have prevented identification of significant differences. In future years, a full data set of 150 isolates per commodity and bacterial species should procure a more accurate description of AMR in the Canadian agri-food sector.

Besides improvements in estimate accuracy, testing a larger number of isolates increases the capacity to identify uncommon AMR patterns. The early detection of rare but potentially harmful events such as multidrug resistance patterns is important from a human and animal health perspective. The *Passive Surveillance* is of use in this regard. First, it is based on a large number of isolates, which increases the capacity to detect unusual patterns. Second, the sample collection essentially represents a sentinel surveillance of a higher risk population (assuming veterinarians send samples to the laboratory, for reasons such as interest in the causative organism, including AMR).

AMR Across Animal Species: The uniform sampling design of the *Abattoir Surveillance* enables investigation of the similarities of AMR for a given bacterial species across different animal species.

According to the *Abattoir Surveillance* data, AMR in generic *E. coli* isolated from animals entering the food chain was less common in beef cattle (70% of isolates fully susceptible), and more common in swine and broiler chicken (20% of isolates fully susceptible in both commodities). Furthermore, resistance to tetracycline, streptomycin and sulfamethoxazole were frequent among chicken and swine generic *E. coli* isolates, yet uncommon among beef cattle generic *E. coli* isolates (Table Appendix A.4.1). Although not tested formally, this may imply that the generic *E. coli* population in beef cattle are different from those harboured by chicken and swine.

The prevalences of individual antimicrobial drug resistance in *Salmonella* spp. obtained through *Abattoir Surveillance* from swine and chicken were different (Appendix Table A.4.4). Chicken isolates tended to be more often resistant to ceftiofur, ampicillin, cefoxitin, and cephalothin, whereas swine isolates tended to be more often resistant to trimethoprim-sulfamethoxazole, amoxicillin-clavulanic acid, sulfamethoxazole, streptomycin, chloramphenicol, and tetracycline (antimicrobials ordered by increasing absolute difference between swine and chicken isolates). Serovar difference may partly explain this, however, further explanation of this observation is beyond the scope of this report. Differences in the use of antimicrobials between these commodities warrant further investigation.

The *Passive Surveillance* indicated similarities between diseased swine and cattle, especially regarding the multiple drug resistance patterns. In both species, the mode of the number of antimicrobials to which resistance was observed in one isolate was five, and the antimicrobials most frequently involved were tetracycline, sulfamethoxazole, streptomycin, ampicillin, and chloramphenicol. Such patterns were not observed as frequently in chicken isolates. However, interpretation of the findings at the *Salmonella* spp. level is not straightforward since serovars are not independent from host species or from AMR patterns.

Abattoir Surveillance data for 2002 confirm that there was correlation between the resistance of *Salmonella* isolates and their serovars and/or phagetypes. Previous Canadian studies have shown that more than 90% of the *S.* Typhimurium DT104 strains isolated from animals, the animal environment, and food of animal origin were resistant to antimicrobials including ampicillin, chloramphenicol, florfenicol, streptomycin, sulfonamides and tetracycline, whereas about 30% of the isolates were additionally resistant to kanamycin and neomycin, and a few to trimethoprim (Poppe et al., 2002). However many isolates belonging to other phagetypes of *S*. Typhimurium (e.g. phagetypes 2, 10, 66 and 108) were susceptible to all antimicrobials in the testing panel. Similar

observations have been made regarding differences in AMR in different serovars of *Salmonella*. In a previous Canadian study, *S*. Derby isolates were nearly uniformly resistant to streptomycin, sulfonamides and tetracycline whereas AMR in *S*. Infantis isolates was nearly absent (Poppe et al., 2001).

A similar correlation between AMR and the serotype of the isolate may be present among *E. coli* isolates. However, little is known about the putative association between resistance and type in generic *E. coli* since *E. coli* isolated from sources such as faeces or carcass rinses from healthy animals are rarely serotyped or phagetyped. In verotoxigenic and other pathogenic *E. coli*, which have been serotyped, and phagetyped, some studies have been conducted to determine possible associations between AMR and serotype or phagetype (Zhao et al., 2001; Grif et al. 1998). In a study on the effect of administration of antimicrobials on AMR of *Salmonella* and *E. coli* isolated from the faeces of calves, it was noted that among "commensal" *E. coli*, isolates of certain serotypes were persistently multiresistant whereas isolates of other serotypes were persistently susceptible to all antimicrobials in the testing panel (Poppe *et al*., manuscript in preparation).

AMR across Bacterial Species, within the Same Animal Species: During the *Abattoir Surveillance*, *Salmonella* testing was performed on all samples, whereas *E. coli* isolation was performed on only a portion of the samples. Based on individual antimicrobial drug resistance, the *Abattoir Surveillance* showed some similarities and some marked differences between *E. coli* and *Salmonella* spp. recovered from broiler chickens. The *E. coli* and *Salmonella* isolates were all susceptible to ceftriaxone, ciprofloxacin, and amikacin and they showed the same level of resistance to ceftiofur, amoxicillin-clavulanic acid, ampicillin, cefoxitin, and cephalothin (Figure 14). The two bacterial species differed on kanamycin, tetracycline, sulfamethoxazole, streptomycin, and trimethoprim-sulfamethoxazole, to which the *E. coli* isolates tended to be more often resistant. Because of this higher prevalence of resistance (for some drugs), *E. coli* was overall more frequently resistant to at least one antimicrobial in comparison to *Salmonella* spp.

E. coli and *Salmonella* isolated from swine tended to have the same individual antimicrobial drug resistance profile with one exception (Figure 20). *E. coli* isolates were twice as often resistant to tetracycline in comparison to *Salmonella* (78% vs. 38%, respectively), with an overall higher resistance to at least one antimicrobial (79% versus 45%, respectively). Only a small proportion of the samples processed in year 2002 yielded both *Salmonella* and *E. coli* isolates. For 2003, in order to investigate more thoroughly the AMR profile of different bacterial species from the same environment, laboratory procedures have been modified so that *E.* coli recovery will be performed on all *Salmonella* positive samples.

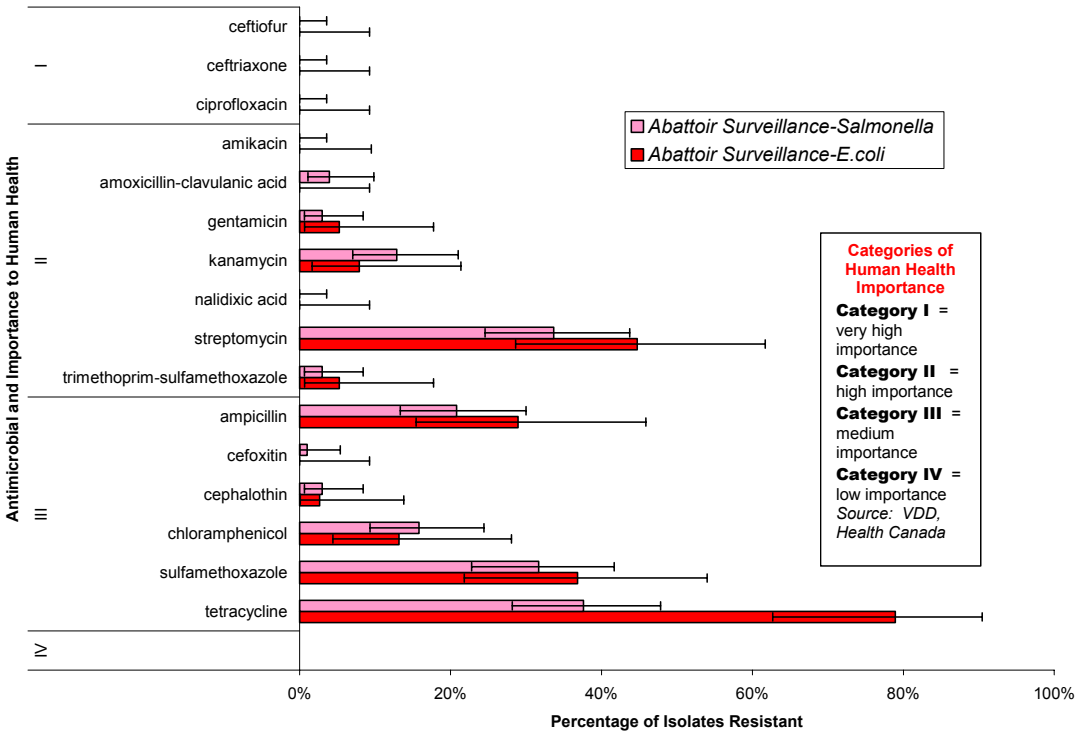


Figure 20. Individual antimicrobial drug resistance in ***E. coli*** (n=37) and ***Salmonella*** (n=101) isolates from **swine**; *Abattoir Surveillance*

Section Three - Antimicrobial Use

Currently, no comprehensive monitoring of antimicrobial use in human medicine, veterinary medicine, or agriculture occurs in Canada. CIPARS is therefore developing a use monitoring system. As part of this development process, Health Canada and its government, academic, and industry partners have undertaken several projects in order to generate preliminary data on antimicrobial use, evaluate the logistics and feasibility of collecting data from potential sources, and assess the quality/validity of the data collected. Highlights from these exploratory studies are summarized in *CIPARS - Background Studies.* Information on the distribution system for antimicrobials used in livestock can be found in Appendix A.5.

In this section, we present data on human use of systemic antimicrobials, representative of antimicrobials dispensed by community pharmacies across Canada. This is one significant component of present and future CIPARS antimicrobial use monitoring systems. In some instances, the antimicrobials are categorized according to Guidelines proposed by the VDD (Appendix A.1). The original intent of these guidelines was to classify antimicrobials used in veterinary medicine. However, this classification system provides a useful way to examine the potential human health impact with respect to AMR concern of using these drugs in humans and animals.

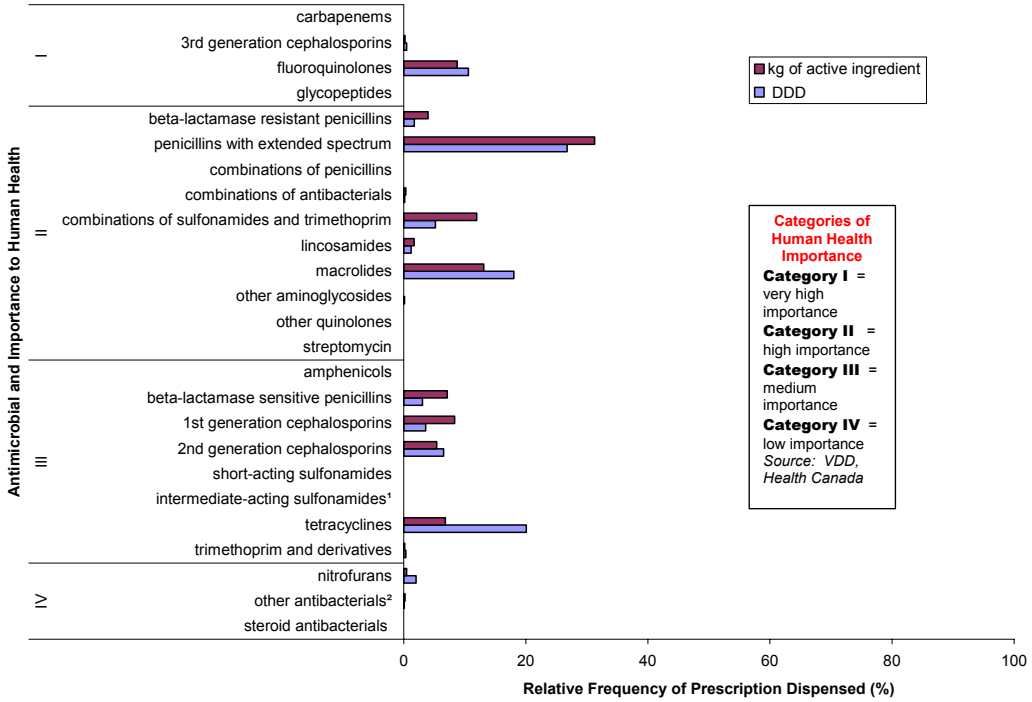
Human Antimicrobial Use

Health Canada has been working with Intercontinental Medical Statistics (IMS) Health to quantify and describe antimicrobial drug use in humans. IMS Health collects information on drug use across Canada via several audit programs. This report focuses on the IMS Health *CompuScript* and *Canadian Disease and Therapeutic Index* (*CDTI*) audits for fiscal year 2000-2001. Further information on IMS Health data collection methods are described in Appendix B.3.

As per international standards of measurement, the volume of active ingredient (kg), the number of Defined Daily Doses (DDDs), and number of DDDs/1,000 inhabitant-days were calculated for each product strength and summed for the year (Appendix Table A.6.1). The relative percentage of total use is presented in Figure 21 and diagnoses associated with antimicrobial use are presented in Figure 22 and Appendix A.6.2.

Between April 2000 and March 2001, 234.7 million DDDs of antimicrobials for systemic use were dispensed in community pharmacies in Canada. This is equivalent to 21.4 DDDs/1,000 inhabitant-days. The most commonly dispensed antimicrobials (based on DDDs) were extended spectrum penicillins (mostly amoxicillin). Other commonly dispensed antimicrobials (based on DDDs) included tetracyclines (mostly minocycline and tetracycline), macrolides (mostly clarithromycin), fluoroquinolones (mostly ciprofloxacin), and cephalosporins (mostly second generation drugs, especially cefuroxime).

Almost half of the antimicrobials prescribed were indicated for respiratory system diseases. Antimicrobials were also commonly prescribed for genitourinary system diseases, nervous system and sense organ diseases (especially otitis), skin and subcutaneous tissue diseases, and infectious and parasitic diseases (Figure 22 and Appendix A.6.2). Approximately 5% of the prescribed antimicrobials were used to treat disorders of the digestive system. While 11% of DDDs of antimicrobials dispensed were in Category I (very high human health importance), the bulk (53%) of the antimicrobials dispensed were in Category II (high human health importance).



Note: [1]1106 units of sulfamethoxazole were dispensed but were not included in this calculation because the product strength was unknown; [2]100 254 units of methenamine were dispensed but were not included in this calculation because the product strength was unknown.

Figure 21. Relative use of antimicrobials dispensed by community pharmacies (IMS Health)

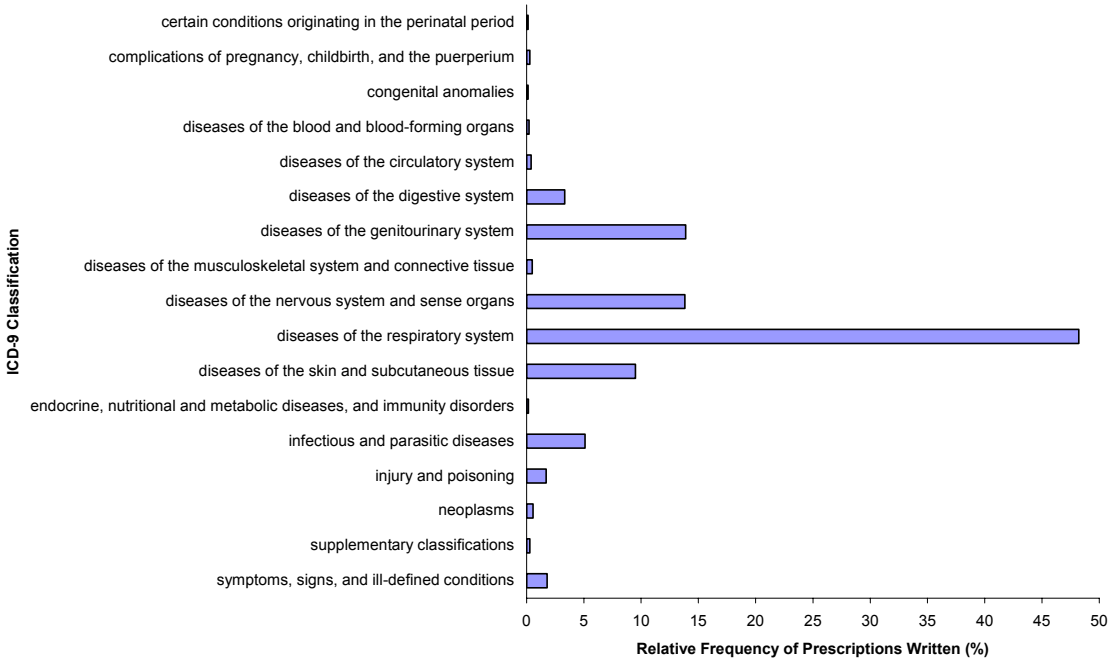


Figure 22. Distribution of antimicrobial use by diagnostic classes, based on office-based physician prescription data (IMS Health)

Discussion and Data Limitations

The information in this section is based on the best currently accessible and available data describing human antimicrobial use in Canada. However, potential limitations exist. *CompuScript* data are generally accurate, however, when analyzing extended units and prescription size alone, this information may be unreliable because of the methods pharmacists use to enter the size of the prescription and the number of units dispensed. Pharmacists enter a number into the quantity field of the database that represents the number of drug units in the prescription. For example, if the product were an oral tablet, the quantity units would be the number of pills dispensed. However, inconsistencies arise for pre-packaged products, such as a vial, where the quantity field could represent either the number of vials dispensed or the number of millilitres per vial. There is no adjustment possible to account for these inconsistencies. To ensure a conservative and consistent approach in our analyses, we assumed that every formulation had the same quantity units (Table B.3.1).

CDTI offers a good estimate of the distribution of illnesses for which Canadian physicians recommend the use of antimicrobials. However, under representation of some diagnoses may occur because some medical specialties are not represented (Appendix Table A.6.2). Furthermore, it is important to note that *CDTI* does not track whether the patients had their prescriptions filled.

The classes of antimicrobials most frequently dispensed by community pharmacies for human medicine (measured by DDDs) were extended spectrum penicillins, tetracyclines, macrolides, fluoroquinolones, and cephalosporins. The majority of these antimicrobials (by number of DDDs) belonged to Category II human health importance (high importance). Of the total antimicrobial DDDs prescribed, approximately 50% were for the treatment of respiratory system diseases and 5% for the treatment of digestive system diseases.

Section Four - Future Plans

In 2002, CIPARS data collection in combination with the results of background research studies (see Summary of Background Studies for CIPARS Development) have been invaluable for creating working partnerships with Canadian stakeholders, identifying future areas of required research, exploring analytical and methodological options, and focussing surveillance expansion efforts.

CIPARS is a program undergoing strategic change with plans for expansion in many areas, including partnerships, geographic locations sampled, commodities represented, and bacterial species evaluated.

