NATIONAL ACTION PLAN TO ADDRESS ANTIBIOTIC RESISTANCE

CANADIAN COMMITTEE ON ANTIBIOTIC RESISTANCE

August 2004

This document builds upon the recommendations from the 2002 National Policy Conference on Antibiotic Resistance and was prepared through wide consultation and the involvement of many Canadian organizations. The document is available on the web site of the Canadian Committee on Antibiotic Resistance at http://www.ccar-ccra.com/national-e.htm

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Executive Summary

In May 1997, Health Canada and the Canadian Infectious Disease Society jointly sponsored *Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians*, the first Canadian consensus conference on antimicrobial resistance. One of the key results of the 1997 Consensus Conference was the widespread recognition of the need for the co-ordination of a focused national approach to resistance issues. In 2002, a second national conference was held to revisit the key recommendations and to test their continuing validity. Stemming from this second event, this updated National Action Plan to Combat Antibiotic Resistance has been formulated to provide renewed focus and vigour to the initiative.

Efforts to control the development and transmission of antibiotic resistance in Canada have met with limited success since they began in earnest in 1997. Canada enjoys considerably lower rates of resistance than many other developed nations and we are experiencing a decline in the total antibiotic use in this country. However, resistance rates continue to rise and resistant pathogens are no longer only found in patients of health care facilities but increasingly in the community.

This Action Plan contains a series of priority action items related to surveillance; optimal antibiotic use; infection prevention and control; and research. Each is intended to have direct impact on resistance by limiting its development or transmission. The Action Items include descriptions of the lead agency that should be responsible for successful implementation and many have specific deliverables and time lines.

While the Canadian Committee on Antibiotic Resistance intends to take a leadership role for some Action Items and play a key facilitation role in others, successful Action Plan implementation will require the commitment and resources of many other organizations. During 2004, CCAR will actively solicit the endorsement of this Action Plan by all of the key organizations that must take a leadership role as well as those responsible for the Action Plan implementation.

Action Item Overview

A summary of actions identified in the four key areas of surveillance, infection prevention and control, optimal use and research have been identified below. Of note, a number of these actions include the revitalization of earlier initiatives that were overtaken by other public health issues.

SURVEILLANCE:

1a: Current surveillance systems, including CNISP and CIPARS, will be expanded to include a wider variety of facilities and organisms. Health Canada, the Canadian Hospital Epidemiology Committee and CCAR will consider a pilot project for a new real time surveillance system to monitor resistance patterns in one key area of interest by the end of 2004.

1b: In 2005**,** Health Canada, provincial Ministries of Health, the Canadian Hospital Epidemiology Committee, CCAR and IMS Health will discuss mechanisms to collect, analyze and compare antibiotic use data from human health care facilities, retail pharmacies and other private and public databases that are available.

2: Health Canada and key provincial Ministries of Health and Agriculture, in conjunction with CCAR and other stakeholders, will form or revitalize Steering Committees on Surveillance in 2004 to escalate current efforts to monitor antibiotic use and resistance in human health and agri-food settings.

3: CEQA-AGAR, with support from Health Canada and provincial laboratories, will restart their efforts by the end of 2005to ensure existing and emerging resistance is monitored and that laboratory methodologies are standardized.

INFECTION PREVENTION AND CONTROL:

4: CHICA and CCAR will work in conjunction with the Alberta Ministry of Health and Wellness identify a Provincial coordinator for infection prevention and control. They will require access to adequate infection prevention and control resources in all health care and selected non-health care public settings (e.g. day cares, prisons) by 2006. This will form a pilot program which can then be implemented widely across Canada with support from Health Canada and Provincial Ministries of Health**.**

5: CHICA, in conjunction with CCAR and Do Bugs Need Drugs, and with funding from Health Canada and the Alberta Ministry of Health and Wellness, will form a Working Group to develop codes of best practice, accreditation standards and performance indicators for hygiene and asepsis outcomes and consider implementation of supportive provincial and national education programs by the end of 2004 as well as examine potential linkages among those activities.

6: CHICA, in conjunction with CCAR and other organizations, will advertise the publication of the RICH report and assist Health Canada to complete the SPICE efforts by the Spring of 2005.

7: CCAR and CHICA will immediately revitalize CCAR's Infection Prevention and Control Working Group to facilitate partnerships between the new National Public Health Agency and infection control practitioners across Canada.

OPTIMAL ANTIBIOTIC USE:

8: Health Canada and the Provincial Ministries of Health will assist CCAR in retaining access to the IMS Health CompuScript database and initiating access to Provincial drug benefit data sets for rapid analysis and results distribution

9: Health Canada and Provincial Ministries of Agriculture, through CIPARS and in conjunction with the Canadian Animal Health Institute, will lead the development of data collection, analysis and reporting efforts on the use of antibiotics in agriculture and aquaculture

10: CCAR will work with Provincial Ministries of Health, Health Canada and others to convert current data to Defined Daily Dose (DDD), compare the data among jurisdictions, provide recommended actions and widely disseminate the information

11: CCAR will work with their professional association members and the Canadian Hospital Epidemiology Committee in 2005 to develop national standards for antibiotic use and to provide continuing education modules funded, in part, by Health Canada's Best Practices Contribution Program

12: The Canadian Veterinary Medical Association, to continue its work promoting the development of animal species and commodity specific antimicrobial prudent use guidelines. It will publish finished antimicrobial use recommendations in its national journal in 2005, as well as working towards development of educational programs for veterinarians and livestock producers on prudent use of antimicrobials.