Ultimately, the surveillance data (both AMR and antimicrobial use) will be utilized in risk assessments to evaluate risk reduction and intervention strategies for new and existing antimicrobial products, with the intent to assist policy decisions. These data will also assist a variety of stakeholders with such things as the development and refinement of prudent/judicious/clinical use programs and targeting future research studies based on identified knowledge gaps.

Human Antimicrobial Resistance

The CIPARS human AMR demonstration project was launched in early 2003, and results will be included in the 2003 report. This demonstration project was developed following a series of background studies carried out between 1999-2001, which systematically evaluated options for acquiring national antimicrobial resistance surveillance data (see Figure 23 and Table 13). Available results from the background studies are compiled in the Summary of Background Studies for CIPARS Development.

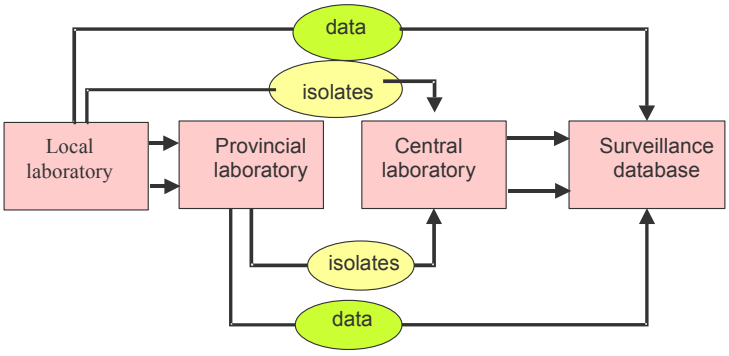


Figure 23. Options for a prospective AMR surveillance system: Human component

Table 13. Advantages and disadvantages of prospective surveillance options

Option	Description	Background Study (Year)	Advantages	Disadvantages
1	TRANSFER AMR DATA from: Local laboratory to surveillance database	NSAGI Canadian Laboratory Survey (2001)	- Use made of existing data - More representative data	- Inconsistent and variable sensitivity testing methods - High cost/effort required to establish and maintain system - Confidentiality issues
2	FORWARD ISOLATES from: Local laboratory to central laboratory	NSAGI Canadian Laboratory Survey (2001)	- Opportunity for consistent testing methodology - Opportunity to integrate Human /Agri/Food AMR surveillance using standard methodology - Central archive for future research - Access to *Campylobacter* isolates	- Isolates bypassing PPHL - Potentially high maintenance cost
3	TRANSFER AMR DATA from: Provincial laboratory to surveillance database	NSAGI AREO Survey (2001) Retrospective Study of AMR in *Salmonella* and *Shigella*	- Use made of existing data - Low cost/effort to establish system	- Not all PPHL's currently do testing - Different sensitivity testing methods - Incomplete and unknown proportion of isolates sent to PPHL's
4	FORWARD ISOLATES from: Provincial laboratory to central laboratory	Multi-provincial S. Typhimurium Case-control Study (1999-2000) CIDPC ARO Survey (2000) CIPARS Demonstration Project (2002-05)	- Opportunity for consistent testing methodology - Opportunity to integrate Human/Agri/Food AMR surveillance using standard methodology - Central archive for future research - Availability of phagetyping, other reference services	- Potentially high maintenance cost - Incomplete and unknown proportion of isolates sent to PPHL's

Note: NSAGI - National Studies on Acute Gastrointestinal Illness; AREO - Antimicrobial Resistant Enteric Organism; CIDPC – Centre for Infectious Disease Prevention and Control; PPHL – Provincial Public Health Laboratory.

Agri-Food Antimicrobial Resistance

For 2003, a full year of data from the *Abattoir Surveillance* will be available, thus the same data exploration will be undertaken to expand the results from 2002. With the implementation of the *Retail Surveillance*, other analytical evaluations of the data will be undertaken to synthesize the animal AMR data in a more comprehensive manner, such as evaluating changes over time, comparison between host species, comparison between bacterial species, and spread through the food chain.

Human Antimicrobial Use

In future CIPARS reports, the intent is to comprehensively analyze human antimicrobial consumption trends in Canada, including those antimicrobials that are used to treat enteric infections. Additional investigations are planned to validate the sampling methods, and to describe associations between use and the demographic characteristics of both the patient and the prescriber (including geographic area, age, and gender).

Animal Antimicrobial Use

In the future, methods will be developed to document antimicrobial use and usage patterns for major food animal species, incorporating where possible information on routes of administration, stage of production and collecting data from various points in the antimicrobial distribution system. In so far as possible, quantitative use information will be reported in a manner that is internationally harmonized in order to facilitate appropriate comparisons.

Integrated Analysis of the Emergence and Spread of AMR

In the future, the intent of this section is to integrate data on antimicrobial use and AMR in human and agri-food sectors, to provide knowledge useful for the containment of AMR based on the following key issues:

Does human antimicrobial use affect AMR in human patients? If so, then how?

Does livestock antimicrobial use affect AMR in food-producing animals? If so, then how?

Does AMR spread from food-producing animals to humans? If so, then how?

Internationally, there has been evidence to answer the above questions, albeit in very specific contexts. This section will attempt to provide a modest contribution to the wealth of such evidences, with the unique asset of being tailored to the Canadian environment. Time is a key dimension in the link between antimicrobial use and resistance, and in the spread of resistance within and between species and will be factored into the analysis.

Demographic Data

Future reports will make greater use of population denominator data to report surveillance results in an internationally harmonized manner. It is expected that animal and human density calculations will facilitate analytical evaluations of the multidimensional nature of AMR development, persistence, and spread through time and space.

Efficiency Improvement and Expansion of Reporting Ability

Currently, the main focus of CIPARS is to systematically integrate the surveillance findings in order to produce an annual report. It is anticipated that in the future, the report itself will become available in different media formats, and that efficient data analysis will be facilitated by the developing central data repository.

The current organisations and centres undertaking AMR surveillance within Health Canada are not linked so as to facilitate the transfer of data. A central integrated repository of information from animals, food and humans will enable the assessment of event relatedness, the detection of time trends and geographical patterns.

CIPARS members have prepared a business case for the development of a central repository for the management of the AMR data generated under the program, and this has been presented to the management team for approval.

The labour-intensive experience involved in production of this first annual CIPARS report highlights the expected benefits to the program from having an integrated data repository. The largest amount of effort was related to the gathering and combining of the data from multiple sources. Under the current situation, annual publication is considered the maximum frequency for such a report, but more regular reports will be possible once the repository is in place. We will also gain the ability to conduct ad hoc reporting in response to specific requests for information.

Appendix A - Additional Information

A.1. Drugs of Human Health Importance

Classification of Antimicrobial Products Based On Importance in Human Medicine

Excerpt from Veterinary Drugs Directorate's Draft Proposed Guidelines on the Microbiological Safety Studies for the Evaluation of Veterinary New Drug Submissions (September 2003)

Different classes of antimicrobials are used in human and animal medicine for the treatment and prevention of bacterial diseases. Some of these antimicrobials are last-line drugs for the treatment of serious life-threatening infections in humans. If these antimicrobials become ineffective due to the development of bacterial resistance, alternative antimicrobials are not available to treat human infections caused by the resistant bacteria. These and newer generation antimicrobials with unique mechanism of action and/or mechanism of resistance are of **V**ery **H**igh **I**mportance (**VHI**) in human medicine. Some antimicrobials that are considered of **H**igh **I**mportance (**HI**) in human medicine have limited alternatives. First-line or second-line antimicrobials may be classified as being of **M**edium **I**mportance or **L**ow **I**mportance in human medicine depending on their therapeutic usefulness.

Rationale for classification:
The criteria for classification of antimicrobials is based on the following factors:

- Spectrum of activity of antimicrobials;
- Mode of action;
- Mechanism of resistance;
- Availability of alternative antimicrobial therapy;
- Potential for transfer of resistance.

1. Category I: Very High Importance
These antimicrobial classes are of highest importance in human medicine and are used for the treatment of life-threatening bacterial infections. There may be no alternative antimicrobials in case of emergence of resistance to these agents. These agents are also considered "last-line" antimicrobials in human medicine. Examples include:

1.1 Fluoroquinolones
1.2 Glycopeptides
1.3 Carbapenems
1.4 3rd - Generation Cephalosporins
1.5 4th - Generation Cephalosporins
1.6 Streptogramins
1.7 Newer Generation Antimicrobial Drugs

2. Category II: High Importance
Antimicrobials classified as category II consist of those that can be used to treat infections caused by bacteria that are resistant to category III antimicrobials. Examples include:

2.1 Penicillins Group 1 (Beta-lactamase resistant penicillins, extended spectrum penicillins)
2.2 Aminoglycosides
2.3 Macrolides
2.4 Lincosamides

3. Category III: Medium Importance

These antimicrobials are generally used as first line drugs for treatment of bacterial infections. Bacteria that are resistant to these drugs can be treated by category II antimicrobials. Examples include:

- 3.1 1st - Generation Cephalosporins
- 3.2 2nd - Generation Cephalosporins
- 3.3 Penicillins Group2 (natural penicillins, aminopenicillins)
- 3.4 Tetracycline
- 3.5 Sulphonamides

4. Category IV: Low Importance

These antimicrobials are of limited use in human medicine. Some, such as the ionophores, are not used under any circumstances in human medicine. Examples include:

- 4.1 Zinc Bacitracin
- 4.2 Polymyxin B
- 4.3 Colistin
- 4.4 Quinoxalines
- 4.5 Flavophospholipols
- 4.6 Ionophores

Note: [1]The proposed classification of antimicrobial drugs is based only on the importance of each drug class to human health but does not reflect the extent of drug use or the degree to which resistance occurs in human bacterial pathogens. A proposed parallel classification based on risk of exposure is being developed and will be integrated with this classification system; For this report, the VDD suggested that products with a combination of antimicrobials be classified one category higher than the highest category of their individual constituents; For comments regarding the Proposed Drug Classification System, please contact the Veterinary Drugs Directorate, Health Canada.

A.2. Demographic Information

The purpose of the demographic section is to provide background information on Canadian population distributions and general health care availability. In addition, demographic data have been used to develop and refine statistically valid sampling strategies, and in future reports updated demographic data will provide the necessary denominators for calculating rates of antimicrobial use and resistance.

Tables A.2.1-A.2.3 outline human and livestock population demographics and general health care availability. As specific demographic data were not available for all categories for 2002, the most recent or most comparable data have been provided, accompanied by the year of data collection. It is important to recognize that Canada is a country with marked clusters of habitation and clusters of agricultural activity. A density map is provided to illustrate human distribution by province (Figure A.2.1). The number of farms, livestock, quantity of food produced, and per capita consumption of the various commodities are shown in Table A.2.2.

Data limitations: For the animal demographics, it was noted that industry statistics often differed from governmental figures. For a compilation of industry and governmental figures (using a mathematical extrapolation) see "Uses of Antimicrobials in Food Animals in Canada: Impact on Resistance and Human Health" (HC, 2002).

Human Demographic Information

Table A.2.1. Population demographics and health care availability

	Population (2002)[1] As of July 1, 2002	Population (2001)[2]	Population Density Per Square Km (2001)[2]	Health Care - Number of Approved Beds (1996-1997)[3]	Number Of Physicians Per 100,000 Population (2001)[4]
Canada	31,414,000	30,007,094	3.3	352,334	188
Northwest Territories	41,400	37,360	0.0	643	92
Nunavut	28,700	26,745	0.0	N/A	24
Yukon Territory	29,900	28,674	0.1	282	182
Newfoundland and Labrador	531,600	512,930	1.4	6,996	177
Saskatchewan	1,011,800	978,933	1.7	18,411	153
Manitoba	1,150,800	1,119,583	2.0	18,146	182
British Columbia	4,141,300	3,907,738	4.2	44,571	197
Alberta	3,113,600	2,974,807	4.6	38,180	167
Quebec	7,455,200	7,237,479	5.3	68,972	214
New Brunswick	756,700	729,498	10.2	12,830	156
Ontario	12,068,300	11,410,046	12.6	128,249	180
Nova Scotia	944,800	908,007	17.2	12,547	200
Prince Edward Island	139,900	135,294	23.8	2,507	137

Note: number of physicians "Excludes residents and physicians who are not licensed to provide clinical practice and have requested to the Business Information Group (formerly Southam Medical Group) that their data not be published… includes physicians in clinical and/or non-clinical practice, including research, teaching or administration"; Sources: [1]Statistics Canada. CANSIM II, table 051-0001, based on postcensal population estimates; [2]Statistics Canada. http://www12.statcan.ca/english/census01/products/standard/popdwell/Table-PR.cfm?T=2&S=9&O=A, Accessed Feb 2003; [3]Statistics Canada and Canadian Institute for Health Information. http://www.statcan.ca/english/Pgdb/health32a.htm, Accessed Feb, 2003; [4] Southam Medical Database, Canadian Institute for Health Information. http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=statistics_results_source_smdb_e. Accessed Feb 2003.

Animal Demographic Information

Table A.2.2. Canadian livestock–demographics, production and per-capita consumption, 2001

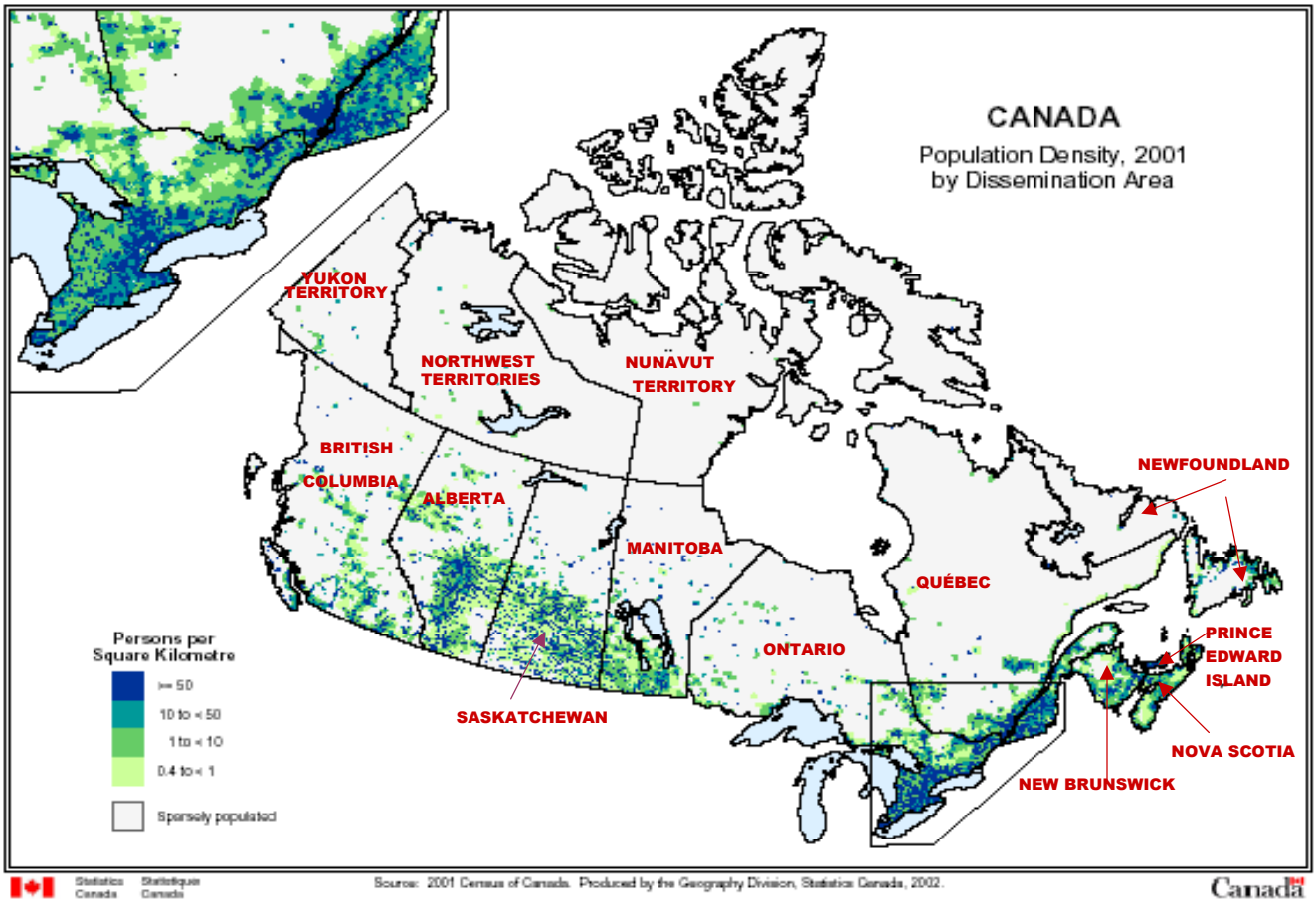
Farmed Species	Number of Farms[1]	Number of Animals[1]	Product Produced[2] Metric Tonnes	Per-Capita Consumption[3] Kg/Person
Cattle	122,066	15,551,449	total cold dressed weight = 1,211,375	beef (carcass weight) = 30.69
beef cows	90,066	4,802,400		
heifers (≥1 year)	83,914	2,492,996		
beef steers (≥1 year)	32,884	1,731,100		
calves (< 1 year)	110,397	5,203,770		
bulls (≥1 year)	78,816	260,218		
dairy cows	21,911	1,060,965	kilolitres milk = 7,560,538[4]	fluid milk = 86.86 (litres/person)
Swine	15,472	13,958,772	total cold trimmed weight = 1,729,127	pork (carcass weight) = 28.88
nursing and weaner pigs, grower and finisher pigs	14,319	12,502,277		
Poultry				
hens and chickens	26,484	126,159,529		
broilers, roasters, and Cornish hens	10,875	87,437,798	broiler, roasters, Cornish hens = 1,084,811.5	chicken (eviscerated weight) = 30.27 stewing hen (eviscerated weight) = 1.74
Turkeys	4,176	8,115,942	turkeys = 178,178	Turkey (eviscerated weight) = 4.19
Ovine	13,232	1,262,448	total cold dressed weight = 12,946	mutton/lamb (carcass weight) = 0.99
Ewes	12,510	621,151		
Fish			all finfish =118,161	fresh and frozen seafish, edible weight = 4.57
salmon	300[5]	25,000,000[5]	salmon = 105,306	
trout	900[5]	10,000,000[5]	trout = 6, 516	freshwater, edible weight = 0.42
				processed seafish (edible weight) = 2.45

Note: These data represent food available for consumption in Canada, and not actual quantities of food consumed; totals represent net availability and account for imports as well exports; Sources: [1]Statistics Canada, Census of Agriculture. http://www.statcan.ca/english/Pgdb. Accessed Feb. 2003; [2]Statistics Canada, Agriculture Division and Census of Agriculture. http://www.statcan.ca. Accessed Feb. 2003; [3]Canada Food Stats, Statistics Canada – Cat. No. 21-020-XIE. http://www.statcan.ca/english/IPS/Data/21-020-XIE.htm. Accessed Feb. 2003; [4]Statistics Canada, CANSIM II tables 003-0008 and 003-0011 and Catalogue no. 23-212 XIB. http://www.statcan.ca. Accessed Feb. 2003; [5]Veterinary Drugs Directorate, Health Canada. 2002. Uses of antimicrobials in food animals in Canada: Impact on resistance and human health. Report of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health.

Table A.2.3. Veterinary services in Alberta, Ontario and Quebec, 2002

Province	Total # Veterinary Practices	Total # Large Animal Practices
Alberta	355	188
Ontario	1154	240
Quebec	600	164

Note: Large animal practices included any practices that had a large animal component. Data was unavailable from the other provincial veterinary licensing organizations; Sources: College of Veterinarians of Ontario, http://www.cvo.org/PRACTICES.HTM, Accessed Feb. 2003; Ordre des Medicins Veterinaires du Quebec, http://www.omvq.qc.ca/regionsetliens.html, Accessed Feb. 2003; Alberta Veterinary Medical Association, http://www.avma.ab.ca/directory/frame.htm, Accessed Feb. 2003.



Note: A dissemination area is a "Small area composed of one or more neighbouring blocks, with a population of 400 to 700 persons." Statistics Canada. http://geodepot.statcan.ca/Diss/Maps/ThematicMaps/population/National/pop_dens_colour_e.pdf . Accessed Feb. 2003.

Figure A.2.1. Human population density 2001; Statistics Canada

The demographic information provided in this section has identified the need for more recent statistics on human health care availability, the need to acquire the most accurate livestock data available, the need for data across all provinces with respect to animal health care availability, and the need for consideration of the spatial clustering of human and livestock populations for future epidemiological analysis of antimicrobial use and resistance.

A.3. Human Antimicrobial Resistance - Current Reporting Structure for Enteric Disease

The surveillance system for enteric diseases in Canada diverges into two pathways following the identification of an enteric infection or disease (Figure A.3.1). One pathway, the *National Notifiable Disease Summary* program (NNDS), channels information through local public health authorities and focuses on collecting demographic and risk factor information for each case. Detailed laboratory information, such as AMR profiles, are rarely included in NNDS data. This surveillance pathway is considered the gold standard, as legislation requires that laboratories and public health authorities report all notifiable enteric diseases (Table A.3.1).

The second reporting pathway, the *National Enteric Surveillance Program* (NESP), captures information on isolates transferred, on a voluntary basis, from local to provincial and national public health reference laboratories. Reference laboratories further characterize isolates by phage typing, serotyping, and occasionally molecular typing and/or AMR testing, and report laboratory findings along with limited demographic data to NESP weekly. The provincial rates of *Salmonella* and *Shigella* reported to the national level by each surveillance pathway are shown in Figures A.3.2 and A.3.3. Although voluntary forwarding of *Salmonella* isolates is very high and in some cases NESP figures exceed NNDS, for most other enteric pathogens, isolates are forwarded less frequently to reference laboratories and the numbers reported by NESP are lower than NNDS.

Underreporting

The steps required for a case to be captured at the national surveillance level are shown in Figure A.3.4. A series of studies initiated by Health Canada, entitled *National Studies on Acute Gastrointestinal Illness* (NSAGI), are currently underway to quantify the loss of information at each level of the surveillance system. This issue is important because the reporting system in Canada typically requires that a case have a laboratory confirmed diagnosis of a reportable disease or condition. If international figures apply (Wheeler *et al*., 1999), only 4.5% of all community cases submit a specimen for analysis and of these, only a fraction are found positive for a reportable enteric pathogen, and are included in national surveillance. Therefore, any surveillance system for AMR based on existing notifiable disease infrastructure will not represent all people ill with enteric infections, just that subset who have sought care and submitted a specimen found positive for a reportable disease.

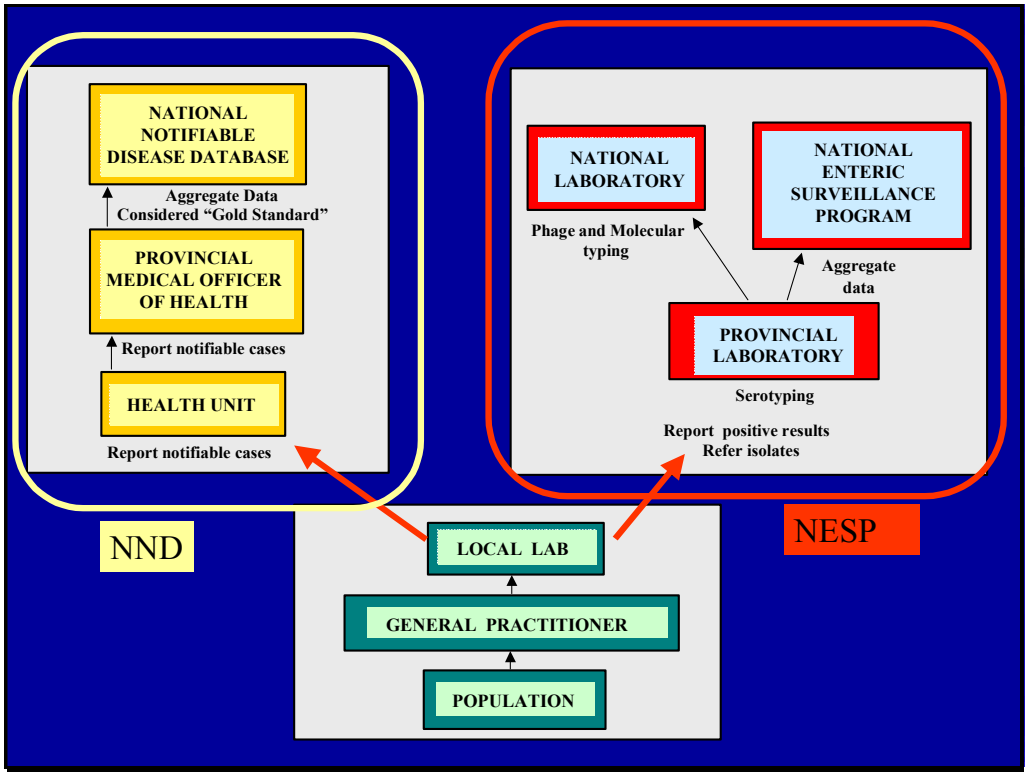
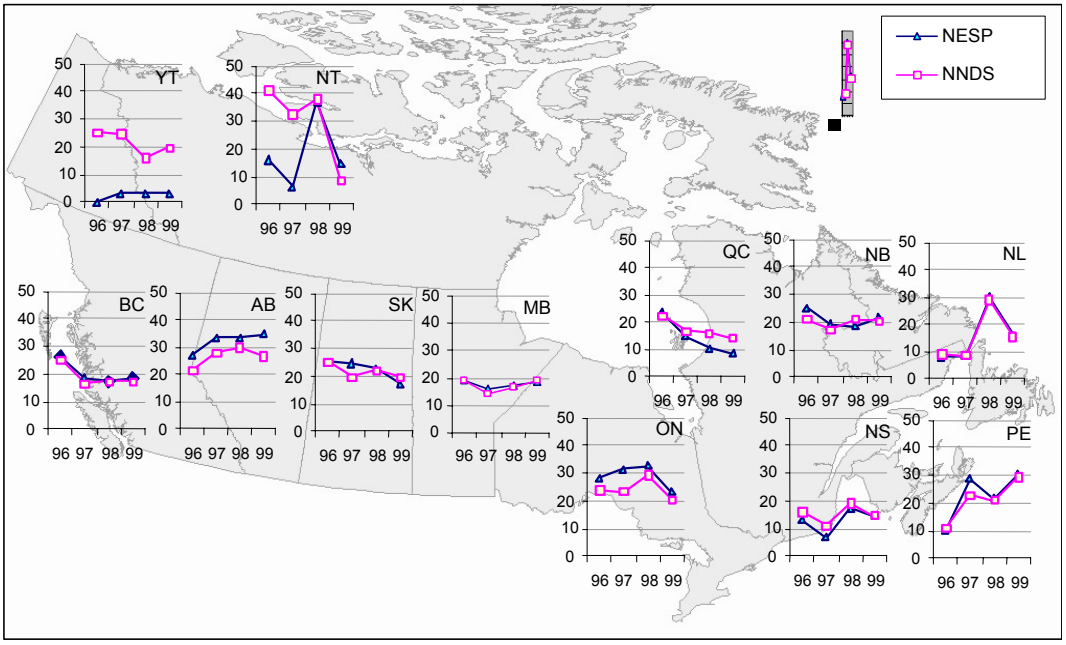


Figure A.3.1. Pathways of surveillance for enteric diseases in Canada

Table A.3.1. Nationally notifiable diseases in Canada

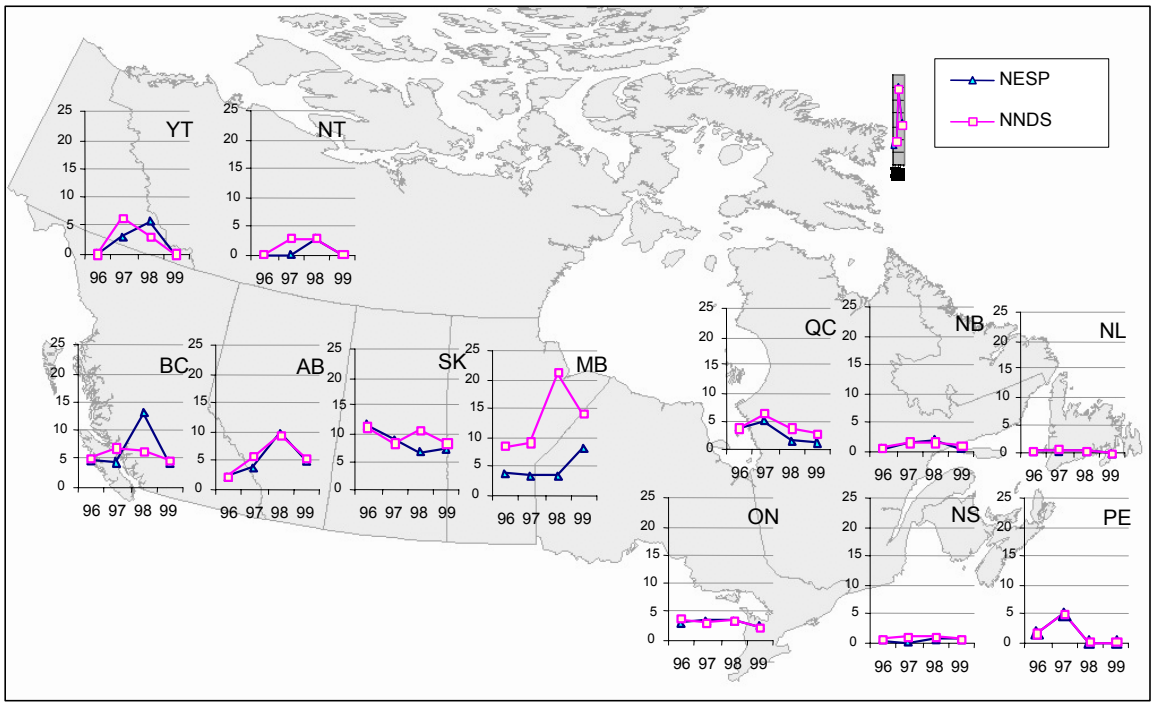
Nationally Notifiable Diseases	
Botulism*	*Cryptosporidium*
Salmonella (also Typhoid)	*Cyclospora*
Campylobacter	*Giardia*
Shigella	Hepatitis A*
Verotoxigenic *Escherichia coli*	
Vibrio (Cholera)	
Others Diseases Reported Through the *National Enteric Surveillance Program* (NESP)	
Yersinia	Rotavirus
Norovirus	*Entamoeba*

**Note: not reported through NESP*



Source: *Health Canada. Canadian Integrated Surveillance Report: Salmonella, Campylobacter, pathogenic E. coli and Shigella, from 1996 to 1999. CCDR 2003;29S1.*
Note: *YT = Yukon, NT = Northwest Territories, BC = British Columbia, AB = Alberta, SK = Saskatchewan, MB = Manitoba, ON = Ontario, QC = Québec, NB = New Brunswick, NS = Nova Scotia, NL = Newfoundland, PE = Prince Edward Island*

Figure A.3.2. Rates of human salmonellosis (per 100,000 people) as reported through the National Notifiable Disease Summary program (NNDS) and the National Microbiology Laboratory and National Enteric Surveillance Program (NML/NESP) by province for 1996 – 1999



Source: *Health Canada. Canadian Integrated Surveillance Report: Salmonella, Campylobacter, pathogenic E. coli and Shigella, from 1996 to 1999. CCDR 2003;29S1.*
Note: *YT = Yukon, NT = Northwest Territories, BC = British Columbia, AB = Alberta, SK = Saskatchewan, MB = Manitoba, ON = Ontario, QC = Québec, NB = New Brunswick, NS = Nova Scotia, NL = Newfoundland, PE = Prince Edward Island.*

Figure A.3.3. Rates of *Shigella* infections (per 100,000 people) as reported through the National Notifiable Disease Summary program (NNDS) and the National Microbiology Laboratory and National Enteric Surveillance Program (NML/NESP) by province for 1996 - 1999

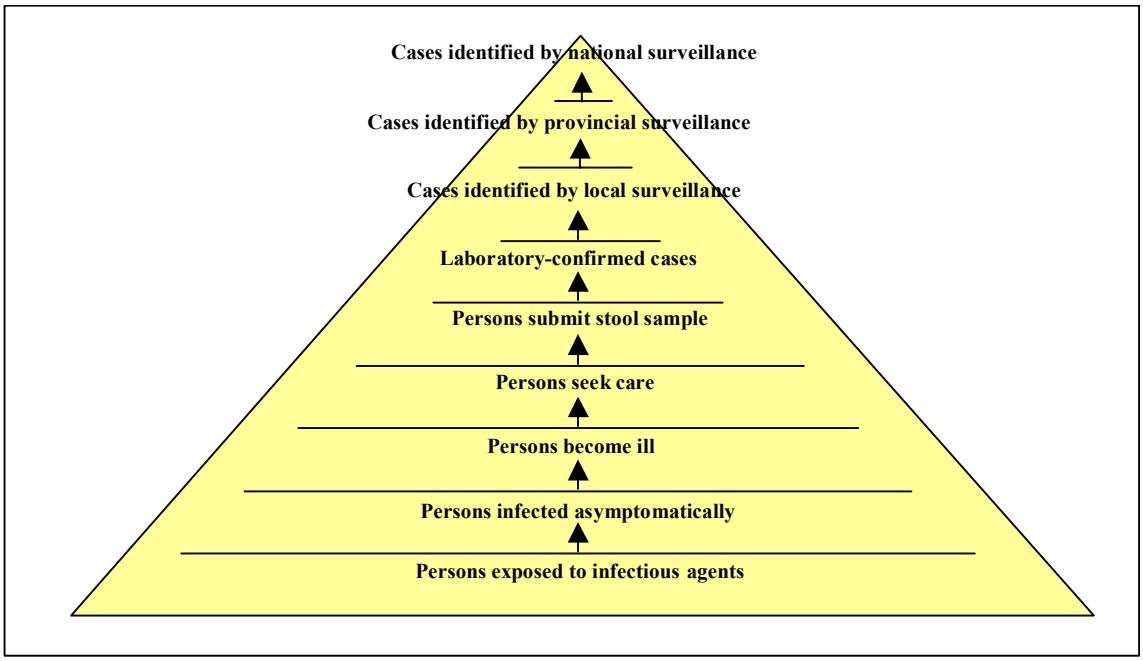


Figure A.3.4. Reporting pyramid for enteric diseases in Canada

A.4. Agri-Food Antimicrobial Resistance

Table A.4.1. Distribution of MICs and resistance in ***E. coli*** recovered from **beef cattle, chicken** and **swine**; *Abattoir Surveillance*

*	Antimicrobial	Animal Species	n	%R	C.I. 95% -	C.I. 95% +	Distribution (%) of MICs <=0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
I	Ceftiofur	Cattle	78	0.0	0.0	4.6				16.7	74.4	9.0											
		Chicken	40	10.0	2.8	23.7					70.0	15.0	5.0			7.5	2.5						
		Swine	38	0.0	0.0	9.3				23.7	73.7	2.6											
	Ceftriaxone	Cattle	78	0.0	0.0	4.6					100												
		Chicken	40	0.0	0.0	8.8					85.0		5.0			5.0	5.0						
		Swine	38	0.0	0.0	9.3					100												
	Ciprofloxacin	Cattle	78	0.0	0.0	4.6	98.7	1.3															
		Chicken	40	0.0	0.0	8.8	100																
		Swine	38	0.0	0.0	9.3	100																
II	Amikacin	Cattle	77	0.0	0.0	4.7							19.2	66.7	12.8	1.3							
		Chicken	40	0.0	0.0	8.8							12.5	67.5	20.0								
		Swine	38	0.0	0.0	9.5							13.2	68.4	15.8	2.6							
	Amoxicillin-Clavulanic Acid	Cattle	78	0.0	0.0	4.6							6.4	25.6	55.1	11.5	1.3						
		Chicken	40	12.5	4.2	26.8							2.5	20.0	32.5	27.5	5.0	2.5	10.0				
		Swine	38	0.0	0.0	9.3							5.3	39.5	21.1	31.6	2.6						
	Gentamicin	Cattle	78	0.0	0.0	4.6					10.3	34.6	53.8	1.3									
		Chicken	40	20.0	9.1	35.6					7.5	25.0	40.0			7.5	5.0	15.0					
		Swine	38	5.3	0.6	17.7					15.8	42.1	34.2			2.6	2.6	2.6					
	Kanamycin	Cattle	78	0.0	0.0	4.6										98.7	1.3						
		Chicken	40	25.0	12.7	41.2										70.0	5.0			25.0			
		Swine	38	7.9	1.7	21.4										92.1				7.9			
	Nalidixic Acid	Cattle	78	0.0	0.0	4.6								12.8	84.6	2.6							
		Chicken	40	0.0	0.0	8.8								20.0	72.5	7.5							
		Swine	38	0.0	0.0	9.3								28.9	63.2	7.9							
	Streptomycin	Cattle	78	11.5	5.4	20.8												88.5	10.3	1.3			
		Chicken	40	52.5	36.1	68.5												47.5	22.5	30.0			
		Swine	38	44.7	28.6	61.7												55.3	21.1	23.7			
	Trimethoprim-Sulfamethoxazole	Cattle	78	0.0	0.0	4.6				87.2	7.7	3.8		1.3									
		Chicken	40	7.5	1.6	20.4				65.0	20.0	5.0	2.5			7.5							
		Swine	38	5.3	0.6	17.7				55.3	31.6	7.9				5.3							
III	Ampicillin	Cattle	78	1.3	0.0	6.9							3.8	48.7	39.7	6.4			1.3				
		Chicken	40	32.5	18.6	49.1								25.0	32.5	10.0			32.5				
		Swine	38	28.9	15.4	45.9							7.9	31.6	28.9	2.6			28.9				
	Cefoxitin	Cattle	78	0.0	0.0	4.6							3.8	26.9	41.0	23.1	5.1						
		Chicken	40	12.5	4.2	26.8								20.0	27.5	22.5	17.5	12.5					
		Swine	38	0.0	0.0	9.3								39.5	39.5	15.8	5.3						
	Cephalothin	Cattle	78	2.6	0.3	9.0								3.8	16.7	55.1	21.8	2.6					
		Chicken	40	22.5	10.8	38.5									7.5	52.5	17.5	7.5	15.0				
		Swine	38	2.6	0.1	13.8								2.6	39.5	47.4	7.9	2.6					
	Chloramphenicol	Cattle	78	1.3	0.0	6.9								2.6	61.5	33.3	1.3		1.3				
		Chicken	40	2.5	0.1	13.2									57.5	40.0			2.5				
		Swine	38	13.2	4.4	28.1								7.9	44.7	31.6	2.6	10.5	2.6				
	Sulfamethoxazole	Cattle	78	9.0	3.7	17.6											91.0						9.0
		Chicken	40	45.0	29.3	61.5											55.0						45.0
		Swine	38	36.8	21.8	54.0											63.2						36.8
	Tetracycline	Cattle	78	26.9	17.5	38.2									65.4	7.7	5.1	1.3	20.5				