RESEARCH:

13: The Institute for Infection and Immunity (III) will adopt the four strategic research priorities listed below and prepare Requests for Proposals from the research community. III will ensure that antibiotic resistance research carried out under its mandate, is linked to this National Action Plan

- Determine the utility and cost benefit of infection prevention measures, screening and alternate therapies as they affect colonization and infection rates
- Better understand the ecology of antibiotic resistance
- Quantify the impact of resistant organisms in non-acute settings in terms of outcome
- Quantify the contribution to antibiotic resistance in humans made through the use of antibiotics in agri-food and veterinary medicine

Summary Table of Action Items

#	ACTION	RESPONSIBLE	TIMING	RESOURCES
1a	Expand current surveillance systems, including CNISP and CIPARS, to include wider variety of facilities and organisms. Establish a pilot project for a new real time surveillance system to monitor resistance patterns in one key area of interest	Health Canada, the Canadian Hospital Epidemiology Committee and CCAR	**2004**	
1b	Discuss mechanisms to collect, analyze and compare antibiotic use data from human health care facilities, retail pharmacies and other private and public databases that are available	Health Canada, provincial Ministries of Health, Canadian Hospital Epidemiology Committee, CCAR and IMS Health	**2005**	
2	Form or revitalize Steering Committees on Surveillance to escalate current efforts to monitor antibiotic use and resistance in human health and agri-food settings	Health Canada and key provincial Ministries of Health and Agriculture, CCAR, other stakeholders	**2004**	
3	Restart efforts to ensure existing and emerging resistance is monitored and that laboratory methodologies are standardized	CEQA-AGAR, Health Canada and provincial laboratories	**2005**	
4	Identify a Provincial coordinator for infection prevention and control. They will require access to adequate infection prevention and control resources in all health care and selected non-health care public settings (e.g. day cares, prisons). This will form a pilot program which can then be implemented widely across Canada	CHICA, CCAR in conjunction with the Alberta Ministry of Health and Wellness, Health Canada and Provincial Ministries of Health	**2006**	
5	Form a Working Group to develop codes of best practice, accreditation standards and performance indicators for hygiene and asepsis outcomes and consider implementation of supportive provincial and national education programs	CHICA, in conjunction with CCAR and Do Bugs Need Drugs	**2004**	Funding from Health Canada and the Alberta Ministry of Health and Wellness
6	Advertise the publication of the RICH report and assist Health Canada to complete the SPICE efforts	CHICA, CCAR and other organizations	**Spring 2005**	
7	Revitalize CCAR's Infection Prevention and Control Working Group to facilitate partnerships between the new National Public Health Agency and infection control practitioners across Canada	CCAR and CHICA	**2004**	
8	Retain access to the IMS Health CompuScript database and initiating access to Provincial drug benefit data sets for rapid analysis and results distribution	Health Canada, Provincial Ministries of Health, CCAR	**2004**	
9	Development of data collection, analysis and reporting efforts on the use of antibiotics in agriculture and aquaculture	Health Canada and Provincial Ministries of Agriculture, CIPARS, Canadian Animal Health Institute	**ongoing**	

10	Convert current data to Defined Daily Dose (DDD), compare the data among jurisdictions, provide recommended actions and widely disseminate the information	CCAR will work with Provincial Ministries of Health, Health Canada and others	**ongoing**	
11	Develop national standards for antibiotic use and to provide continuing education modules funded, in part, by Health Canada's Best Practices Contribution Program	CCAR professional association members, Canadian Hospital Epidemiology Committee	**2005**	
12	The Canadian Veterinary Medical Association, to continue its work promoting the development of animal species and commodity specific antimicrobial prudent use guidelines	The Canadian Veterinary Medical Association, provincial counterparts and producer associations	**2005**	
13	Adopt the four strategic research priorities listed below and prepare Requests for Proposals from the research community. III will ensure that antibiotic resistance research carried out under its mandate, is linked to this National Action Plan - Determine the utility and cost benefit of infection prevention measures, screening and alternate therapies as they affect colonization and infection rates - Better understand the ecology of antibiotic resistance - Quantify the impact of resistant organisms in non-acute settings in terms of outcome - Quantify the contribution to antibiotic resistance in humans made through the use of antibiotics in agri-food and veterinary medicine	The Institute for Infection and Immunity (III)	**ongoing**	

PROCESS DESCRIPTION

In May 1997, Health Canada and the Canadian Infectious Disease Society (now Association of Medical Microbiology and Infectious Disease Canada) jointly sponsored *Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians*[1], the first Canadian consensus conference on antimicrobial resistance. One of the key results of the 1997 Consensus Conference was the widespread recognition of the need for the co-ordination of a focused national approach to resistance issues. In response to this recommendation, the Canadian Committee on Antibiotic Resistance (CCAR) was established in 1998 and is now the central, coordinating body for Canadian activities in the field of antimicrobial resistance. A Report Card on all the other recommendations from the 1997 Consensus Conference is included in Appendix A. It clearly shows that Canada has achieved only limited success on implementing the recommendations and that considerably more effort is required if we are to successfully limit the development and transmission of resistance.

CCAR hosted the 2002 National Policy Conference on Antibiotic Resistance to revisit key recommendations emanating from the 1997 conference and to test their continuing validity. The conference attendees also marked the milestones already achieved in the struggle against resistance, identified areas of consensus and debate among subject-matter experts and set priorities for the next phase in the development of an integrated action plan.

The 1997 conference focused primarily on human health aspects of antimicrobial resistance and the impact of antimicrobial usage in the agri-food sector was not generally discussed. The 2002 conference considered both human health care and agriculture/aquaculture in four key areas: surveillance, optimal antibiotic use, infection prevention and control, and research.

CCAR Working Groups were activated with a mandate to feed into a multi-stakeholder National Action Plan Task Force, made up of members from the CCAR Executive Committee. The Task Force is responsible for developing the National Action Plan and continues to assist in soliciting input and commitment from the broader community and various levels of government.

INTRODUCTION

A global trend of increasing drug resistance, with wide variations at local levels, is well-documented in the research literature. Antimicrobial resistance is now a global problem. Widespread resistance to "first line" antimicrobial drugs is accelerating rapidly although resistance rates differ considerably from country to country and among geographic regions of larger nations.

In many cases, national governments have taken it upon themselves to develop strategies to address the problem of resistance within their borders. Recognizing that these resistant infections do not respect national boundaries, the World Health Organization has developed a series of recommendations to address antimicrobial resistance, to protect the international community and to provide guidance for those countries that can not, or have not, developed national strategies of their own. Both the United States Food and Drug Administration[2] and the World Health Organization have called for the development of complex, coordinated interventions which target both health care providers and their patients while simultaneously exerting a positive influence on the environments in which they operate.