*	Antimicrobial	Animal Species	n	%R	C.I. 95% -	C.I. 95% +	Distribution (%) of MICs <=0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
		Chicken	40	65.0	48.3	79.4									30.0	5.0			65.0				
		Swine	38	78.9	62.7	90.4									21.1			5.3	73.7				

*Note: * = Ranking of human health importance, VDD; The white fields denote the ranges tested for each antimicrobial; vertical bars denote breakpoints.*

Table A.4.2. Multiple drug resistance patterns in **bovine *E. coli;*** *Abattoir Surveillance*

Pattern	*E. coli*; n=78 % (n)
None	69.2 (54)
TCY-	14.1 (11)
SMS-TCY-	2.6 (2)
STR-SMX-TCY-	5.1 (4)
STR-TCY-	2.6 (2)
CEP-	2.6 (2)
CHL-STR-SMX-TCY-	1.3 (1)
STR-	1.3 (1)
AMP-STR-TCY-	1.3 (1)

Table A.4.3. Resistance patterns in ***E. coli*** and ***Salmonella*** isolates from **swine** and **pork meat** specimens; *Abattoir Surveillance, Passive Surveillance*

Pattern	*Abattoir Surveillance E. coli;* n=38 % (n)	*Abattoir Surveillance Salmonella;* n=101 % (n)	Pork from *Passive Surveillance Salmonella;* n=33 % (n)
None	21.05 (8)	55.45 (56)	69.7 (23)
ACSSuT		7.92 (8)	9.09 (3)
STR-SMX-TCY-	2.63 (1)	7.92 (8)	3.03 (1)
TCY-	15.79 (6)	5.94 (6)	3.03 (1)
ACKSSuT+SXT-		2.97 (3)	
AKSSuT		1.98 (2)	
KAN-STR-SMX-TCY-		1.98 (2)	
STR-TCY-	18.42 (7)	1.98 (2)	
ACSSuT+AMC		1.98 (2)	
AMP-CEP-		1.98 (2)	
GEN-KAN-STR-SMX-TCY-		1.98 (2)	
STR-SMX-		1.98 (2)	
ACKSSuT		0.99 (1)	9.09 (3)
ACKSSuT+AMC		0.99 (1)	
AKSSuT+GEN-		0.99 (1)	
AMC-AMP-CEP-		0.99 (1)	
FOX-CHL-		0.99 (1)	
KAN-		0.99 (1)	
A3C+AMP-STR-SMX-TCY-			3.03 (1)
SMX-SXT-			3.03 (1)
AMP-CEP-STR-SMX-TCY-	2.63 (1)		
AMP-TCY-	2.63 (1)		
AMP-STR-SMX-TCY-	10.53 (4)		
ACKSSuT+GEN-	2.63 (1)		
AMP-CHL-SMX-TCY-	2.63 (1)		
AMP-KAN-TCY-	2.63 (1)		

Pattern	*Abattoir Surveillance E. coli;* n=38 % (n)	*Abattoir Surveillance Salmonella;* n=101 % (n)	Pork from *Passive Surveillance Salmonella;* n=33 % (n)
AMP-STR-SMX-TCY-SXT-	2.63 (1)		
AMP-SMX-TCY-	2,63 (1)		
CHL-GEN-STR-SMX-TCY-	2,63 (1)		
CHL-STR-SMX-TCY-	2,63 (1)		
CHL-SMX-TCY-	2,63 (1)		
KAN-TCY-	2,63 (1)		
SMX-TCY-SXT-	2,63 (1)		

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic acid, Cefoxitin, Ceftiofur and Cephalothin.

Table A.4.4. Distribution of MICs and resistance in ***Salmonella*** recovered from **beef cattle, chicken and swine**; *Abattoir Surveillance*

*	Antimicrobial	Animal Species	n	%R	C.I.95% -	C.I.95% +	Distribution (%) of MICs <=0.01	0.03	0.0	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	51	>512
I	Ceftiofur	Cattle	1	0.0	0.0	8.5						100											
		Chicken	25	12.0	2.5	31.2					4.0	80.0	4.0				12.0						
		Swine	101	0.0	0.0	3.6						69.3	27.7	3.0									
	Ceftriaxone	Cattle	1	0.0	0.0	8.5					100												
		Chicken	25	0.0	0.0	13.7					88.0					4.0	8.0						
		Swine	101	0.0	0.0	3.6					100												
	Ciprofloxacin	Cattle	1	0.0	0.0	8.5	100																
		Chicken	25	0.0	0.0	13.7	80.0	20.0															
		Swine	101	0.0	0.0	3.6	71.3	25.7	3.0														
II	Amikacin	Cattle	1	0.0	0.0	8.5							100										
		Chicken	25	0.0	0.0	13.7						12.0	76.0	12.0									
		Swine	101	0.0	0.0	3.6						5.0	58.4	32.7	4.0								
	Amoxicillin-Clavulanic Acid	Cattle	1	0.0	0.0	8.5							100										
		Chicken	25	12.0	2.5	31.2							64.0			4.0	20.0		12.0				
		Swine	101	4.0	1.1	9.8							60.4	16.8	2.0	5.9	10.9	4.0					
	Gentamicin	Cattle	1	0.0	0.0	8.5							100										
		Chicken	25	12.0	2.5	31.2					72.0	12.0	4.0				4.0	8.0					
		Swine	101	3.0	0.6	8.4					60.4	23.8	12.9				1.0	2.0					
	Kanamycin	Cattle	1	0.0	0.0	8.5										100							
		Chicken	25	0.0	0.0	13.7										100							
		Swine	101	12.9	7.0	21.0										87.1				12.9			
	Nalidixic Acid	Cattle	1	0.0	0.0	8.5									100								
		Chicken	25	4.0	0.0	20.3									28.0	64.0	4.0	4.0					
		Swine	101	0.0	0.0	3.6									31.7	60.4	7.9						
	Streptomycin	Cattle	1	0.0	0.0	8.5												100					
		Chicken	25	20.0	6.8	40.7												80.0	4.0	16.0			
		Swine	101	33.7	24.5	43.8												66.3	14.9	18.8			
	Trimethoprim-Sulfamethoxazole	Cattle	1	0.0	0.0	8.5				100													
		Chicken	25	0.0	0.0	13.7				96.0	4.0												
		Swine	101	3.0	0.6	8.4				55.4	32.7	5.9	2.0	1.0		3.0							
III	Ampicillin	Cattle	1	0.0	0.0	8.5							100										
		Chicken	25	36.0	18.0	57.4							48.0	16.0					36.0				
		Swine	101	20.8	13.3	30.0							40.6	28.7	6.9	3.0			20.8				
	Cefoxitin	Cattle	1	0.0	0.0	8.5								100									
		Chicken	25	12.0	2.5	31.2								72.0	16.0			12.0					
		Swine	101	1.0	0.0	2.9								30.7	47.5	16.8	4.0	1.0					
	Cephalothin	Cattle	1	0.0	0.0	8.5								100									
		Chicken	25	20.0	6.8	40.7								60.0	8.0		12.0	8.0	12.0				
		Swine	101	3.0	0.6	8.4								33.7	53.5	7.9	2.0	2.0	1.0				
	Chloramphenicol	Cattle	1	0.0	0.0	8.5								100									
		Chicken	25	0.0	0.0	13.7								4.0	24.0	72.0							
		Swine	101	15.8	9.3	24.4									21.8	55.4	6.9	1.0	14.9				
	Sulfamethoxazole	Cattle	1	0.0	0.0	8.5											100						
		Chicken	25	12.0	2.5	31.2											80.0	8.0					12.0
		Swine	101	31.7	22.8	41.7											45.5	19.8	2.0	1.0			31.7
	Tetracycline	Cattle	1	100	0.0	25.3											100						
		Chicken	25	8.0	1.0	26.0									92.0			4.0	4.0				
		Swine	101	37.6	28.2	47.8									61.4	1.0	2.0	8.9	26.7				

*Note: * = Ranking of human health importance, VDD; The white fields denote the ranges tested for each antimicrobial; vertical bars denote breakpoints.*

Table A.4.5. *Salmonella* serovars, phagetypes, and resistance patterns from **swine** isolates; *Abattoir Surveillance* and *Passive Surveillance (pork)*

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Abattoir Surveillance n=101			
Typhimurium 104	7	ACKSSuT+TMP	3
Typhimurium var Copenhagen 104	7	ACKSSuT+AMC	1
Heidelberg 29	6	AKSSuT+GEN	1
Typhimurium 104	6	ACKSSuT+	1
Typhimurium var Copenhagen 104	6	ACSSuT+AMC	2
Mbandaka	5	GEN-KAN-STR-SMX-TCY	2
Typhimurium var Copenhagen 208	5	AKSSuT+	2
Typhimurium var Copenhagen 104	5	ACSSuT+	8
Typhimurium var Copenhagen 208	4	KAN-STR-SMX-TCY	2
Derby	3	STR-SMX-TCY	7
Heidelberg	3	AMC-AMP-CEP	1
Mbandaka	3	STR-SMX-TCY	1
Derby	2	STR-SMX	2
Hadar	2	STR-TCY	2
Heidelberg 18	2	AMP-CEP	2
Senftenberg	2	FOX-CHL	1
I:4,12:-:-	1	TCY	1
Agona	1	TCY	1
Derby	1	TCY	4
Typhimurium var Copenhagen 104	1	KAN	1
1:6,7:-:1,w	0	None	1
Salmonella bovi	0	None	2
1:ROUGH-0:d:1,2	0	None	1
291	0	None	1
Agona	0	None	1
Berta	0	None	1
Brandenburg	0	None	5
California	0	None	2
Derby	0	None	1
Give	0	None	2
Heidelberg 27	0	None	2
Heidelberg 4	0	None	1
Infantis	0	None	6
Krefeld	0	None	2
Livingstone	0	None	1
Mbandaka	0	None	1
Montevideo	0	None	2
Muenchen	0	None	5
Ohio	0	None	3
Rubislaw	0	None	1
Schwarzengrund	0	None	2
Senftenberg	0	None	3
Tennessee	0	None	1
Typhimurium 170	0	None	1
Typhimurium 208	0	None	2
Typhimurium 291	0	None	1
Typhimurium 73	0	None	1

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Typhimurium var Copenhagen 104	0	None	3
Typhimurium var Copenhagen 169	0	None	1
***Passive Surveillance* (pork)** n=33			
Derby	8	A3C-AMP-STR-SMX-TCY	1
Typhimurium 104	6	ACKSSuT+	3
Typhimurium	5	ACSSuT+	1
Typhimurium 101	5	ACSSuT+	1
Typhimurium 104	5	ACSSuT+	1
Derby	3	STR-SMX-TCY	1
Typhimurium 104	2	SMX-TMP	1
Typhimurium 208	1	TCY	1
Cerro	0	None	1
Infantis	0	None	10
London	0	None	1
Muenchen	0	None	1
Salmonella spp.	0	None	7
Typhimurium 104	0	None	1
Typhimurium 108	0	None	2

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.6. Resistance patterns in ***E. coli*** and ***Salmonella*** isolates from **broiler chicken**; *Abattoir Surveillance*

Pattern	*Abattoir Surveillance* *E. coli* n=40 % (n)	*Abattoir Surveillance* *Salmonella* n=25 % (n)
None	20.0 (8)	52.0 (13)
A3C+AMP		12.0 (3)
AMP-CEP-		8.0 (2)
GEN-STR-SMX-	2.5 (1)	8.0 (2)
AMP-	2.5 (1)	4.0 (1)
AMP-GEN-STR-SMX-		4.0 (1)
AMP-NAL-		4.0 (1)
AMP-STR-TCY-	2.5 (1)	4.0 (1)
STR-TCY-	7.5 (3)	4.0 (1)
KAN-STR-SMX-TCY-	7.5 (3)	
TCY-	7.5 (3)	
AMP-CEP-STR-SMX-TCY-	5.0 (2)	
GEN-KAN-STR-SMX-TCY-	5.0 (2)	
A3C+AMP-GEN-STR-SMX-TCY-	2.5 (1)	
A3C+AMP-STR-SMX-TCY-	2.5 (1)	
A3C+AMP-TCY-	2.5 (1)	
ACSSuT+A3C+GEN-SXT-	2.5 (1)	
AKSSuT+	2.5 (1)	
AMC-AMP-FOX-CEP-TCY-	2.5 (1)	
AMP-GEN-STR-SMX-TCY-	2.5 (1)	
AMP-SMX-SXT-	2.5 (1)	
AMP-TCY-	2.5 (1)	
CEP-	2.5 (1)	
CEP-GEN-STR-SMX-TCY-	2.5 (1)	
GEN-KAN-STR-SMX-	2.5 (1)	
KAN-STR-	2.5 (1)	
KAN-STR-SMX-TCY-SXT-	2.5 (1)	
KAN-TCY-	2.5 (1)	
SMX-TCY-	2.5 (1)	

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin.

Table A.4.7. *Salmonella* serovars, phagetypes, and resistance patterns from **broiler chicken** isolates*; Abattoir Surveillance* n=25

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Heidelberg 29	5	A3C+AMP	2
Heidelberg 4	5	A3C+AMP	1
Heidelberg 29	4	AMP-GEN-STR-SUL-	1
Hadar	3	AMP-STR-TCY-	1
Heidelberg 18	3	GEN-STR-SMX-	1
Heidelberg 26	3	GEN-STR-SMX-	1
Heidelberg 18	2	AMP-CEP-	1
Heidelberg 18	2	AMP-NAL-	1
Heidelberg 19	2	AMP-CEP-	1
1:6,8:-:enx	2	STR-TCY	1
Heidelberg 9	1	AMP	1
Bradford	0	None	1
Heidelberg 18	0	None	2
Heidelberg 19	0	None	1
Heidelberg 26	0	None	4
Kentucky	0	None	4
Thompson	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.8. Details regarding the data obtained from the *Passive Surveillance* of clinical ***Salmonella*** isolates

Zoological species (n)	Specimen (n)	Province (n)	Year of sample collection (n)
Bovine (480) Porcine (309) Chicken (146) Turkey (87) Equine (74) Canine (15) Feline (18) Others (197)	Organs (677) Faeces (525) Culture (91) Eggs (11) Others	ON (927) AB (276) MA (73) NS (54) SK (25) NB (20) QC (18) PE (16) NF (6) BC (1) Unknown (117)	1999 (3) 2000 (89) 2001 (853) 2002 (579)

Table A.4.9. Distribution of MICs and resistance in ***Salmonella*** from **bovine** and **porcine** clinical isolates; *Passive Surveillance*

*	Antimicrobial	Animal species	n	%R	Distribution (%) of MICs															
					<=0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
I	Ceftiofur	Cattle	480	8.3					0.2	66.5	24.4	0.6		1.5	5.0	1.9					
		Swine	309	2.9					0.6	58.3	38.2			0.6	1.9	0.3					
	Ceftriaxone	Cattle	480	0.0					91.7				2.1	2.1	1.7	2.5					
		Swine	309	0.0					97.1				0.6	0.3	1.0	1.0					
	Ciprofloxacin	Cattle	480	0.0	92.9	6.9	0.2														
		Swine	309	0.0	87.1	12.6	0.3														
	Imipenem	Cattle	247	0.0					98.8	1.2											
		Swine	192	0.0					100.0												
II	Amikacin	Cattle	480	0.0						1.0	31.7	14.4	52.7	0.2							
		Swine	309	0.0						1.6	23.9	11.0	63.4								
	Amoxicillin-Clavulanic Acid	Cattle	480	10.8						0.2	35.4	3.3	0.4	21.3	28.5	2.3	8.5				
		Swine	309	5.8						0.6	48.5	5.2		12.3	27.5	3.6	2.3				
	Gentamicin	Cattle	480	6.7					37.3	45.2	10.6	0.2			1.9	4.8					
		Swine	309	5.8					23.6	54.7	14.9	1.0			3.9	1.9					
	Kanamycin	Cattle	480	40.2										32.1	27.7			40.2			
		Swine	309	19.4										31.1	49.5			19.4			
	Nalidixic Acid	Cattle	480	0.0									80.8	18.1	1.0						
		Swine	309	0.0									81.6	18.1	0.3						
	Streptomycin	Cattle	478	55.4												44.6	26.4	29.1			
		Swine	309	55.0												45.0	24.3	30.7			
	Trimethoprim-Sulfamethoxazole	Cattle	480	11.7				34.8	41.0	12.3		0.2		11.7							
		Swine	309	7.8				37.5	38.2	16.2	0.3		0.3	7.4							
III	Ampicillin	Cattle	480	60.8							19.0	18.5	1.7				60.8				
		Swine	309	45.6							13.3	38.5	2.6				45.6				
	Apramycin	Cattle	247	3.6								35.2	55.5	5.7			3.6				
		Swine	192	4.7								34.4	51.6	8.9	0.5		4.7				
	Cefoxitin	Cattle	480	6.9							0.6	22.7	58.5	8.1	3.1	5.2	1.7				
		Swine	309	2.6							0.3	15.2	70.6	11.0	0.3	2.3	0.3				
	Cephalothin	Cattle	480	12.5								27.7	34.0	21.7	4.2	1.5	11.0				
		Swine	309	3.9							0.3	36.2	44.3	12.0	3.2	1.0	2.9				
	Chloramphenicol	Cattle	480	36.9								1.7	34.4	26.7	0.4		36.9				
		Swine	309	33.7								0.3	19.1	46.9		0.6	33.0				
	Sulfamethoxazole	Cattle	480	62.1											17.1	5.0		15.8			62.1
		Swine	309	60.2											13.9	1.3	0.3	24.3			60.2
	Tetracycline	Cattle	480	62.9									21.9	15.2	0.6	46.5	15.8				
		Swine	309	61.8									14.2	23.9	0.3	46.0	15.5				

*Note: * Ranking of human importance, VDD; The white fields denote the ranges tested for each antimicrobial. The solid area refers to the 2002 antimicrobial panel and the light shaded area refers to the 2001 antimicrobial panel. The dark shaded area refers to an overlap of both the 2002 and 2001 antimicrobial panels; vertical bars denote breakpoints.*

Table A.4.10. Resistance patterns in clinical **bovine *Salmonella*** isolates; *Passive Surveillance* (n=478)[a]

Pattern	% (n)	Pattern	% (n)
None	36.19 (173)	ACKSSuT+AMC-TIO-CEP-GEN-SXT-	0.21 (1)
AKSSuT[b]	16.53 (79)	ACKSSuT+AMC-CEP-SXT-	0.21 (1)
ACSSuT	13.81 (66)	ACKSSuT+FOX-CEP-SXT-	0.21 (1)
AMP-KAN-SUL-TCY-	5.65 (27)	ACKSSuT+SXT-	0.21 (1)
ACKSSuT	3.35 (16)	ACSSuT+A3C+SXT-	0.21 (1)
ACKSSuT+CEP-SXT-	3.14 (15)	AKSSuT+AMC	0.21 (1)
ACKSSuT+GEN-SXT-	3.14 (15)	AKSSuT+CEP-SXT-	0.21 (1)
ACSSuT+A3C	2.93 (14)	AKSSuT+GEN-SXT-	0.21 (1)
ACSSuT+AMC	1.88 (9)	AMP-CEP-	0.21 (1)
ACKSSuT+A3C	1.67 (8)	AMP-CEP-KAN-SMX-TCY-	0.21 (1)
ACSSuT+AMC-TIO-CEP-	1.46 (7)	AMP-CHL-GEN-KAN-TCY-	0.21 (1)
AKSSuT+SXT-	0.84 (4)	AMP-KAN-STR-SMX-SXT-	0.21 (1)
ACKSSuT+A3C+GEN-SXT-	0.63 (3)	AMP-KAN-SMX-TCY-SXT-	0.21 (1)
ACKSSuT+A3C+SXT-	0.63 (3)	AMP-KAN-TCY-	0.21 (1)
AMP-CHL-GEN-KAN-SMX-TCY-SXT-	0.63 (3)	AMP-STR-SMX-	0.21 (1)
CHL-GEN-STR-SMX-TCY-SXT-	0.63 (3)	CHL-GEN-STR-SMX-TCY-	0.21 (1)
STR-TCY-	0.63 (3)	CHL-STR-SMX-TCY-	0.21 (1)
ACKSSuT+A3C+GEN-	0.42 (2)	CHL-STR-SMX-TCY-SXT-	0.21 (1)
ACKSSuT+GEN-	0.42 (2)	CHL-SMX-TCY-	0.21 (1)
TCY-	0.42 (2)	KAN-STR-SMX-TCY-	0.21 (1)
A3C+AMP	0.21 (1)	STR-SMX-TCY-	0.21 (1)
ACKSSuT+AMC	0.21 (1)	SMX-	0.21 (1)

Note: a) two isolates were excluded from analysis because results for one antimicrobial were invalid. b) ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin.

Table A.4.11. ***Salmonella*** serovars, phagetypes, and resistance patterns from **bovine** clinical isolates; *Passive Surveillance* (n=478)

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Salmonella spp.	13	ACKSSuT-A3C-GEN-SXT-	1
Typhimurium var Copenhagen 104	12	ACKSSuT-A3C-GEN-	1
Heidelberg	12	ACKSSuT-A3C-GEN-SXT-	1
Typhimurium var Copenhagen	12	ACKSSuT-A3C-GEN-SXT-	1
Newport	11	ACKSSuT-A3C-GEN-	1
Salmonella spp.	11	ACKSSuT-A3C-SXT-	1
Typhimurium var Copenhagen	11	ACKSSuT-A3C-SXT-	1
Typhimurium var Copenhagen 208	11	ACKSSuT-A3C-SXT-	1
Typhimurium var Copenhagen	11	ACKSSuT-AMC-TIO-CEP-GEN-SXT-	1
Newport	10	ACKSSuT-A3C-	7
Saintpaul	10	ACKSSuT-A3C-	1
Mbandaka	10	ACSSuT-A3C-SXT-	1
Typhimurium	9	ACKSSuT-AMC-CEP-SXT-	1
Typhimurium	9	ACKSSuT-FOX-CEP-SXT-	1
Salmonella 208	9	ACKSSuT-GEN-SXT-	1
Typhimurium var Copenhagen	9	ACKSSuT-GEN-SXT-	1
Typhimurium 108	9	ACSSuT-A3C-	8
Newport	9	ACSSuT-A3C-	4
Typhimurium 170	9	ACSSuT-A3C-	2
Typhimurium	8	ACKSSuT-CEP-SXT-	11
Typhimurium 208	8	ACKSSuT-CEP-SXT-	2
Typhimurium 132	8	ACKSSuT-CEP-SXT-	1
Typhimurium 302	8	ACKSSuT-CEP-SXT-	1
Salmonella spp.	8	ACKSSuT-GEN-	1
Typhimurium var Copenhagen 208	8	ACKSSuT-GEN-SXT-	4
Typhimurium	8	ACKSSuT-GEN-SXT-	3
Typhimurium var Copenhagen	8	ACKSSuT-GEN-SXT-	3
Salmonella 208	8	ACKSSuT-GEN-SXT-	1
Typhimurium 208	8	ACKSSuT-GEN-SXT-	1
Typhimurium var Copenhagen 302	8	ACKSSuT-GEN-SXT-	1
Typhimurium 108	8	ACSSuT-AMC-TIO-CEP-	5
Typhimurium 12	8	ACSSuT-AMC-TIO-CEP-	1
Typhimurium 170	8	ACSSuT-AMC-TIO-CEP-	1
Typhimurium 104	7	ACKSSuT-AMC	1
I:ROUGH O:i:1,2	7	ACKSSuT-GEN-	1
Typhimurium var Copenhagen 104	7	ACKSSuT-SXT-	1
Typhimurium var Copenhagen 208	7	AKSSuT-CEP-SXT-	1

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Typhimurium var Copenhagen 208	7	AKSSuT-GEN-SXT-	1
Typhimurium	7	AMP-CHL-GEN-KAN-SMX-TCY-SXT-	2
Typhimurium var Copenhagen	7	AMP-CHL-GEN-KAN-SMX-TCY-SXT-	1
Stanley	7	CHL-GEN-STR-SMX-TCY-SXT-	3
Typhimurium 104	6	ACKSSuT-	12
Muenster	6	ACKSSuT-	1
Salmonella spp.	6	ACKSSuT-	1
Typhimurium var Copenhagen 104	6	ACKSSuT-	1
Typhimurium var Copenhagen 208	6	ACKSSuT-	1
Typhimurium 104	6	ACSSuT-AMC	7
Typhimurium var Copenhagen 104	6	ACSSuT-AMC	2
Typhimurium var Copenhagen 208	6	AKSSuT-AMC	1
Typhimurium var Copenhagen 208	6	AKSSuT-SXT-	4
Stanley	6	CHL-GEN-STR-SMX-TCY-	1
Heidelberg 29	5	A3C-AMP	1
Typhimurium 104	5	ACSSuT-	55
Typhimurium var Copenhagen 104	5	ACSSuT-	8
Typhimurium	5	ACSSuT-	2
Typhimurium 302	5	ACSSuT-	1
Typhimurium var Copenhagen 208	5	AKSSuT-	47
Typhimurium var Copenhagen	5	AKSSuT-	15
Typhimurium	5	AKSSuT-	7
Typhimurium 208	5	AKSSuT-	6
I:ROUGH O:i:	5	AKSSuT-	1
Salmonella sp. 208	5	AKSSuT-	1
Typhimurium 132	5	AKSSuT-	1
Typhimurium var Copenhagen 21	5	AKSSuT-	1
Typhimurium var Copenhagen 208	5	AMP-CEP-KAN-SMX-TCY-	1
Typhimurium	5	AMP-CHL-GEN-KAN-TCY-	1
Typhimurium var Copenhagen 208	5	AMP-KAN-STR-SMX-SXT-	1
Typhimurium var Copenhagen 208	5	AMP-KAN-SMX-TCY-SXT-	1
Mbandaka	5	CHL-STR-SMX-TCY-SXT-	1
Typhimurium var Copenhagen 208	4	AMP-KAN-SMX-TCY-	22
Typhimurium var Copenhagen	4	AMP-KAN-SMX-TCY-	5
Typhimurium	4	AMP-KAN-SMX-TCY-	1
Typhimurium 208	4	AMP-KAN-SMX-TCY-	1
Mbandaka	4	CHL-STR-SMX-TCY-	1
Kentucky	4	KAN-STR-SMX-TCY-	1
Typhimurium var Copenhagen 208	3	AMP-KAN-TCY-	1
Dublin	3	AMP-STR-SMX-	1
Typhimurium var Copenhagen 104	3	CHL-SMX-TCY-	1
Stanley	3	STR-SMX-TCY-	1
Heidelberg 19	2	AMP-CEP-	1
Hadar	2	STR-TCY-	1
Heidelberg	2	STR-TCY-	1

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Salmonella spp.	2	STR-TCY-	1
Dublin	1	SMX-	1
Agona	1	TCY-	1
Heidelberg 32	1	TCY-	1
Kentucky	0	None	42
Muenster	0	None	30
Cerro	0	None	16
Salmonella spp.	0	None	7
Typhimurium 108	0	None	6
I:18: :	0	None	4
I:4,12:i: 291	0	None	4
I:ROUGH O: :	0	None	4
Typhimurium 10	0	None	4
Brandenburg	0	None	3
Heidelberg	0	None	3
Infantis	0	None	3
Orionvar15-	0	None	3
Typhimurium var Copenhagen 104, 170, 2	0	None	3
Agona	0	None	2
Anatum	0	None	2
Dublin	0	None	2
Give	0	None	2
I:ROUGH O:z4,z23:	0	None	2
Stanley	0	None	2
Typhimurium 104	0	None	2
Typhimurium 107	0	None	2
Typhimurium 186	0	None	2
Typhimurium 2	0	None	2
Typhimurium 284	0	None	2
Typhimurium 40	0	None	2
Bredeney	0	None	1
Heidelberg 19	0	None	1
Heidelberg 35	0	None	1
Heidelberg 8	0	None	1
I:4,5,12:b:	0	None	1
I:4,5,12:i:	0	None	1
I:4,5:i: 291	0	None	1
I:8,20:i:	0	None	1
Mbandaka	0	None	1
Orionvar.15-34-	0	None	1
Salmonella 302	0	None	1
Senftenberg	0	None	1
Thompson	0	None	1
Typhimurium	0	None	1
Typhimurium 208	0	None	1
Typhimurium 66	0	None	1
Worthington	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.12. Resistance patterns in **porcine** clinical ***Salmonella*** isolates; *Passive Surveillance* (N=309)

Pattern	% (n)	Pattern	% (n)
None	33.01 (102)	STR-SMX-	0.65 (2)
ACSSuT	20.39 (63)	SMX-TCY-	0.65 (2)
AKSSuT	7.12 (22)	SMX-TCY-SXT-	0.65 (2)
STR-SMX-TCY	7.12 (22)	A3C-AMP-STR-SMX-TCY-	0.32 (1)
ACKSSuT	3.88 (12)	A3C-AMP-TCY-	0.32 (1)
TCY-	2.91 (9)	ACKSSuT-AMC	0.32 (1)
ACKSSuT-GEN-	1.94 (6)	ACKSSuT-AMC-CEP-GEN-SXT-	0.32 (1)
ACSSuT-AMC	1.62 (5)	ACKSSuT-SXT-	0.32 (1)
SMX-SXT-	1.62 (5)	ACSSuT-A3C-GEN-	0.32 (1)
AMP-STR-SMX-TCY-	1.29 (4)	ACSSuT-AMC-TIO-CEP-	0.32 (1)
STR-TCY-	1.29 (4)	AKSSuT-SXT-	0.32 (1)
ACSSuT-A3C	0.97 (3)	AMP-CHL-KAN-SMX-TCY-SXT-	0.32 (1)
AMP-KAN-STR-TCY-	0.97 (3)	AMP-CHL-SMX-TCY-	0.32 (1)
GEN-SMX-TCY-SXT-	0.97 (3)	AMP-GEN-STR-SMX-	0.32 (1)
KAN-STR-SMX-TCY-SXT-	0.97 (3)	AMP-STR-SXT-	0.32 (1)
SMX	0.97 (3)	AMP-SMX-TCY-SXT-	0.32 (1)
ACKSSuT-A3C-GEN-SXT-	0.65 (2)	CHL-STR-SMX-TCY-	0.32 (1)
ACKSSuT-AMC-GEN-	0.65 (2)	CHL-SMX-TCY-	0.32 (1)
ACSSuT-CEP-	0.65 (2)	KAN-	0.32 (1)
AMP-STR-TCY-	0.65 (2)	KAN-STR-SMX-TCY-	0.32 (1)
AMP-SMX-	0.65 (2)	KAN-SMX-TCY-SXT-	0.32 (1)
GEN-SMX-TCY-	0.65 (2)	STR-SMX-SXT-	0.32 (1)
KAN-SMX-TCY-	0.65 (2)	STR-SMX-TCY-SXT-	0.32 (1)

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin.

Table A.4.13. *Salmonella* serovars, phagetypes, and resistance patterns from **porcine** clinical isolates; *Passive Surveillance* (n=309)

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Ohio-	12	ACKSSuT-A3C-GEN-SXT-	2
Agona-	10	ACKSSuT-AMC-CEP-GEN-SXT-	1
Typhimurium-104	10	ACSSuT-A3C-GEN-	1
Typhimurium-104	9	ACKSSuT-AMC-GEN-	2
Typhimurium-108	9	ACSSuT-A3C-	2
Infantis-	9	ACSSuT-A3C-	1
Derby-	8	A3C-AMP-STR-SMX-TCY-	1
Salmonella spp.	8	ACKSSuT-GEN-	4
Livingstone-	8	ACKSSuT-GEN-	1
Typhimurium-108	8	ACSSuT-AMC-TIO-CEP-	1
Typhimurium var Copenhag-104	7	ACKSSuT-AMC	1
I:6,7:-:l,w-	7	ACKSSuT-GEN-	1
Typhimurium-302	7	ACKSSuT-SXT-	1
Derby-	6	A3C-AMP-TCY-	1
Typhimurium-104	6	ACKSSuT-	4
Typhimurium var Copenhag-104	6	ACKSSuT-	4
Salmonella spp.	6	ACKSSuT-	1
Typhimurium-302	6	ACKSSuT-	1
Typhimurium var Copenhag-120	6	ACKSSuT-	1
Krefeld-	6	ACKSSuT-	1
Typhimurium-104	6	ACSSuT-AMC	2
Typhimurium-	6	ACSSuT-AMC	1
Typhimuriumvar.copenhag-104	6	ACSSuT-AMC	1
I:4,12:i:--104	6	ACSSuT-AMC	1
Typhimurium-	6	ACSSuT-CEP-	2
Typhimurium-208	6	AKSSuT-SXT-	1
Typhimuriumvar.copenhag-104	6	AMP-CHL-KAN-SMX-TCY-SXT-	1
Typhimurium-104	5	ACSSuT-	45
Typhimuriumvar.copenhag-104	5	ACSSuT-	13
Typhimurium-	5	ACSSuT-	2
Typhimuriumvar.copenhag-302	5	ACSSuT-	1
Typhimuriumvar.copenhag-110	5	ACSSuT-	1
Krefeld-	5	ACSSuT-	1
Typhimurium-208	5	AKSSuT-	8
Typhimurium-	5	AKSSuT-	3
Typhimurium-186	5	AKSSuT-	2
Typhimurium var Copenhag-	5	AKSSuT-	2
Typhimuriumvar.copenhag-208	5	AKSSuT-	2
Typhimurium-193	5	AKSSuT-	1
Typhimurium-35	5	AKSSuT-	1
Typhimurium-195	5	AKSSuT-	1
Typhimuriumvar.copenhag-186	5	AKSSuT-	1
Typhimur.varcopenhagen-208	5	AKSSuT-	1
Typhimuriumvar.copenhag-194	5	GEN-SMX-TCY-SXT-	1
Typhimuriumvar.copenhag-27	5	GEN-SMX-TCY-SXT-	1
Typhimuriumvar.copenhag-104	5	KAN-STR-SMX-TCY-SXT-	3