The confluence of economic and globalization pressures are forcing many pharmaceutical companies to abandon their efforts to identify, develop and commercialize new antibiotics. Over the past few years, Bristol Myers Squibb, Abbott Laboratories, Eli Lilly and Wyeth have discontinued or significantly scaled back their research efforts on antibiotics to focus on other therapies for other diseases. As well, a number of antibiotics are no longer being manufactured due to small profit margins and declining sales.

As resistance rates rise, newer and much more costly antibiotics are required to replace the cheaper first and second line choices which are becoming ineffective for treating resistant pathogens. As well, hospitalization costs rise due to the need for special patient handling and infection prevention and control measures.

In order to ascertain the economic and social impact of antibiotic resistance, in 2002 CCAR commissioned the report *Antimicrobial Resistance: A Deadly Burden No Country Can Afford to Ignore*[3].

A number of important conclusions were reached in this study which estimated the cost to the Canadian health care system if levels of resistance rose to those that currently exist in USA. Rapid escalation in drug costs alone could increase from the current $660 million per year to over $1.8 billion. As well, direct hospitalization costs could soar from a current minimum of $14 million to a projected $187 million per year. From a societal aspect, the quality of lives will be further diminished by the personal tolls which drug resistance can add to already serious medical conditions. Finally, the important public policy implication in this report is recognition that Canada needs persistent, coordinated leadership and support for efforts consistent with current national and international action plans against a growing global public health menace.

The extent of drug resistance varies on a global, regional and even institutional basis. While Canada enjoys considerably lower rates of resistance than the US we have considerably higher rates than in some developed nations, including Denmark and Iceland. Within institutions, risk tends to be highest in certain areas such as medical or surgical intensive care units or burns units.

Risk to an institution also can be affected by increased levels of resistance within neighboring institutions

Each year thousands of cases of food-derived infections occur, many of which are resistant to antibiotics. Key reservoirs of these pathogens exist in our food animals. While little is understood about the development of these organisms, it is widely believed that antibiotic use in animal agriculture is a contributing factor to resistance in human pathogens. Key reservoirs of these pathogens exist in our food animals, the most prominent include *Salmonella enterica* and *Campylobacter jejuni*.

Although routine surveillance activities and outbreak investigations of enteric illnesses often yield considerable epidemiological and microbiological information, confirmed routes of transmission (ie food, water or person-to-person contact) are not commonly reported for these illnesses. Therefore, one cannot directly quantify the magnitude of antimicrobial resistance in foodborne and waterborne infections. However, the following information, compiled from laboratories across Canada, describes the extent of resistance in enteric pathogens such as *Salmonella*, *E. coli*, *Shigella*, and *Campylobacter*.

In 2001, the Health Canada Foodborne, Waterborne, and Zoonotic Infections Division (FWZID) surveyed 408 hospital and private laboratories in Canada to gain a better understanding of key laboratory practices relevant to enteric pathogens, including the frequency and scope of antimicrobial susceptibility testing. Across the country, 236 laboratories (86%) were involved in testing one or more enteric pathogens for antimicrobial resistance (AMR). The proportion of these laboratories that reported *always* conducting antimicrobial susceptibility testing differed by pathogen: 72% for *Shigella spp*, 68% for *Salmonella* Typhi, 65% for *Salmonella* Paratyphi, 53% for *Salmonella* Typhimurium, 53% for other *Salmonella spp.*, 29% for *E. coli* O157, and 8% for *Campylobacter spp*.[4]. In addition, FWZID surveyed 14 provincial laboratories in 2000-2001 to describe existing surveillance and research initiatives monitoring AMR. Of the 11 laboratories that responded, the proportion that monitored AMR differed by pathogen: 80% for *Shigella*, 80% for *Salmonella*, 50% for *E. coli*, and 20% for *Campylobacter*[5].

Using information from these background studies, Health Canada, in collaboration with numerous federal, provincial and private partners, initiated the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) in order to develop a nationally representative and methodologically unified surveillance program for antimicrobial resistance in humans, livestock and food. The first CIPARS report[6] describes a retrospective study of AMR among human *Salmonella* and *Shigella* isolates tested between 1993-2001 in Alberta, Newfoundland, Ontario, Prince Edward Island, and Saskatchewan[7]. The most commonly tested *Salmonella* serotypes were Typhimurium (n=2826), Heidelberg (n=874), and Enteritidis (n=788). Rates of resistance to at least one antimicrobial among these serotypes were 54%, 33%, and 28%, respectively. Data on 2224 *Shigella* isolates (1607 *S. sonnei*, 510 *S. flexneri*, 73 *S. boydii*, and 34 *S. dysenteriae*) showed that rates of resistance to at least one antimicrobial were 94% for *S. flexneri*, 88% for *S. sonnei*, 79% for *S. dysenteriae*, and 75% for *S. boydii*. Future CIPARS reports will present *Salmonella* AMR rates and patterns using prospectively collected data from all Canadian provinces.

Due to limited testing, relatively little information from Canada is available on antimicrobial resistance rates among *Campylobacter* isolates. However, a recent study conducted in Ontario examined antimicrobial resistance rates among 79 *C. jejuni* and seven *C. coli* isolates obtained

from human cases between 2001-2003 and found that 93% were resistant to trimethoprim-sulphamethoxazole, 53.5% to tetracycline, 5% to clindamycin, 5% to erythromycin, 3.5% to ampicillin, 3.5% to ciprofloxacin, and 3.5% to nalidixic acid[8].

Similar strides in assigning resources from Health Canada were not forthcoming for the human health activities related to resistance. There is a considerable lack of balance between what is being done on the animal side versus the human side relative to antibiotic resistance. Considering the documented evidence of the direct link to resistance from antibiotic over-use, as well as nosocomial transmission, much more effort is required in the human health sector.