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Typhimuriumvar.copenhag-110	4	AMP-CHL-SMX-TCY-	1
Typhimurium-110	4	AMP-GEN-STR-SMX-	1
Enteritidis-29	4	AMP-KAN-STR-TCY-	3
Typhimuriumvar.copenhag-302	4	AMP-STR-SMX-TCY-	3
Typhimurium-104	4	AMP-STR-SMX-TCY-	1
Berta-	4	AMP-SMX-TCY-SXT-	1
Derby-	4	CHL-STR-SMX-TCY-	1
Typhimuriumvar.copenhag-208	4	GEN-SMX-TCY-SXT-	1
California-	4	KAN-STR-SMX-TCY-	1
Agona-	4	KAN-SMX-TCY-SXT-	1
Agona-	4	STR-SMX-TCY-SXT-	1
Typhimuriumvar.copenhag-194	3	AMP-STR-SXT-	1
Heidelberg-22	3	AMP-STR-TCY-	1
Anatum-	3	AMP-STR-TCY-	1
Heidelberg-8	3	CHL-SMX-TCY-	1
Typhimuriumvar.copenhag-27	3	GEN-SMX-TCY-	1
Oranienburg-	3	GEN-SMX-TCY-	1
Agona-	3	KAN-SMX-TCY-	2
Typhimurium-104	3	STR-SMX-SXT-	1
Derby-	3	STR-SMX-TCY-	15
Typhimurium var Copenhag-	3	STR-SMX-TCY-	2
Typhimurium var Copenhag-194	3	STR-SMX-TCY-	2
Typhimurium-	3	STR-SMX-TCY-	1
Typhimurium-194	3	STR-SMX-TCY-	1
Schwarzengrund-	3	STR-SMX-TCY-	1
Typhimurium-208	3	SMX-TCY-SXT-	2
Typhimurium-208	2	AMP-SMX-	1
Typhimurium-104	2	AMP-SMX-	1
Typhimurium-104	2	STR-SMX-	2
Salmonella spp.	2	STR-TCY-	1
Mbandaka-	2	STR-TCY-	1
Heidelberg-8	2	STR-TCY-	1
Heidelberg-	2	STR-TCY-	1
Typhimurium-104	2	SMX-SXT-	3
Typhimurium-12	2	SMX-SXT-	1
Typhimurium-66	2	SMX-SXT-	1
Agona-	2	SMX-TCY-	2
Typhimuriumvar.copenhag-108	1	KAN-	1
Typhimurium-108	1	SMX-	1
Typhimuriumvar.copenhag-186	1	SMX-	1
Typhimuriumvar.copenhag-302	1	SMX-	1
Derby-	1	TCY-	3
Typhimuriumvar.copenhag-108	1	TCY-	1
Typhimuriumvar.copenhag-104	1	TCY-	1
Heidelberg-8	1	TCY-	1
Heidelberg-22	1	TCY-	1
Cerro-	1	TCY-	1

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
I:4,12:i:--	1	TCY-	1
Salmonella spp.	0	None	7
Typhimurium-104	0	None	7
Typhimurium-108	0	None	7
Derby-	0	None	7
Mbandaka-	0	None	5
Brandenburg-	0	None	5
Typhimuriumvar.copenhag-12	0	None	4
Infantis-	0	None	4
Typhimurium-	0	None	3
Typhimurium-10	0	None	3
Typhimurium-27	0	None	3
Typhimuriumvar.copenhag-27	0	None	3
Krefeld-	0	None	3
Kentucky-	0	None	3
Berta-	0	None	3
Agona-	0	None	3
Typhimurium-186	0	None	2
Typhimuriumvar.copenhag-108	0	None	2
Typhimurium var.Copenhag-	0	None	2
Heidelberg-	0	None	2
Worthington-	0	None	1
Typhimurium-208	0	None	1
Typhimurium-12	0	None	1
Typhimurium-170	0	None	1
Typhimurium-110	0	None	1
Thompson-	0	None	1
Typhimurium var. Copenhag-186	0	None	1
Typhimurium var. Copenhag-170	0	None	1
Typhimurium var. Copenhag-208	0	None	1
Typhimurium var. Copenhag-2	0	None	1
Muenster-	0	None	1
Muenchen-	0	None	1
Meleagridis-	0	None	1
Livingstone-	0	None	1
Litchfield-	0	None	1
Havana-	0	None	1
Anatum-	0	None	1
Orion-	0	None	1
IIIb:61:-:1,5-	0	None	1
I:ROUGH-O:-:--	0	None	1
I:6,7:z10:--	0	None	1
I:6,7,14:-:l,w-	0	None	1
I:4,12:a:--	0	None	1
I:4,12:-:--	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.14. Distribution of MICs and resistance in ***Salmonella*** from **chicken** and **turkey** clinical isolates; *Passive Surveillance*

*	Antimicrobial	Animal species	n	%R	Distribution (%) of MICs																
					<=0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
I	Ceftiofur	Chicken	146	2.7						69.2	27.4	0.7			2.7						
		Turkey	87	5.7						56.3	34.5	2.3	1.1		2.3	3.4					
	Ceftriaxone	Chicken	146	0.0					97.3				0.7	0.7	0.7	0.7					
		Turkey	87	1.1					93.1				1.1			4.6	1.1				
	Ciprofloxacin	Chicken	146	0.0	81.5	17.8	0.7														
		Turkey	87	0.0	90.8	4.6		1.1	3.4												
	Imipenem	Chicken	96	0.0					97.9	2.1											
		Turkey	52	0.0					98.1	1.9											
II	Amikacin	Chicken	146	0.0						2.1	25.3	6.2	65.8	0.7							
		Turkey	87	0.0						3.4	16.1	17.2	63.2								
	Amoxicillin- Clavulanic Acid	Chicken	146	4.1							68.5	11.6		5.5	10.3	1.4	2.7				
		Turkey	87	6.9						1.1	58.6	9.2	1.1	4.6	18.4	1.1	5.7				
	Gentamicin	Chicken	146	7.5					45.9	38.4	7.5			0.7	3.4	4.1					
		Turkey	87	28.7					36.8	27.6	2.3	3.4	1.1		4.6	24.1					
	Kanamycin	Chicken	146	7.5										30.1	62.3		0.7	6.8			
		Turkey	87	24.1										27.6	47.1	1.1	10.3	13.8			
	Nalidixic Acid	Chicken	146	0.0									70.5	28.8	0.7						
		Turkey	87	3.4									71.3	25.3			1.1	2.3			
	Streptomycin	Chicken	146	30.1												69.9	17.1	13.0			
		Turkey	87	39.1												60.9	11.5	27.6			
	Trimethoprim-Sulfamethoxazole	Chicken	146	0.0				78.1	19.9	2.1											
		Turkey	87	2.3				70.1	27.6					2.3							
III	Ampicillin	Chicken	146	19.2							18.5	55.5	6.2	0.7			19.2				
		Turkey	87	31.0							16.1	44.8	8.0				31.0				
	Apramycin	Chicken	96	0.0								47.9	42.7	8.3	1.0						
		Turkey	52	0.0								48.1	44.2	7.7							
	Cefoxitin	Chicken	146	0.7							0.7	26.7	64.4	4.1	2.1	2.1					
		Turkey	87	3.4							3.4	11.5	60.9	17.2	1.1	2.3	3.4				
	Cephalothin	Chicken	146	6.2								58.2	24.0	6.8	4.8	2.7	3.4				
		Turkey	87	23.0								35.6	29.9	6.9	4.6	13.8	9.2				
	Chloramphenicol	Chicken	146	4.1									43.2	52.7			4.1				
		Turkey	87	1.1									43.7	52.9	2.3		1.1				
	Sulfamethoxazole	Chicken	146	21.9											28.1			50.0		21.9	
		Turkey	87	25.3											21.8	9.2		43.7		25.3	
	Tetracycline	Chicken	146	30.1									24.0	45.9	1.4	20.5	8.2				
		Turkey	87	35.6									23.0	41.4		19.5	16.1				

*Note: * Ranking of human importance, VDD; The white fields denote the ranges tested for each antimicrobial. The solid area refers to the 2002 antimicrobial panel and the light shaded area refers to the 2001 antimicrobial panel. The dark shaded area refers to an overlap of both the 2002 and 2001 antimicrobial panels; vertical bars denote breakpoints.*

Table A.4.15. Resistance patterns in clinical ***Salmonella*** isolates from **chicken;** *Passive Surveillance* (N=146)

Pattern	% (n)	Pattern	% (n)
None	56.85 (83)	ACSSuT-A3C-	0.68 (1)
STR-TCY-	6.16 (9)	AKSSuT-A3C-GEN-	0.68 (1)
TCY-	6.16 (9)	AMC-AMP-TIO-CEP-STR-TCY-	0.68 (1)
STR-SMX-TCY-	4.79 (7)	AMC-AMP-CEP-	0.68 (1)
ACSSuT-	2.74 (4)	AMC-AMP-CEP-STR-TCY-	0.68 (1)
AKSSuT-	2.74 (4)	AMP-GEN-SMX-	0.68 (1)
GEN-STR-SMX-	2.74 (4)	AMP-KAN-STR-TCY-	0.68 (1)
AMP-CEP-	2.05 (3)	AMP-STR-	0.68 (1)
AMP-GEN-STR-SMX-	2.05 (3)	AMP-STR-SMX-	0.68 (1)
AMP-	1.37 (2)	GEN-STR-SMX-TCY-	0.68 (1)
AMP-KAN-SMX-TCY-	1.37 (2)	KAN-STR-SMX-	0.68 (1)
STR-	1.37 (2)	KAN-STR-TCY-	0.68 (1)
ACKSSuT-A3C-GEN-	0.68 (1)	SMX-TCY-	0.68 (1)

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic acid, Cefoxitin, Ceftiofur and Cephalothin.

Table A.4.16. Serovars, phagetypes, and resistance patterns of clinical ***Salmonella*** isolates from **chicken**; *Passive Surveillance* (N=146)

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Heidelberg-	11	ACKSSuT-A3C-GEN-	1
Bredeney-	10	AKSSuT-A3C-GEN-	1
Heidelberg-6	9	ACSSuT-A3C-	1
Hadar-	6	AMC-AMP-TIO-CEP-STR-TET-	1
Typhimuriumvar.copenhag-104	5	ACSSuT-	2
Salmonella-302	5	ACSSuT-	1
Typhimurium-104	5	ACSSuT-	1
Typhimurium-	5	AKSSuT-	2
Typhimuriumvar.copenhag-208	5	AKSSuT-	2
Heidelberg-32	5	AMC-AMP-CEP-STR-TCY-	1
Heidelberg-19	4	AMP-GEN-STR-SMX-	2
Salmonella spp.	4	AMP-GEN-STR-SMX-	1
Heidelberg-	4	AMP-KAN-STR-TCY-	1
Typhimurium-	4	AMP-KAN-SMX-TCY-	1
Typhimuriumvar.copenhag-208	4	AMP-KAN-SMX-TCY-	1
Typhimurium-2	4	GEN-STR-SMX-TCY-	1
Heidelberg-5	3	AMC-AMP-CEP-	1
Heidelberg-	3	AMP-GEN-SMX-	1
Heidelberg-	3	AMP-STR-SMX-	1
Salmonella spp.	3	GEN-STR-SMX-	1
Heidelberg-19	3	GEN-STR-SMX-	1
Heidelberg-	3	GEN-STR-SMX-	1
Heidelberg-5	3	GEN-STR-SMX-	1
Heidelberg-29	3	KAN-STR-SMX-	1
Heidelberg-	3	KAN-STR-TCY-	1
Schwarzengrund-	3	STR-SMX-TCY-	6
Salmonella spp.	3	STR-SMX-TCY-	1
Heidelberg-19	2	AMP-CEP-	2
Heidelberg-17	2	AMP-CEP-	1
Heidelberg-29	2	AMP-STR-	1
Hadar-	2	STR-TCY-	7

Serovar and phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Salmonella spp.	2	STR-TCY-	1
Heidelberg-35	2	STR-TCY-	1
Kentucky-	2	SMX-TCY-	1
Heidelberg-	1	AMP-	2
Heidelberg-19	1	STR-	1
Heidelberg-	1	STR-	1
Putten-	1	TCY-	6
Indiana-	1	TCY-	1
Heidelberg-8	1	TCY-	1
Heidelberg-29	1	TCY-	1
Heidelberg-	0	None	20
Typhimurium-2	0	None	9
Heidelberg-19	0	None	7
Enteritidis-8	0	None	6
Salmonella spp.	0	None	4
Senftenberg-	0	None	4
Heidelberg 20	0	None	4
Enteritidis-28	0	None	4
Typhimurium-107	0	None	3
Typhimurium-	0	None	2
Kentucky-	0	None	2
Heidelberg-41	0	None	2
Typhimurium-22	0	None	1
Typhimurium-170	0	None	1
Thompson-	0	None	1
Muenchen-	0	None	1
Mbandaka-	0	None	1
Heidelberg-35	0	None	1
Heidelberg-17	0	None	1
Heidelberg-11	0	None	1
Heidelberg-47	0	None	1
Heidelberg-6	0	None	1
Heidelberg-13	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.17. Most frequent serovars, phagetypes, resistance patterns of clinical ***Salmonella*** isolates from **turkey**; *Passive Surveillance* (n=87)

Serovar and Phagetype	Number of antimicrobials in resistance pattern	Pattern	Number of isolates
Bredeney-	11	AKSSuT-A3C-CRO-GEN-	1
Bredeney-	10	AKSSuT-A3C-GEN-	4
Montevideo-	8	AKSSuT-AMC-CEP-GEN-	1
Muenster-	8	AKSSuT-CEP-GEN-NAL-	1
Typhimurium-194	7	AKSSuT-GEN-SXT-	1
Heidelberg-	6	AKSSuT-GEN-	1
Bredeney-	6	AKSSuT-GEN-	1
Anatum-	6	AMP-CEP-STR-SUL-TCY-SXT-	1
Heidelberg-32	5	ACSSuT-	1
Senftenberg-	5	AMP-CEP-GEN-KAN-STR-	3
Senftenberg-	5	GEN-KAN-NAL-STR-SMX-	1
Tennessee-	5	GEN-KAN-STR-SMX-TCY-	1
Montevideo-	5	GEN-KAN-STR-SMX-TCY-	1
Heidelberg-8	5	GEN-KAN-STR-SMX-TCY-	1
Senftenberg-	4	AMP-CEP-KAN-STR-	1
Senftenberg-	3	AMP-CEP-GEN-	2
Senftenberg-	3	AMP-CEP-KAN-	1
Senftenberg-	3	AMP-CEP-STR-	1
Senftenberg-	3	GEN-KAN-STR-	1
Heidelberg-	3	GEN-STR-SMX-	1
Heidelberg-47	3	GEN-STR-SMX-	1
Heidelberg-29	3	GEN-STR-SMX-	1
Berta-	3	GEN-STR-SMX-	1
Schwarzengrund-	3	STR-SMX-TCY-	2
Senftenberg-	2	AMP-CEP-	3
Saintpaul-	2	AMP-CEP-	1
Muenster-	2	AMP-STR-	1
Senftenberg-	2	KAN-STR-	1
Hadar-	2	STR-TCY-	2
Typhimurium-193	2	STR-TCY-	1
Mbandaka-	2	STR-TCY-	1
Heidelberg-6	1	AMP-	2
Senftenberg-	1	GEN-	1
Senftenberg-	1	NAL-	1
Heidelberg-32	1	TCY-	7
Heidelberg-	1	TCY-	2
Agona-	1	TCY-	1
Senftenberg-	0	None	4
Muenster-	0	None	4
Heidelberg-	0	None	4
Heidelberg-47	0	None	4
Salmonella spp.	0	None	2
Newport-	0	None	2
Heidelberg-13	0	None	2
Heidelberg-29	0	None	2
Heidelberg-6	0	None	2
Saint Paul	0	None	1
Typhimurium var Copenhagen	0	None	1
Muenchen-	0	None	1
Heidelberg-26	0	None	1
Brandenburg-	0	None	1
Agona-	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

Table A.4.18. Serovars, phagetypes, and resistance patterns in ***Salmonella*** isolates from **feed and rendered ingredients**; *Passive Surveillance* (n=65)

Serovar and phagetype	Number of antimicrobials in resistance pattern	Patterns	Number of Isolates
Newport	10	ACSSuT-A3C-SXT-	1
Typhimurium 108	9	ACSSuT-A3C	1
Derby	3	STR-SMX-TCY-	1
Mbandaka	2	STR-TCY-	3
Hadar	2	STR-TCY-	1
Tennessee	1	STR-	1
Salmonella spp.	0	None	11
Senftenberg	0	None	5
Tennessee	0	None	5
Cubana	0	None	4
Montevideo	0	None	4
Orionvar15-	0	None	4
Brandenburg	0	None	3
Livingstone	0	None	3
Oranienburg	0	None	3
Molade	0	None	2
Agona	0	None	1
Anatum	0	None	1
Cerro	0	None	1
Havana	0	None	1
I:19: :	0	None	1
I:40: :enx	0	None	1
I:ROUGH O: :	0	None	1
Johannesburg	0	None	1
Kentucky	0	None	1
Mbandaka	0	None	1
Meleagridis	0	None	1
Ohio	0	None	1
Putten	0	None	1

Note: ACSSuT=Resistant to Ampicillin, Chloramphenicol, Streptomycin, Sulfamethoxazole and Tetracycline; AKSSuT= Resistant to Ampicillin, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; ACKSSuT= Resistant to Ampicillin, Chloramphenicol, Kanamycin, Streptomycin, Sulfamethoxazole and Tetracycline; A3C=Resistant to Amoxicillin-Clavulanic Acid, Cefoxitin, Ceftiofur and Cephalothin; numbers after Typhimurium, Heidelberg and Enteritidis indicate the phagetype pattern.

A.5. Antimicrobial Use - Animal

Monitoring antimicrobial use in animal health and production has been identified by a number of organizations including the WHO, OIE and the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, as an essential component of the effort to control AMR in the bacteria affecting humans and animals. The purpose of a national antimicrobial use monitoring system for agriculture and veterinary medicine is to provide baseline data on usage in order to: facilitate the interpretation of trends in AMR monitored in humans, animals, food and the environment; evaluate the need for and effectiveness of interventions for the control of AMR including education, prudent use guidelines, clinical practice guidelines and on-farm management strategies; contribute to qualitative and quantitative risk assessments; facilitate the (re-) evaluation of submissions of antimicrobial drugs for regulatory approval. The distribution of antimicrobials from manufacturers/importers to end-users is complex and governed by legislation at both the federal and provincial level (Figure A.5.1). The development of a credible, timely and accurate antimicrobial use monitoring system for Canada will require collaboration between government agencies, the animal health and animal nutrition industries, veterinarians and producers.