To date, most Canadian projects pertaining to antibiotic resistance and its effects on human and animal health have been individual initiatives, organized to address specific concerns of their sponsors. These projects have generally been short term and limited in scope. This situation has resulted in a fragmented approach to issue management with considerable duplication of effort and extensive, strategic gaps.

A multifaceted, national approach is needed to address the many dimensions of this problem as resistance within a wide range of microbes is emerging not only in hospitalized populations, but also in human communities and food animal production businesses. These resistant organisms spread rapidly once introduced and established, in part, by cross-border commerce and travel.

This National Action Plan is intended to have components to limit antibiotic resistance that would:

- Facilitate national and provincial vision and leadership;
- Encourage and identify adequate resourcing (human and financial) for local, regional, provincial and national antimicrobial resistance programs; and
- Support the provision of objective, Canadian data concerning antibiotic use, and the extent of resistance to particular drugs and among particular pathogens.

Methicillin Resistant *Staphylococcus aureus*

The percentage of *Staphylococcus aureus* isolates identified as MRSA (methicillin-resistant *Staphylococcus aureus*) in all Canadian Nosocomial Infection Surveillance Program[9] (CNISP) hospitals was estimated at less than 1% in 1995. As shown in Table 3.1, this figure rose every subsequent year to over 5% by 1998 and 8.3% by 2000. The 2002 annual report from Ontario's Chief Medical Officer of Health noted that "in Ontario alone, new cases of MRSA increased 20 fold between 1994 and 2000". Although alarming, as shown in Table 3.2, these levels of resistance compare favorably to current rates of over 50% in many US hospitals.

Table 3.1 MRSA Rate per 100 *Staphylococcus aureus* 1995 – 2002
Source: Canadian Noscocomial Infection Surveillance Program

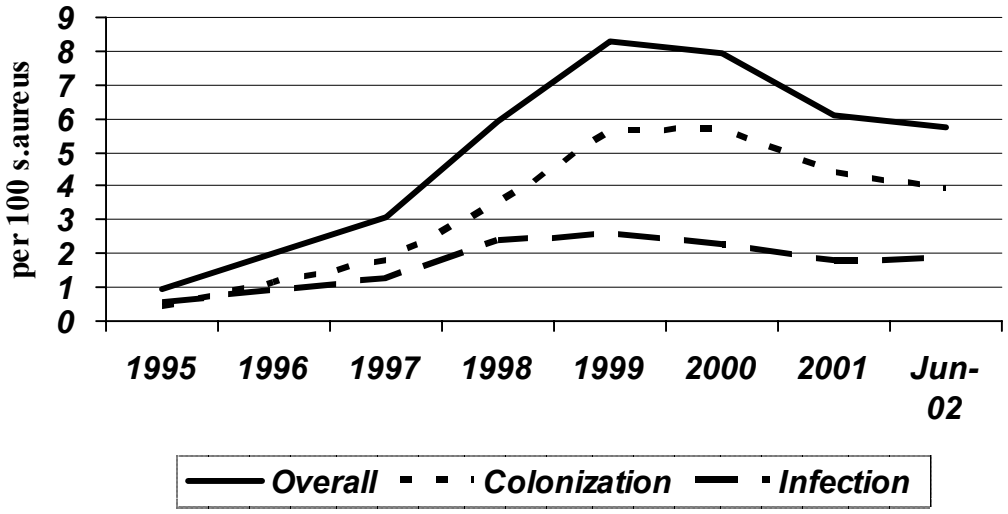
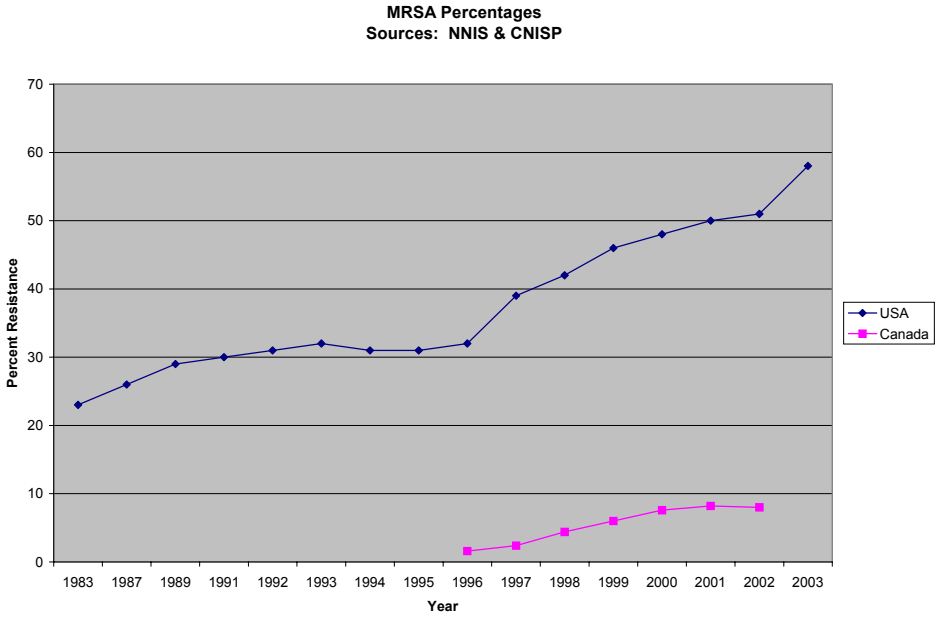


Table 3.2 MRSA Incidence in Canada and USA



Vancomycin Resistant Enterococci (VRE)

Monitoring of other drug resistant organisms largely relies on passive, anecdotal reporting. CNISP initiated prospective studies of VRE (vancomycin-resistant enterococci) in 1999. Studies were then extended to include extended spectrum beta-lactamase (ESBL) resistance among gram-negative organisms in 2001. Canada's first major VRE outbreaks in Toronto (1995), Saskatoon (1996), and Montérégie, Quebec (1998) began some two years after this organism was first detected in Canada. VRE prevalence has stabilized at around 0.5% of isolates in Canada versus 0.3% in 1989, 7.9% in 1993, and upward of 25% today in US facilities.

Extended Spectrum Beta-Lactamase (ESBL)

Thirty-five percent of gram-negative clinical isolates exhibited new forms of beta-lactamase-mediated resistance in a 1992 study of one hospital's ICU and hospital-wide antibiograms. A 1998 CNISP survey of 15 labs found ESBL resistance in 0.1-0.7% of *E. coli* and 0.2-2.5% of *K. pneumoniae* isolates.

Others

The National Centre for Streptococcus found diminished penicillin sensitivity when comparing *Streptococcus pneumoniae* isolates received during the 1992-1995 period (7.8%) compared to those received in the 1996-1997 timeframe (10.2%). This compared with an increase from 7.9% to 25.3% from 1996 to 1998 according to a Quebec reference lab's experience or higher rates for 1999-2000 in British Columbia. (US reports from 1997-1999 indicated 25% resistance along with rising macrolide and fluoroquinolone resistance rates). Similarly, 9.6% of 52 *Neisseria meningitidis* isolates from Ontario exhibited decreased susceptibility to penicillin in 1997 versus 34.6% of 55 in 2000. *S. pneumoniae* and *N. meningitidis* are leading causes of meningitis and sepsis in children and young adults.

Although routine surveillance activities and outbreak investigations of enteric illnesses often yield considerable epidemiological and microbiological information, confirmed routes of transmission (ie food, water or person-to-person contact) are not commonly reported for these illnesses. Therefore, one cannot directly quantify the magnitude of antimicrobial resistance in foodborne and waterborne infections. However, the following information, compiled from laboratories across Canada, describes the extent of resistance in enteric pathogens such as *Salmonella*, *E. coli*, *Shigella*, and *Campylobacter.*

In 2001, Health Canada's Foodborne, Waterborne, and Zoonotic Infections Division (FWZID) surveyed all hospital and private community laboratories across Canada to gain a better understanding of key laboratory practices relevant to enteric pathogens, including the frequency and scope of antimicrobial susceptibility testing. Of the 274/408 laboratories which tested stool specimens on-site, 236 (86%) reported testing one or more enteric pathogens for antimicrobial resistance (AMR). The proportion of these laboratories that reported *always* conducting antimicrobial susceptibility testing differed by pathogen: 72% for *Shigella spp*, 68% for *Salmonella* Typhi, 65% for *Salmonella* Paratyphi, 53% for *Salmonella* Typhimurium, 53% for other *Salmonella spp.*, 29% for *E. coli* O157, and 8% for *Campylobacter spp.*. In addition, FWZID surveyed 14 provincial laboratories in 2000-2001 to describe existing surveillance and research initiatives monitoring AMR. Of the 11 laboratories that responded, the proportion that monitored AMR differed by pathogen: 80% for *Shigella*, 80% for *Salmonella*, 50% for *E. coli*, and 20% for *Campylobacter*.

Using information from these background studies, Health Canada, in collaboration with numerous federal, provincial and private partners, initiated the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) in order to develop a nationally representative and methodologically unified surveillance program for antimicrobial resistance in humans, livestock and food. The first CIPARS report describes a retrospective study of AMR among human *Salmonella* and *Shigella* isolates tested between 1993-2001 in Alberta, Newfoundland, Ontario, Prince Edward Island, and Saskatchewan. The most commonly tested *Salmonella* serotypes were Typhimurium (n=2826), Heidelberg (n=874), and Enteritidis (n=788). Rates of resistance to at least one antimicrobial among these serotypes were 54%, 33%, and 28%, respectively. Data on 2224 *Shigella* isolates (1607 *S. sonnei*, 510 *S. flexneri*, 73 *S. boydii*, and 34 *S. dysenteriae*) showed that rates of resistance to at least one antimicrobial were 94% for *S. flexneri*, 88% for *S. sonnei*, 79% for *S. dysenteriae*, and 75% for *S. boydii*[7]. Future CIPARS reports will present *Salmonella* AMR rates and patterns using prospectively collected data from all Canadian provinces.

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Resistance has also been increasing in organisms that tend to infect Canadians in community settings. Many Canadians suffer from food or water borne infections. In 1998 over 7,000 cases of salmonellosis, 14,000 cases of campylobacteriosis and almost 1,500 cases of *E. coli* infection were reported. An ESBL *E. coli* outbreak in a long-term care facility reportedly contributed to three deaths. While outbreaks of this nature receive considerable media attention, most cases go unreported. Because of the lack of data on these and other enteric pathogens, we have a poor understanding about the development and transmission of resistant strains. While antibiotic use in agriculture is an important factor in increased rates of resistance, other factors are also involved including current intense production systems and food handling in the home and food service industry.

Canada's Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health published a report[10] in June 2002 which discussed the agricultural issues. The content and recommendations from that report provide considerable detail on the key issues and is an excellent information resource for those with an interest in the agri-food sector. The recommendations related to the agri-food sector made in this National Action Plan support the findings of the Advisory Committee.

KEY ISSUES

Four key issue areas have been selected for attention in this Action Plan: Integrated Surveillance, Infection Prevention and Control, Optimal Antibiotic Use and Research. Each issue area is described in greater detail below and separated into human health and agriculture. A series of recommendations provided from the 2002 National Policy Conference is provided as well as the actions taken to address the issue since the Policy Conference took place. Finally specific Action Items stemming from each recommendation is described. The Action Items are summarized on page 2.

A. Integrated Surveillance

Human Health

A true population-based national surveillance network for community acquired drug resistant micro-organisms does not exist and represents the most pressing current need in Canada. Available data sets and reports provide a fragmented and incomplete picture to guide our understanding of the evolving situation.

For example, the most recent Canadian national infection-site-specific incidence density rates are from 1986. More current information is available but it is often incomplete and provides a fragmented, non-representative view of the situation.

CNISP is an important voluntary network and holds our best promise to produce useful information concerning hospital-based care. However, it over-represents large teaching hospitals, encompasses roughly 5% of all Canadian hospitals and is hampered by meager resources. CNISP is a joint effort by the Canadian Hospital Epidemiology Committee and Health Canada.