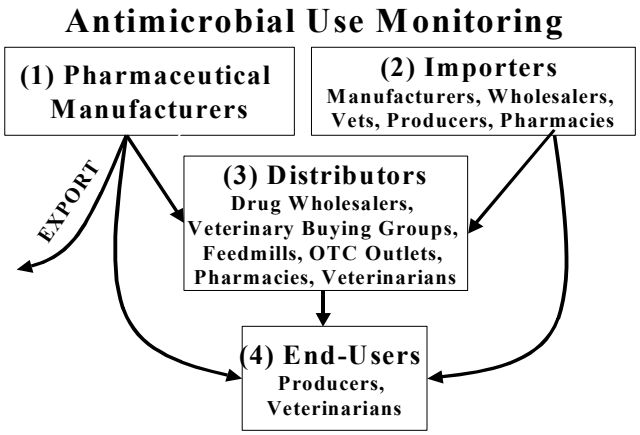


Figure A.5.1. Distribution system for antimicrobials used in livestock

A.6. Antimicrobial Use - Human

Table A.6.1. Systemic antimicrobials dispensed by selected pharmacies in Canada, April 2000-March 2001

ATC Group	Therapeutic group	Total Kg Active Ingredient	Total No. DDD	DDD / 1,000 inhabitant-days***
J01AA	Tetracyclines	13827	47,101,500	4.301
J01B	Amphenicols	1	202	0.000
J01CA	Penicillins with extended spectrum	63512	62,768,729	5.731
J01CE	Beta-lactamase sensitive penicillins	14453	7,212,678	0.659
J01CF	Beta-lactamase resistant penicillins	8113	4,056,404	0.370
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	22	1,572	0.000
J01DA	Cephalosporins and related substances	28320	24,857,454	2.270
	First Generation Cephalosporins	*16943*	*8456521*	*0.772*
	Second Generation Cephalosporins	*10924*	*15307642*	*1.398*
	Third Generation Cephalosporins	*453*	*1093290*	*0.100*
J01DH	Carbapenems	1	289	0.000
J01EA	Trimethoprim and derivatives	318	795,093	0.073
J01EB	Short-acting sulfonamides	87	73,216	0.007
J01EC	Intermediate-acting sulfonamides*	21	33,596	0.003
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	24258	12,212,458	1.115
J01FA	Macrolides	26608	42,318,937	3.864
J01FF	Lincosamides	3446	2,859,167	0.261
J01GA	Streptomycin	0	265	0.000
J01GB	Other aminoglycosides	74	279,726	0.026
J01MA	Fluoroquinolones	17809	24,861,214	2.270
J01MB	Other quinolones	78	19,539	0.002
J01RA	Combinations of antibacterials	668	327,260	0.030
J01XA	Glycopeptides	47	23,315	0.002
J01XC	Steroid antibacterials	38	25,696	0.002
J01XE	Nitrofuran derivatives	944	4,720,059	0.431
J01XD	Imidazoles	34	22,418	0.002
J01XX	Other antibacterials**	458	166,594	0.015
J01	**Antibacterials for systemic use (Total)**	**203136**	**234,737,379**	**21.432**

*Note: * 1106 units of sulfamethoxazole were dispensed but are not included in this calculation because the product strength was unknown; ** 100254 units of methenamine were dispensed but are not included in this calculation because the product strength was unknown; *** based on 2001 census; To calculate the number of DDDs per 1000 inhabitant days, the division factor was determined by using the population for Canada from the 2001 census; formula: Number of days in fiscal year x (2001 population of Canada / 1,000 inhabitants) Source: IMS Health CompuScript audit.*

Table A.6.2. Most common ICD-9 diagnostic classes and codes for which systemic antibacterials were recommended by a sample of 652 physicians* in Canada, April 2000-March 2001

ATC Group	Therapeutic group	ICD-9 Diagnostic Class		Specific ICD-9 Diagnostic Code			Total no. patient visits in which a drug in this therapeutic group was recommended, regardless of diagnosis	%
		Name	No. patient visits in which drug from this diagnostic class was recommended (% of no. visits in which drug in this therapeutic group was recommended)	Code	Description	No. patient visits		
J01AA	Tetracyclines	Diseases of the skin and subcutaneous tissue	230 (71%)	706.5	Diseases of sebaceous glands (no description available)	56	325	5%
J01B	Amphenicols	No information available						
J01CA	Penicillins with extended spectrum	Diseases of the respiratory system	927 (57%)	462.0	Acute pharyngitis	157	1635	24%
		Diseases of the nervous system and sense organs	344 (21%)	382.9	Unspecified otitis media	323		
J01CE	Beta-lactamase sensitive penicillins	Diseases of the respiratory system	134 (62%)	462.0	Acute pharyngitis	65	215	3%
J01CF	Beta-lactamase resistant penicillins	Diseases of the skin and subcutaneous tissue	121 (61%)	682.9	Other cellulitis and abscess, unspecified site	20	199	3%
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	Diseases of the skin and subcutaneous tissue	61 (28%)	682.3	Other cellulitis and abscess, upper arm and forearm	2	221	3%
J01DA	Cephalosporins and related substances	Diseases of the respiratory system	528 (46%)	461.9	Acute sinusitis, unspecified	108	1145	17%
J01DH	Carbapenems	Diseases of the respiratory system	2 (33%)	486.0	Pneumonia, organism unspecified	1	6	0%
				466.0	Acute bronchitis	1		
J01EA	Trimethoprim and derivatives	Diseases of the genitourinary system	14 (67%)	595.9	Cystitis, unspecified	2	21	0%
				596.8	Other specified disorders of bladder	2		
				599.0	Urinary tract infection, site not specified	2		
				599.7	Hematuria	2		
		Neoplasms	5 (24%)	188.9	Bladder, part unspecified	4		
J01EB	Short-acting sulfonamides	No information available						
J01EC	Intermediate-acting sulfonamides	Diseases of the musculoskeletal system and connective tissue	1 (100%)	714.9	Rheumatoid arthritis and other inflammatory polyarthropathies, unspecified	1	1	0%
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	Diseases of the genitourinary system	230 (57%)	599.0	Urinary tract infection, site not specified	118	406	6%
J01FA	Macrolides	Diseases of the respiratory system	1093 (72%)	466.0	Acute bronchitis	349	1509	22%

*Note: * sampled physicians included general practitioners and the following specialists: internists, cardiologists, gastroenterologists, neurologists, psychiatrists, respirologists, rheumatologists, obstetricians/gynecologists, ear, nose, throat specialists, ophthalmologists, general surgeons, orthopedic surgeons, pediatricians, urologists, and dermatologists; Source: IMS Health CDTI audit.*

ATC Group	Therapeutic group	ICD-9 Diagnostic Class		Specific ICD-9 Diagnostic Code			Total no. patient visits in which a drug in this therapeutic group was recommended, regardless of diagnosis	%
		Name	No. patient visits in which drug from this diagnostic class was recommended (% of no. visits in which drug in this therapeutic group was recommended)	Code	Description	No. patient visits		
J01FF	Lincosamides	Diseases of the respiratory system	18 (26%)	486.0	Pneumonia, organism unspecified	5	68	1%
J01GA	Streptomycin	No information available						
J01GB	Other aminoglycosides	Infectious and parasitic diseases	3 (11%)	038.9	Unspecified septicemia	3	28	0%
		Diseases of the genitourinary system	7 (25%)	599.0	Unspecified disorder of urethra and urinary tract	3		
J01MA	Fluoroquinolones	Diseases of the genitourinary system	378 (45%)	599.0	Unspecified disorder of urethra and urinary tract	113	849	12%
J01MB	Other quinolones	Diseases of the genitourinary system	1 (100%)	599.0	Unspecified disorder of urethra and urinary tract	1	1	0%
J01RA	Combinations of antibacterials	Diseases of the nervous system and sense organs	18 (56%)	382.9	Unspecified otitis media	16	32	0%
J01XA	Glycopeptides	Infectious and parasitic diseases	5 (28%)	038.1	Staphylococcal septicemia, unspecified	3	18	0%
		Injury and poisoning	6 (33%)	996.6	Complications peculiar to certain specified procedures-Infection and inflammatory reaction due to internal prosthetic device, implant, and graft	3		
J01XC	Steroid antibacterials	Diseases of the skin and subcutaneous tissue	11 (61%)	681.9	Cellulitis and abscess of finger and toe, unspecified digit	2	18	0%
				706.2	Diseases of sebaceous glands, Sebaceous cyst	2		
		Injury and poisoning	5 (28%)	892.0	Open wound of foot except toe(s) alone, without mention of complication	2		
J01XD	Imidazoles	Diseases of the digestive system	12 (48%)	556.0	Ulcerative (chronic) enterocolitis	3	25	0%
		Diseases of the respiratory system	4 (16%)	486.0	Pneumonia, organism unspecified	3		
J01XE	Nitrofuran derivatives	Diseases of the genitourinary system	157 (97%)	599.0	Unspecified disorder of urethra and urinary tract	89	162	2%
J01XX	Other antibacterials	Diseases of the genitourinary system	13 (100%)	599.0	Unspecified disorder of urethra and urinary tract	9	13	0%
J01					**Antibacterials for systemic use**		**6897**	**100%**

*Note: * sampled physicians included general practitioners and the following specialists: internists, cardiologists, gastroenterologists, neurologists, psychiatrists, respirologists, rheumatologists, obstetricians/gynecologists, ear, nose, throat specialists, ophthalmologists, general surgeons, orthopedic surgeons, pediatricians, urologists, and dermatologists; Source: IMS Health CDTI audit.*

Appendix B - Methods

B.1. Human Antimicrobial Resistance

Antimicrobial Resistance Data Collection & Analysis

In May 2001, all provincial laboratory directors participated in a survey designed to document current provincial laboratory practices in relation to AMR testing of enteric pathogens. This study identified five provincial laboratories that routinely received and tested all, or a defined subset of, enteric pathogens for AMR and that were interested in participating in additional AMR studies: Alberta, Newfoundland and Labrador, Ontario, Prince Edward Island, and Saskatchewan. Across Canada there are 536 laboratories licensed to perform microbiological testing on stool specimens. Of these laboratories, 129 are located in the five provinces that participated in the retrospective *Salmonella* and *Shigella* AMR study. Within these five provinces there were 108 hospital based laboratories and 21 private laboratories. Although laboratory notification of reportable diseases is mandatory and captured in the NNDS dataset, forwarding *Salmonella* and *Shigella* isolates to the province is voluntary and passive in nature; the proportion of isolates varies by pathogen and laboratory. Figure B.1.1 summarises the frequency with which the hospital-based and private laboratories in each provide send all their *Salmonella* and *Shigella* isolates to the provincial public health reference laboratory for testing.

Overall, the five provincial laboratories sent FWZID information on 10195 isolates. After removing 1024 isolates from the data that were missing AMR results, not human in origin (either animal or environmental samples), of unknown origin, or missing data on genus, 9171 isolates remained in the dataset. Table B.1.1 summarizes the information included in the dataset. Pathogen names were standardized, all minimum inhibitory concentrations (MICs) and resistance profiles were interpreted in accordance with National Committee on Clinical Laboratory Standards (NCCLS) guidelines (January 2001). The data was analyzed using SAS® V8.0, conducting univariate and bivariate analyses. Significance of relationships was determined using Student's t-tests and simple odds ratios with a p-value of ≤0.05 defined as significant.

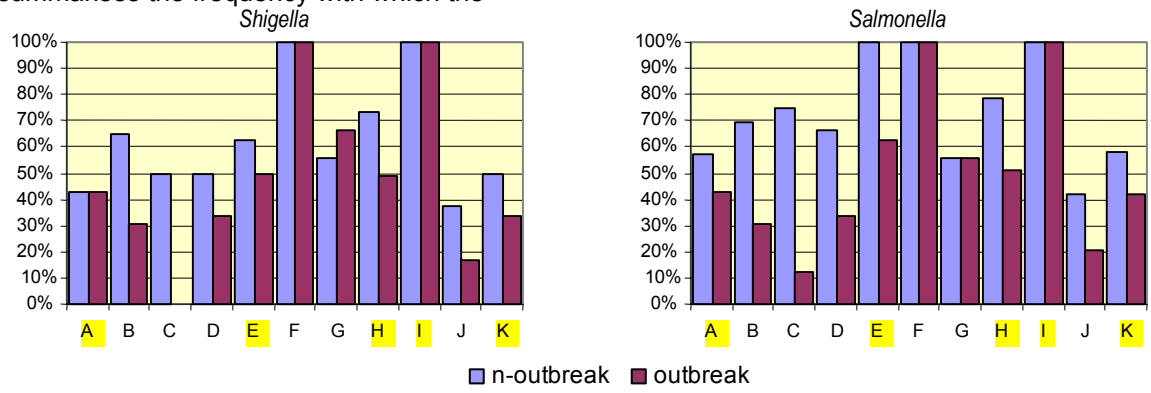


Figure B.1.1. Laboratories sending all isolates (non-outbreak and outbreak) to provincial public health laboratories; comparison between provinces. (Denoted A – K). Provincial laboratories participating in the Retrospective AMR study are highlighted

Source: *NSAGI Laboratory Survey. Report of the 2001 Canadian Laboratory Survey; National Studies on Acute Gastrointestinal Illness. Health Canada, April 2002. Available electronically at http://www.hc-sc.gc.ca/pphb-dgspsp/nsagi-enmga/lab_e.html)*

Table B.1.1. Description of provincial data

Variable	Alberta	Newfoundland	Ontario	Prince Edward Island	Saskatchewan
Number of records provided [a]	3107	75	4905	107	977
Years provided	1993-2001 [b]	1999-2001	1997-2000	1996-2001	1996-2001
Date isolate received by laboratory	X	X	X	X	X
Patient age	X	X	X	X	X
Patient gender	X	X	X	X	X
Location of isolation (name of hospital, lab, referred isolate)	X	X	X	X	
Patient city and province of residence	X	X	X	X	X
Source of specimen (i.e. stool, blood, tissue, organism)	X	X	X	X	
Travel reported by patient (location)	X				
Outbreak related (yes/no) [c]	X				
Serotype	X	X	X	X	X
Phage type [c]	X		X	X	

Note: *X = provided data; [a] Number of records is the number of isolates, not necessarily the number of people who submitted an isolate; [b] Data was not available for all months of each year; [c] Not provided for all isolates*

Laboratory Testing Methodologies

Bacterial Isolation Methods

The diagnostic submissions were examined according to the standard procedures used by the participating laboratories. Culture methods likely varied from one laboratory to another.

Antimicrobial Susceptibility Testing Methods

Antimicrobial susceptibility testing methods varied from province to province. Alberta used the VITEK™ system, Newfoundland used the disk diffusion method, and Ontario used the agar dilution method. The Microscan™ system was used in Prince Edward Island and Saskatchewan. The VITEK™ and Microscan™ system are automated microbroth dilution systems capable of performing susceptibility testing of most rapidly growing gram-positive and gram-negative aerobic bacteria. The disk diffusion method involves diffusion of an antimicrobial agent of a specified concentration from disks, tablets or strips, into solid agar seeded with a standardised bacterial inoculum. The diffusion of the antimicrobial into the agar results in an antimicrobial concentration gradient. When the concentration becomes so dilute that it can no longer inhibit the growth of the bacterium, a zone of inhibition is formed. The edge of the zone correlates with the minimum inhibitory concentration (MIC). The agar dilution method involves the incorporation of an antimicrobial agent into an agar medium in a geometrical progression of concentration, followed by the application of a defined bacterial inoculum to the agar surface. Results are expressed in MIC.

Table B.1.2. Antimicrobials tested by class and province, 1993-2001

Antimicrobial	Alberta	Newfoundland	Ontario	Prince Edward Island	Saskatchewan
Aminoglycosides					
Amikacin	X		X	X	X
Gentamicin	X	X	X	X	X
Netilmicin				X	
Streptomycin			X		
Tobramycin	X		X	X	X
Total # antimicrobials tested in class by province	**3**	**1**	**4**	**4**	**3**
Penicillins					
Amoxicillin/K. Clavulanate	X			X	X
Ampicillin	X	X	X	X	X
Ampicillin/Sulbactam				X	X
Carbenicillin	X				X
Mezlocillin				X	
Piperacillin	X		X	X	X
Pip/Tazobactam	X		X		X
Ticarcillin	X*		X	X	X
Ticarcillin/K. Clavulanate				X	X
Total # antimicrobials tested in class by province	**6**	**1**	**4**	**7**	**8**
Cephalosporins					
Cefamandole	X*				X
Cefazolin	X			X	X
Cefaperazone				X	
Cefotaxime	X		X	X	X
Cefotetan				X	
Cefoxitin	X		X	X	X
Cefpodoxime	X			X	
Ceftazidime	X		X	X	X
Ceftizoxime				X	
Ceftriaxone	X			X	X
Cefuroxime (oral)	X			X	
Cefuroxime (parenteral)	X				X
Cefonicid	X				
Cefixime	X				X
Cefepime	X*				X
Cephalothin	X	X	X	X	X
Total # antimicrobials tested in class by province	**13**	**1**	**4**	**11**	**10**
Other β-Lactams					
Aztreonam				X	X
Imipenem	X			X	X
Loracarbef					X
Meropenem				X	X
Total # antimicrobials tested in class by province	**1**	**0**	**0**	**3**	**4**

Antimicrobial	Alberta	Newfoundland	Ontario	Prince Edward Island	Saskatchewan
Folate Pathway Inhibitors					
Sulfamethoxazole			X	X	X
Trimethoprim		X		X	X
Trimethoprim/Sulfamethoxazole	X	X	X	X	X
Total # antimicrobials tested in class by province	**1**	**2**	**2**	**3**	**3**
Quinolones					
Ciprofloxacin	X		X	X	X
Levofloxacin				X	X
Lomafloxacin				X	X
Nalidixic Acid	X				X
Norfloxacin	X	X		X	X
Ofloxacin	X			X	X
Total # antimicrobials tested in class by province	**4**	**1**	**1**	**5**	**6**
Tetracyclines					
Tetracycline	X		X	X	X
Total # antimicrobials tested in class by province	**1**	**0**	**1**	**1**	**1**
Other					
Chloramphenicol	X		X		X
Nitrofurantoin	X	X		X	X
Total no. antimicrobials tested in class by province	**2**	**1**	**1**	**1**	**2**
Total no. antimicrobials tested overall by province	**31**	**7**	**17**	**35**	**37**
Total no. antimicrobials for which isolates were tested (range, mean)	**1-24, 14**	**7, 7**	**10-14, 13**	**29-32, 32**	**7-19, 13**

***Note**: *Province tested <5 isolates for these antimicrobials.*

B.2. Agri-Food Antimicrobial Resistance

CIPARS *Abattoir Surveillance* Sampling Design

The CIPARS Active *Abattoir Surveillance* aims to provide nationally representative and valid annual antimicrobial susceptibility data from bacteria isolated from animals entering the food chain. Initially, the program has targeted generic *E. coli* and *Salmonella* spp. from beef cattle, hogs, and broiler chicken. The unit of concern is the bacterial isolate tested for antimicrobial susceptibility to a panel of 16 antimicrobials. The bacteria of interest are sampled from the caecal content of slaughtered food-producing animals, as cecal contents most closely represent the farm of origin

The number of isolates expected to be yielded by the sampling is set at 150 per targeted bacterial species, for each of the three commodities, across Canada, and over a 12-month period. This number is a trade-off between acceptable statistical precision and affordable costs (Ravel, 2001). The actual number of specimens to be collected is derived for each commodity according to the expected caecal prevalence of the bacteria for this commodity, e.g. 1500 specimens have to be collected and submitted for bacterial isolation if the bacteria prevalence in the population is expected to be 10%.