IMS Health monitors prescriptions of a wide range of drugs including antibiotics. This information is provided for a fee to data users. It is also provided at no charge to the Canadian Committee on Antibiotic Resistance (CCAR) which posts the information annually on its web site (www.ccar-ccra.org). The information facilitates interprovincial comparisons as well as provides trend information for each antibiotic class.

CNISP is threatened every year due to lack of long-term funding from Health Canada and competing priorities. Although CNISP is the only national surveillance system that we currently have to monitor resistance in health care facilities, it is inadequate and receives considerably less human and financial resources than the comparable system in the agri-food sector (CIPARS).

Agri-Food and Veterinary Medicine

It is difficult to understand the impact that antibiotic use in food animals has on resistance rates in the human population. Current information is inadequate to even begin to quantify the magnitude of the problem. There is almost a total absence of surveillance systems for determining the presence of resistant strains and few mechanisms are available for data collection and sharing for agricultural antibiotic use. The data that are available tend to be non-standardized, collected in an unsystematic way and generally do not meet international standards such as the US NARMS system.

The 2002 CIPARS Report offers the most current, valid and national data available on antibiotic resistance in the food chain. Future surveillance data will be more comprehensive, enabling in-depth analysis of trends and correlations between antimicrobial use and resistance in livestock, food and human populations.

CIPARS will eventually permit analysis of temporal trends of use and resistance, and their correlation among livestock populations. Potential explanations for species differences include differing antimicrobial exposures, animal husbandry practices and species-specific bacterial populations may also be identified. In an effort to better understand the complexities of antibiotic use in our agri-food system, epidemiologic research is being conducted to identify risk factors for the development and spread of resistance along the food chain.

Recommendation 1:
A series of population-based, real time surveillance systems should be established to monitor resistance patterns, drug use, costs and outcomes and to demonstrate the extent of the problem in both humans and animals. Both existing and emerging resistance must be effectively and accurately captured by testing laboratories. These systems should be rolled out based on the results of local pilot programs.

Action Taken: CNISP continues track resistance rates among hospitals currently in the system. No expansion plans are being considered at this time.

Action Taken: CIPARS has initiated a series of pilot projects to provide key data sets on antibiotic resistance in selected agri-food sectors.

Action Taken: CCAR has completed an inventory of information collection methodologies for invasive *Streptococcus pneumonia* from various provincial and territorial stakeholders.

Action Item 1a: Current surveillance systems, including CNISP and CIPARS, will be expanded to include a wider variety of facilities and organisms. Health Canada, the Canadian Hospital Epidemiology Committee and CCAR will consider a pilot project for a new real time surveillance system to monitor resistance patterns in one key area of interest by the end of 2004.

Action Item 1b: In 2005**,** Health Canada, provincial Ministries of Health, the Canadian Hospital Epidemiology Committee, CCAR and IMS Health will discuss mechanisms to collect, analyze and compare antibiotic use data from human health care facilities, retail pharmacies and other private and public databases that are available.

Recommendation 2:
Identify champions, especially in the federal government, and create a working group to move agenda for surveillance forward (including both human and animal experts)

Action Taken: Health Canada has created inter-departmental science and policy committees led by the Veterinary Drugs Directorate to address the development of departmental policies on antimicrobial resistance.

Action Taken: A National Steering Committee on Antibiotic Resistant Enterics has been formed between Health Canada, Canadian Food Inspection Agency and the provincial departments of agriculture in Alberta, Ontario and Quebec.

Action Taken: In April 2003, the Steering Committee on Monitoring Antimicrobial Use in Agri-Food and Veterinary Medicine was formed with Health Canada, Fisheries and Oceans Canada, Canadian Food Inspection Agency and the provinces of British Columbia, Alberta, Ontario and Quebec.

Action Taken: The Canadian Committee on Antibiotic Resistance formed a Surveillance Working Group which meets on an infrequent basis in response to specific issues to be addressed.

Action Item 2: Health Canada and key provincial Ministries of Health and Agriculture, in conjunction with CCAR and other stakeholders, will form or revitalize Steering Committees on Surveillance in 2004 to escalate current efforts to monitor antibiotic use and resistance in human health and agri-food settings

Recommendation 3:
Ensure that external quality assurance is an integral part of the process.

Action Taken: CEQA-AGAR has distributed laboratory guidelines on the identification, testing and reporting of MRSA, VRE, PSRP and ESBLs to Canadian clinical microbiology labs. Consistent proficiency testing has not yet been implemented in some provinces. Funding for CEQA-AGAR has been discontinued.

Action Item 3: CEQA-AGAR, with support from Health Canada and provincial laboratories, will restart their efforts by 2005 to ensure that laboratory methodologies are standardized

B. Infection Prevention and Control

Human Health

The National Advisory Committee on SARS and Public Health was established in May 2003 to provide a third party assessment of current public health efforts and lessons learned for ongoing and future infectious disease control. The report identified many systemic deficiencies in the response to SARS, many of which reflect on our ability to deal with infection prevention and control for antibiotic resistant pathogens. Among these were: lack of surge capacity in the clinical and public health systems; difficulties with timely access to laboratory testing and results; absence of protocols for data or information sharing among levels of government; uncertainties about data ownership; inadequate capacity for epidemiologic investigation of outbreaks; lack of coordinated business processes across institutions and jurisdictions for outbreak management and emergency response; inadequacies in institutional outbreak management protocols, infection control, and infectious disease surveillance; and weak links between public health and the personal health services system, including primary care, institutions, and home care.

These deficiencies are widespread across Canada and place Canadians in jeopardy for a variety of infectious diseases including those resistant to antibiotics.

Agri-Food and Veterinary Medicine

A number of alternatives to the use of antibiotics in food animals have been identified by the National Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health (report released June 2002). These include the use of on-farm management practices and other infection prevention strategies which are consistent with farm quality assurance programs. These can include the use of vaccines, herbs, probiotics, novel peptides or antibodies and immune potentiators. As well, research is needed to explore new alternatives for disease control, growth promotion and enhancing feed efficiency.

Recommendation 4:
Expand and adequately resource infection prevention and control systems in acute and long term care facilities as well as in community settings and identify a Provincial Coordinator for infection prevention and control

> **Action Taken:** Alberta Health and Wellness has developed a Provincial Action Plan to deal with antibiotic resistance with a focus on surveillance, optimal antibiotic use and infection prevention.

Action Item 4: CHICA and CCAR will work in conjunction with the Alberta Ministry of Health and Wellness identify a Provincial coordinator for infection prevention and control. They will require access to adequate infection prevention and control resources in all health care and selected non-health care public settings (e.g. day cares, prisons) by 2006. This will form a pilot program which can then be implemented widely across Canada with support from Health Canada and Provincial Ministries of Health

Recommendation 5:
Develop codes of best practice and performance indicators for hygiene and asepsis outcomes and deliver supportive educational campaigns (including a hand hygiene effort).

> **Action Item 5:** CHICA, in conjunction with CCAR and Do Bugs Need Drugs, and with funding from Health Canada and the Alberta Ministry of Health and Wellness, will form a Working Group to develop codes of best practice, accreditation standards and performance indicators for hygiene and asepsis outcomes and consider implementation of supportive education programs by the end of 2004 as well as examine potential linkages among those activities.

Recommendation 6:
Finalize the infection control resource reports (SPICE and RICH), disseminate to key stakeholders within 6 months and encourage implementation

Action Taken: The RICH report was published in 2003.

> **Action Item 6:** CHICA, in conjunction with CCAR and other organizations, will advertise the publication of the RICH report and assist Health Canada to complete the SPICE efforts by the Spring of 2005

Recommendation 7:
Develop local and regional partnerships, where they do not exist, among public health and infection control practitioners

> **Action Item 7:** CCAR and CHICA will immediately revitalize CCAR's Infection Prevention and Control Working Group to facilitate partnerships between the new National Public Health Agency and infection control practitioners across Canada

C. Optimal Antibiotic Use

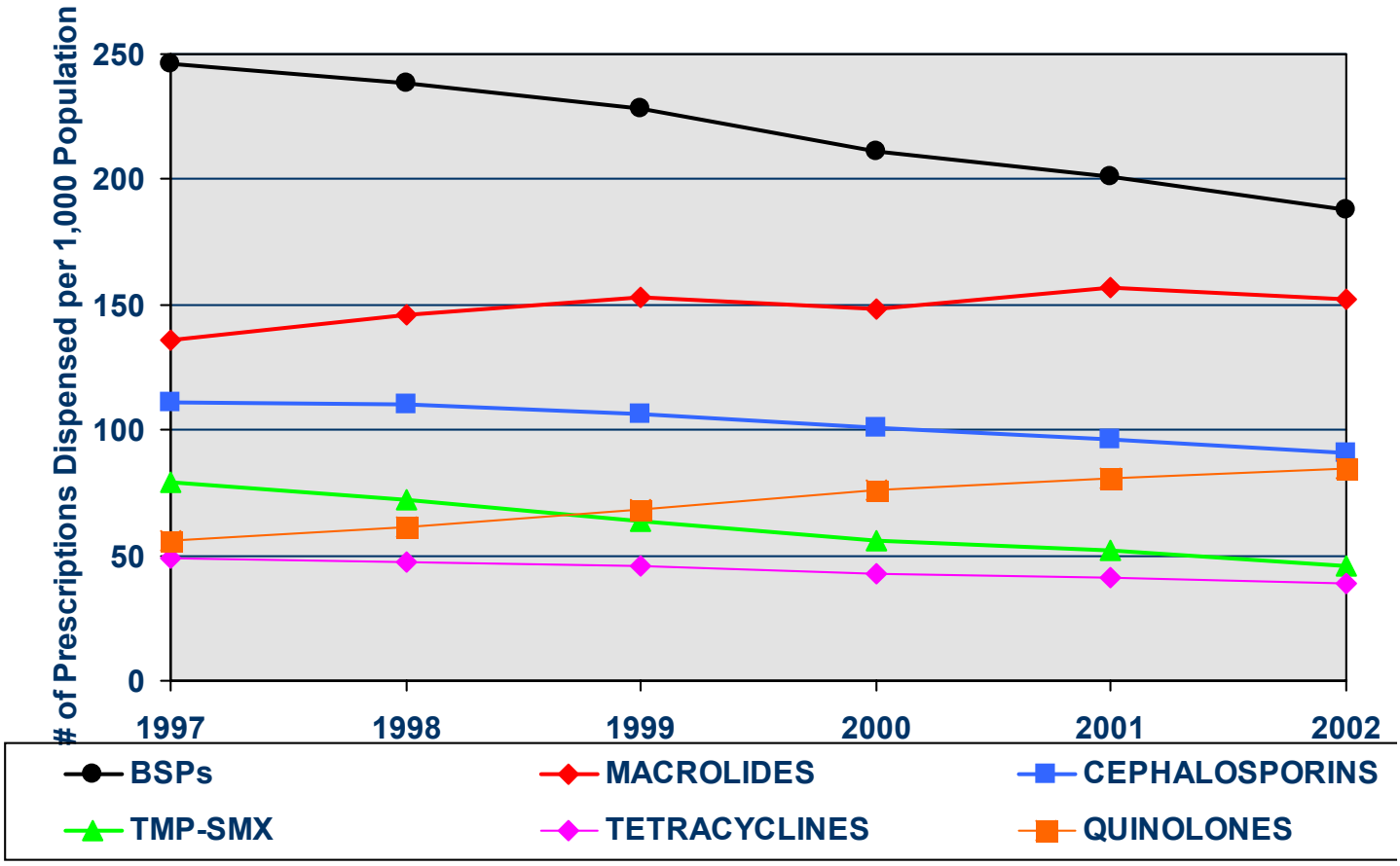
Human Health

While some success has been achieved in reducing the number of prescriptions of first line antibiotics, we continue to see an increase in the prescriptions for newer, broad spectrum antibiotics (i.e. macrolides and quinolones). Table 5.1 shows the trends in prescriptions per thousand population from 1997 to 2002 (data provided by IMS Health). Detailed prescription data by province is available on the CCAR Web site at:
http://www.ccar-ccra.ca

Several regional efforts are underway to curb inappropriate prescribing including the Do Bugs Need Drugs program and the Partners for Appropriate Anti-infective Community Therapy (PAACT). More information on each of these programs is provided in Appendix B.