The sampling design is based on an annual two-stage sampling of food animals in slaughterhouses, each commodity being handled separately. The first stage is a random selection of federally inspected slaughterhouses; the probability for an abattoir to be selected is proportional to its annual slaughter volume. Federally inspected abattoirs slaughter over 90% of all food-producing animals in Canada. The second stage is a systematic selection of animals on the slaughter line. The number of caecal specimens collected yearly, by each selected abattoir, is proportional to its slaughter volume amongst all participating slaughterhouses. In order for each abattoir to minimize shipping costs and for more efficient use of time, the annual total number of samples to be collected is divided by five

(for swine, divided by 10), leading to a given number of collection periods. Collection periods are uniformly distributed over the year, leading to an abattoir-specific schedule for collecting caecal contents. For a sampling week, the five caecal samples are collected within 12 to 36 hours, at the slaughterhouse's convenience, provided the five animals/samples come from different lots. Sampling from different lots is important to maximize diversity and avoid bias due to over-representation of particular producers. The uniform distribution of the collection periods over a 12-month course avoids any potential seasonal bias in bacteria prevalence and in the susceptibility test results.

CIPARS 2002 *Abattoir Surveillance* Data Collection

Fifty-one federally inspected slaughter plants (20 poultry plants, 20 swine plants, and 11 beef plants), from across Canada, were randomly selected to participate in the first developmental phase of the abattoir component of CIPARS. As stated above, the number of samples required was based on the requirement for 150 *Salmonella* and 150 generic *E. coli* isolates per commodity and the expected prevalence of *Salmonella* and generic *E. coli* in each commodity. However, due to the very low expected prevalence of *Salmonella* in beef, the sample size for beef was based only on generating 150 *E. coli*. *Salmonella* isolation procedures were conducted on all beef samples received but only a small number of *Salmonella* were anticipated. Samples were taken according to a pre-determined protocol, with modifications to accommodate various line configurations in the different plants. Protocols were designed in order to avoid conflict with: current inspection methodology, plant specific HACCP/Food

Safety Enhancement Program, Health and Safety requirements, and industry's ability to salvage viscera. They were also designed to avoid situations of potential cross-contamination. The samples were collected by industry personnel under the guidance of the CFIA Veterinarian-in-Charge.

CIPARS 2002 *Passive Surveillance* Data Collection

The veterinary diagnostic isolates included in the passive veterinary component were received by the *Salmonella* Typing Laboratory at LFZ. These isolates came from veterinary diagnostic laboratories from across the country and the isolation methodology varies for each laboratory. Since the samples were submitted for diagnostic purposes, private practitioners and/or producers carry out the sample collection. Therefore, the sample collection methodology varies both between and within laboratories. Other *Salmonella* isolates were also received from various other sources such as inspection agencies or private laboratories, which also use different sampling techniques and isolation methods.

Data Analysis

All data from animal sources were integrated into a common database, and serotypes and phagetypes were standardized. Forty-two duplicate isolates from *Passive Surveillance* were excluded.

Values of MIC's outside of testing range were replaced by missing data (for example, an MIC of 2 for streptomycin was replaced by a missing value). The breakpoints used for the interpretation of susceptibility results (Table B.1.2) were those from the National Committee for Clinical Laboratory Standards (NCCLS) when established or from NARMS. In 2002, the range tested for amikacin did not include the breakpoint. If the MIC of amikacin was > 4 ug/ml, the sensitivity interpretation was set to a missing value. All analyses were performed using SAS® V8.01.

Bacterial Isolation Methods

Abattoir Surveillance (*Salmonella*)

The *Abattoir Surveillance* used a modification of the MFLP-75 method of the *Compendium of Analytical Methods, Health Protection Branch, Methods of Microbiological Analysis of Food, Government of Canada*. This method isolates motile and viable *Salmonella* from caecal content of broilers, swine and beef samples. The method was based on the capacity of *Salmonella* to multiply and be motile in Modified Semi-Solid Rappaport Vassiliadis (MSRV) media at a temperature of 42^0C. Porcine and bovine samples were mixed with a non-selective pre-enrichment broth, and 10 g of caecal content were mixed with 20 ml of buffered peptone water (BPW). In the same manner, avian caecal contents were weighed and BPW was added in a proportion of 1:2. The samples were incubated at 35^0C for 24 hours. Then a MSRV plate was inoculated with 0.1 ml of the pre-enrichment broth and was incubated at 42^0C for 24 to 72 hours. Suspect colonies were inoculated on MacConkey Agar (MAK) to screen for purity and transferred on to Triple Sugar Iron (TSI) and urea agar slants. Presumptive *Salmonella* isolates were verified by slide agglutination using Poly A-I & Vi *Salmonella* antiserum

Abattoir Surveillance (*E. coli*)

A drop of BPW aliquot prepared for the *Salmonella* isolation was inoculated on a MacConkey (MAC) agar and incubated at 35^0C for 18 to 24 hours. Suspect lactose fermenting colonies were screened for purity and transferred onto Luria-Bertani (LB) agar. Presumptive colonies were identified using Simmons citrate and indole test. All bacterial isolates from food animals were stored at -70^0C for potential future study.

Passive Surveillance (*Salmonella*)

Submitting laboratories isolated *Salmonella* according to their standard procedures, which varied from one laboratory to another. Nevertheless, most methods for examining products for the presence of *Salmonella* are

similar in principle and involve pre-enrichment, selective enrichment, differential and selective plating, and biochemical and serological confirmation of the selected isolates.

Antimicrobial Susceptibility Testing Methods

CIPARS 2002 used the Sensititre™ Automated Antimicrobial Susceptibility System (Trek™ Diagnostic Systems Ltd) for AMR testing. Sensititre™ is a commercially available broth microdilution technique using dehydrated antimicrobials in microtitre wells. Results are given in minimum inhibitory concentration (MIC). NARMS Sensititre™ susceptibility panels CMV6CNCD in 2001 and CMV7CNCD in 2002 were used. Wells were incubated aerobically at 37^0C for 18 hours. The MIC was defined as the lowest concentration of antimicrobial with no visible growth. The following strains were used for quality control: *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginose* ATCC 27853 and *Enterococcus faecalis* ATCC 29212.

Table B.2.1. Minimum inhibitory concentrations of antimicrobials tested for agri-food isolates

Surveillance Project	Antimicrobial	Breakpoint ug/ml	Range ug/ml
Abattoir, Passive 2002	Amikacin	>= 64	0.5-4
Passive 2001	Amikacin	>= 64	4-32
Abattoir, Passive 2002	Amoxicillin-Clavulanic Acid	>= 32/16	1-32
Passive 2001	Amoxicillin-Clavulanic Acid	>= 32/16	0.5-32
Abattoir, Passive 2002	Ampicillin	>= 32	1-32
Passive 2001	Ampicillin	>= 32	2-32
Passive 2001	Apramycin	>= 32	2-32
Abattoir, Passive 2002	Cefoxitin	>= 32	0.5-16
Passive 2001	Cefoxitin	>= 32	4-32
Abattoir, Passive 2001, Passive 2002	Ceftriaxone	>= 64	0.25-64
Abattoir, Passive 2002	Ceftiofur	>= 8	0.12-8
Passive 2001	Ceftiofur	>= 8	0.5-16
Abattoir, Passive 2001, Passive 2002	Cephalothin	>= 32	2-32
Abattoir, Passive 2002	Chloramphenicol	>= 32	2-32
Passive 2001	Chloramphenicol	>= 32	4-32
Abattoir, Passive 2001, Passive 2002	Ciprofloxacin	>= 4	0.015-4
Abattoir, Passive 2001, Passive 2002	Gentamicin	>= 16	0.25-16
Passive 2001	Imipenem	>= 16	0.25-8
Abattoir, Passive 2002	Kanamycin	>= 64	8-64
Passive 2001	Kanamycin	>= 64	16-64
Abattoir, Passive 2002	Nalidixic Acid	>= 32	0.5-32
Passive 2001	Nalidixic Acid	>= 32	4-64
Abattoir, Passive 2001, Passive 2002	Streptomycin	>=64	32-64
Abattoir, Passive 2002	Sulfamethoxazole	>= 512	16-512
Passive 2001	Sulfamethoxazole	>= 512	128-512
Abattoir, Passive 2002	Tetracycline	>= 16	4-32
Passive 2001	Tetracycline	>= 16	8-16
Abattoir, Passive 2001, Passive 2002	Trimethoprim-Sulfamethoxazole	>= 4/76	0.12-4

Note: The range for amikacin in 2002 did not include the breakpoint.

B.3. Human Antimicrobial Use Data Collection & Analysis

IMS Health compiles information on drug use across Canada via several audit programs. This report focuses on the IMS Health *CompuScript* and *Canadian Disease and Therapeutic Index* (*CDTI*) audits for fiscal year 2000-2001.

CompuScript

CompuScript tracks the number and size of prescriptions dispensed (not the number written) in Canada. Information includes drug name, form, strength, and therapeutic class. The sampling frame (or "universe") for this dataset consisted of approximately 6,974 pharmacies, including 4,904 chain stores (2,213 large and 2,691 small) and 2,070 independent stores (285 large and 1,785 small), which covers nearly all the pharmacies in Canada. IMS Health stratifies the "universe" by store size (based on purchase volumes), type (chain or independent), and region (10 provinces). The sample design requires approximately 1,373 stores; however, IMS Health utilizes more stores because they have a large sample base. In 2001, approximately 2,500 stores were used to create the estimates. From this sample, IMS Health calculates a projection factor by dividing the number of stores in the "universe" by the number of stores in the sample. The projection factor is used to extrapolate the number of prescriptions dispensed in the sample to that of the "universe" (6,974 pharmacies).

Canadian Disease and Therapeutic Index

CDTI is a quarterly profile designed to provide information about the patterns and treatments of disease encountered by office-based physicians. Every quarter, 652 physicians (specialists and general practitioners) from five regions (the Maritimes, Quebec, Ontario, the Prairies, and British Columbia) are surveyed. For the most part, physicians are consistent from quarter to quarter. These physicians are selected using a two-stage sampling process: first by region and specialty and second by each 48-hour period in the quarter. For four consecutive quarters, each physician maintains a practice diary describing information on every patient visit during a randomly selected 48-hour period. Information includes patient age and sex, reason for visit, diagnosis, name(s) of the drug(s) recommended or discussed, desired therapeutic effect(s), and the presence of concomitant therapies. We used *CDTI* data to determine the most common diagnoses, defined by the International Classification of Diseases Ninth Revision System (ICD-9), associated with antimicrobial use for the sampled physicians.

Data Analysis Methods

Data were analyzed using SAS®V8.0. Drug products were classified according to the Anatomical Therapeutic Chemical (ATC) classification system (2003 ATC DDD Index online at the WHO Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/atcddd/). For every product strength within each ATC group, the total number of drug units dispensed was calculated for the fiscal year. Data from IMS Health were compared to information in the Health Canada Drug Products Database (DPD) (http://www.hc-sc.gc.ca/hpb/drugs-dpd/index.html) and the Compendium of Pharmaceuticals and Specialties (CPS, 2001). If the strength provided by IMS Health did not correspond with information in the DPD and/or CPS, the data were adjusted to reflect product information provided by the latter resources. In some cases, no product strength was available from IMS Health. We omitted these drugs from calculations because we could not determine accurate DDDs. It was assumed that the drug units dispensed were based on the product formulations provided by IMS Health (Table B.3.1). Some products dispensed as ampules, vials, or minibags were available in various sizes, but no information on the size dispensed was available. In these cases, information from DPD and CPS was used to determine unit sizes, and the smallest size available was

used to calculate the most conservative estimate of the number of antimicrobial units dispensed.

To determine the Defined Daily Doses (DDDs) for each antimicrobial, the 2003 ATC DDD Index online at the WHO Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/atcddd/) was used. For antimicrobials not listed in the index or for those with unknown DDD values (e.g. trimethoprim-sulfamethoxazole and gatifloxacin), the WHO Collaborating Centre was contacted for additional guidance. For pediazole, the DDD for erythromycin ethyl succinate was used, and for trisulfaminic, the DDD for sulfamerazine was used to determine the total number of DDDs. Some drugs were not assigned DDDs and these were omitted from the calculations.

From the *CDTI* dataset, for each ATC therapeutic group in the J01 range (antibacterials for systemic use), the most common ICD-9 diagnostic class and the most common ICD-9 diagnostic code were determined. If the most common code was associated with a different class, both were listed.

Note: Benzathine benzylpenicillin and benzathine phenoxymethylpenicillin did not have DDDs assigned at the time of our analyses, therefore overall human antimicrobial drug use was slightly underestimated, and particularly underestimated were the beta-lactamase sensitive penicillins. The veterinary drug orbenin and all antimicrobials prescribed in the form of enemas or suppositories were removed from the dataset.

Table B.3.1. Quantity units used for each product formulation for human antimicrobial prescription data

Formulation	Quantity units
Tablets, caplets	Pills
Suspension, liquid	Millilitres
Vial, syringe, Tubex®, minibag	Vials, syringes, Tubex® needles, minibags
Ampule	Ampules
Nebulizer solution	Dispensers
Sachet	Sachets

Appendix C - References

Canadian Committee on Antibiotic Resistance (CCAR) (2002). Antimicrobial resistance: A deadly burden no country can afford to ignore. Journal of Infectious Disease. 14(1):1-4.

Canadian Pharmacists Association (2001). Compendium of Pharmaceuticals and Specialties (CPS). The Canadian Drug Reference for Health Professionals. Ottawa, Canada.

Centers for Disease Control and Prevention. Outbreak of Multidrug-Resistant Salmonella Newport - United States, January - April 2002. MMWR 2002;51:545-48.

Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) (2002). DANMAP 2001 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. Copenhagen, Denmark.

Delarocque-Astagneau E, Bouillant C, Vaillant V, Bouvet P, Grimont P, Desenclos, J-C (2000). Risk factors for the occurrence of sporadic *Salmonella enterica* serotype Typhimurium infections in children in France: a national case-control study. Clin Inf Dis. 31: 488-92.

Demczuk W, Ahmed R, Woodward D, Clark C, Rodgers F (2001). Laboratory surveillance data for enteric pathogens in Canada: 2000 annual summary. Health Canada.

Fone D, Barker R (1994). Associations between human and farm animal infections with *Salmonella* Typhimurium DT104 in Herefordshire. Communicable Disease Report Rev 4:R136-40.

Glynn M, Reddy S, Fiorentino T. *et al*. (1998). Antimicrobial agent use increases infections with resistant bacteria: a FoodNet case-control study of sporadic, multiresistant *Salmonella* Typhimurium DT104 infections, 1996-1997. Program and abstracts of the 36th annual meeting of the infectious diseases society of America; 1998 November 12-15; Denver, CO. Alexandria, VA: Infectious Diseases Society of America, 84 [abstract 52].

Grif K, Dierich M, Karch H, Allerberger F (1998). Strain-specific differences in the amount of Shiga toxin released from enterohemorrhagic *Escherichia coli* O157 following exposure to subinhibitory concentrations of antimicrobial agents. Eur. J. Clin. Microbiol Infect Dis. 17:761-766.

Health Canada (HC) (2002). Uses of antimicrobials in food animals in Canada: impact on resistance and human health. Report of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health. Prepared for the Veterinary Drugs Directorate, Health Canada. 165 p.

Health Canada (HC) (2003). Canadian Integrated Surveillance Report: *Salmonella,* C*ampylobacter*, pathogenic *E. coli* and *Shigella*, from 1996 to 1999. CCDR. 29S1.

Joint Expert Advisory Committee on Antibiotic Resistance (JETACAR) (1999). Report of the Joint Expert Advisory Committee on Antibiotic Resistance. Commonwealth of Australia.

Marano N, Rossiter S, Stamey K, *et al*. (2000). The National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria, 1996-1999: surveillance for action. J Am Vet Med Assoc. 217: 1829-30.

Mølbak K, Baggesen D, Aarestrup F, Ebbesen J, Engberg J, Frydendahl K, Gerner-Smidt P, Petersen A, Wegener H (1999). An outbreak of multidrug-resistant, quinolone-resistant

Salmonella enterica serotype Typhimurium DT104. The New England Journal of Medicine. 341:1420-1425.

Poppe C, Smart N, Khakhria R, Johnson W, Spika J, Prescott J (1998). *Salmonella* Typhimurium DT104: a virulent and drug-resistant pathogen. Canadian Veterinary Journal. Sep; 39:559-565.

Poppe C, Ayroud M, Ollis G, Chirino-Trejo M, Smart N, Quessy S, Michel P (2001). Trends in antimicrobial resistance of *Salmonella* isolated from animals, foods of animal origin, and the environment of animal production in Canada, 1994-1997. Microbial Drug Resist. 7(2):197-212.

Poppe C, Ziebell K, Martin L, Allen K (2002). Diversity in antimicrobial resistance and other characteristics among *Salmonella* Typhimurium DT104 isolates. Microbial Drug Resist. 8(2):107-122.

Ravel A (2001). Development of the Canadian antimicrobial resistance surveillance system (agri-food sector) – sampling design options. Presented to the National Steering Committee on Antimicrobial Resistance in Enterics, Canada. 79 p.

Replogle ML, Fleming DW, Cieslack PR (2000). Emergence of antimicrobial-resistant shigellosis in Oregon. CID. 30:515-9.

Veterinary Drugs Directorate (VDD), Health Canada (2003). Draft - Proposed guidelines on the microbiological safety studies for the evaluation of veterinary new drug submissions. Appendix: Classification of antimicrobial products based on importance in human medicine.

Wall P, Morgan D, Lamden L, Ryan M, Griffin M, Threlfall E, Ward L, Rowe B (1994). A case control study of infection with an epidemic strain of multiresistant *Salmonella* Typhimurium DT104 in England and Wales. Communicable Disease Report. 4(11):R130-R134.

Wheeler J, Sethi D, Cowden J, Wall P, Rodrigues L, Tompkins D, *et al*. (1999). Study of infectious intestinal disease in England: rates in the community, presenting to general practice, and reported to national surveillance. The Infectious Intestinal Disease Study Executive. *BMJ*. 318:1046-50.

World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology. ATCvet index. 2002. http://www.whocc.no/atcvet. Accessed April 2003.

World Health Organization (WHO) (2000). Global Strategy for Containment of Antimicrobial Resistance. WHO, Geneva. Switzerland.

Zhao S, White D, Ge B, Ayers S, Friedman S, English L, *et al*. (2001). Identification and characterization of integron-mediated antibiotic resistance among Shiga toxin-producing *Escherichia coli* isolates. Appl. Environm. Microbiol. 67:1558-1564.