Practitioners in Ontario and Alberta have endorsed the Dutch antibiotic sparing guidelines. These guidelines are also expected to be endorsed by the American Academies of Pediatrics and Family Physicians. National professional societies in Canada have yet to consider endorsing these guidelines.

Table 5.1 Trends in Prescriptions Per Thousand Population from 1997 to 2002 (data provided by IMS Health)



Agri-Food and Veterinary Medicine

The Canadian agricultural antibiotic distribution system is diverse and highly fragmented. Due to the lack of stringent procedures for antibiotic importation, distribution and use, control measures and data capture face considerable barriers. Further complicating the situation are the current practices of over the counter (OTC) sale of antimicrobials, drug use without prescription, economic dispensing incentive among veterinarians, extra label use and direct importation of active ingredients.

Availability and accessibility of antibiotics for agricultural use also provide additional complicating factors related to increased antibiotic resistance. Farmers are able to legally import antimicrobials from overseas retailers (or through Internet) for use in their own animals under 'own-use' provisions.

While the Canadian Veterinary Medical Association has issued general and specific prudent antibiotic use principles, there are few incentives to implement them. There is also a lack of awareness on resistance issues among producers and veterinarians alike.

Recommendation 8:
Implement measures to facilitate the collection, analysis and reporting of the quantity and distribution of antibiotics being used in our human health care system to compare with other jurisdictions and to facilitate the formulation of appropriate interventions

> **Action Taken:** CCAR and IMS Health (CompuScript database) continue to share data on the number of antibiotic prescriptions filled through retail pharmacies and annually post the information on the CCAR Web site.

Action Item 8: Health Canada and the Provincial Ministries of Health will assist CCAR in retaining access to the IMS Health CompuScript database and initiating access to Provincial drug benefit data sets for rapid analysis and results distribution

Recommendation 9:
Implement measures to facilitate the collection, analysis and reporting of antibiotic use monitoring data to track the use of antibiotics for growth promotion, prophylaxis and therapy in agriculture and aquaculture to compare with other jurisdictions and to facilitate the formulation of appropriate interventions

> **Action Taken:** CIPARS has initiated a series of pilot projects to provide key data sets on antibiotic use in agriculture.

Action Item 9: Health Canada and Provincial Ministries of Agriculture, through CIPARS and in conjunction with the Canadian Animal Health Institute, will lead the development of data collection, analysis and reporting efforts on the use of antibiotics in agriculture and aquaculture

Recommendation 10:
Obtain, analyze and disseminate data/information on antibiotic use in humans and animals in a timely manner and present it in standard formats which can be used for comparison (e.g. Defined Daily Dose)

Action Taken: The BC Ministry of Health, in a pilot program, has converted their antibiotic use data to Defined Daily Dose (DDD).

Action Taken: CIPARS is undertaking a series of pilot projects some of which are intended to facilitate the collection of data on antibiotic use in agriculture.

Action Item 10: CCAR will work with Provincial Ministries of Health, Health Canada and others to convert current data to Defined Daily Dose (DDD), compare the data among jurisdictions, provide recommended actions and widely disseminate the information

Recommendation 11:
Develop national standards for continuing competency for health care professionals involved in antibiotic use

Action Item 11: CCAR will work with their professional association members and the Canadian Hospital Epidemiology Committee in 2005 to develop national standards for antibiotic use and to provide continuing education modules funded, in part, by Health Canada's Best Practices Contribution Program

Recommendation 12:
Convene expert groups to develop practice specific guidelines on prudent use of antimicrobials in animals and promote prudent antibiotic use through case-based veterinary and producer education programs

Action Item 12: The Canadian Veterinary Medical Association, will continue its work promoting the development of animal species and commodity specific antimicrobial prudent use guidelines. It will publish finished antimicrobial use recommendations in its national journal in 2005, as well as working towards development of educational programs for veterinarians and livestock producers on prudent use of antimicrobials.

D. Research

Human Health

The Canadian Institutes of Health Research – Institute on Infection and Immunity (CIHR-III) identified antibiotic resistance as a priority funding area starting in fiscal year 2003/04.

In March 2003, CCAR provided a list of research priorities to the CIHR-III, for their review and implementation (see recommendation 14).

ii. Agri-Food and Veterinary Medicine

Consumers and many players in the agricultural community are calling for reductions in antimicrobial use in animals for disease prevention or for feed efficiency and growth promotion. Many non-antimicrobial approaches can potentially be used including improved management practices, feed additives and probiotics. Commercial validation on safety, efficacy and economics of the alternatives is required. Programs in Sweden and Denmark are already in place and could be used as models for Canadian producers. These programs should also be monitored to ascertain if the actions taken have positive human outcomes.

Recommendation 13:

CIHR Institute for Infection and Immunity (III) should undertake research to:

- Determine the utility and cost benefit of infection prevention measures, screening procedures and alternate therapies as they affect colonization and infection rates
- Better understand the ecology of antibiotic resistance
- Quantify the impact of resistant organisms in non-acute settings
- Quantify the contribution to antibiotic resistance in humans made through the use of antibiotics in agri-food and veterinary medicine

Action Item 13: The Institute for Infection and Immunity (III) will adopt these four strategic research priorities listed above and prepare Requests for Proposals from the research community. III will ensure that antibiotic resistance research carried out under its mandate, is linked to this National Action Plan

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APPENDICES

A. Report Card on Recommendations from 1997 Consensus Conference on Antimicrobial Resistance
B. List of Currently Active Agri-Food Programs in Antibiotic Resistance
C. List of Currently Active Human Health Care Programs in Antibiotic Resistance