

Canadian Public Health Laboratory Network Working Group



- › The CPHLN AMR Working Group will provide a focus for microbiological expertise, guidance and recommendations regarding AMR surveillance initiatives and other AMR-related issues in Canada.

The Canadian Public Health Laboratory Network (CPHLN) is a forum of federal and provincial public health laboratories mandated to provide leadership and consultation in all aspects of the public health system.

Public health laboratories are a key partner in AMR surveillance and response through detection, reference testing, surveillance, technology uptake, and data collection, analysis and interpretation. In light of the public health issues related to AMR, a working group has been formed specifically for AMR to ensure ongoing focused discussion and collaboration.

The CPHLN AMR Working Group provides recommendations on AMR surveillance and microbiological expertise to the CPHLN. This includes addressing provincial laboratory needs and reducing duplication between federal and provincial laboratories, developing relationships with community and acute care laboratories, and working towards a harmonized approach across Canadian laboratories for AMR analysis and interpretation.

Developing laboratory-specific guidelines, and standards for consistent and comparable data analysis—including national definitions for multi-drug resistance and extreme drug resistance, and potential reporting of specific AMR numbers for emerging AMR organisms—will be particularly important. More specifically, the Working Group is developing a national

eXtensively Drug Resistant (XDR) definition for the most common gram-negative organism. These efforts will also facilitate enhanced collection and analysis of AMU and AMR data in the community-setting.

Other jurisdictions may wish to leverage the Working Group model and terms of reference to facilitate greater collaboration across various laboratories, as well as the definitions and standardized data collection.

Timescale: 2014–2016, with the possibility of extension.

The owners and organisation involved in the project

Public Health Agency of Canada
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<https://www.nml-lnm.gc.ca/cphln-rlspc/index-eng.htm>

Implementation of surveillance for MDR bacteria of EU concern



- › To implement laboratory diagnosis and surveillance for anti-microbial-resistant infections and drug-resistant tuberculosis in Italy. To describe the molecular epidemiology of some MR pathogens with particular regard to their clonal structure. To continue quality assessment of anti-biogram for *M. tuberculosis* infections, involving other laboratories.

The Department for Infective Disease (MIPI) of the Italian Institute of Health (ISS) is the scientific institution involved in the laboratory surveillance of infections of public health concern representing the Italian reference centre in this. In recent years, AMR infections have been considered as a relevant issue due to the growing spread of MRSA, carbapenem-resistant *K. pneumonia*, multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis.

This project therefore aims to implement the national system of laboratory surveillance for AMR infections and drug resistant TB.

The implementation process requires the straightness of the 30-lab network involved in AMR infections and MR TB surveillance improving technologies, molecular epidemiology and data management.

Timescale: February 2013 to July 2015

The owner and organisation involved in the project

Istituto Superiore di Sanità

Prevention and risk analysis of MDR infections in transplant surgery



- To obtain a national estimation of potentially infected donors. To perform a risk analysis of the colonisation/infection of organ-recipient patients by KCP and other MDR microorganisms colonised/infected persons, especially with a focus on new resistance profiles. To estimate the prevalence of the colonisation/infection by MDR microorganisms among transplant patients. To provide guidelines for decision-makers. To perform a microbiological analysis of MDR microorganisms circulating.

Infections, and multidrug-resistant infections in particular, represent a feared event after a transplant especially in subjects undergoing invasive procedures, in a long-term stay or immunosuppressed. Therefore, the control of the spread of these infections, as well as the risk analysis of post-transplant infection, have become more necessary now than ever.

Timescale: November 2012 to October 2014, extended to April 2015

The owners and organisations involved in the project

- Istituto Superiore di Sanità
- National Transplant Center
- Emilia Romagna Region
- Spallanzani National Institute for Communicable Diseases
- Policlinico Sant'Orsola Malpighi
- University of Insubria-Varese

Surveillance of bioterroristic agents and pathogens of EU concern



- › To implement and improve laboratory diagnosis and surveillance for legionella, burdetella pertussis, diphtheria, atypical agents or bioterrorism agents, AMR infections, drug-resistant tuberculosis in at-risk groups such as migrants.

The Department for Infectious Disease (MIPI) of the Istituto Superiore di Sanità (ISS) is the scientific institution involved in the laboratory surveillance of infections of public health concern. This project thus aims to implement the national system of laboratory surveillance for legionella, burdetella pertussis, diphtheria, atypical agents or bioterrorism infections, AMR infections and drug-resistant tuberculosis in at-risk groups such as migrants.

The owner and organisation involved in the project

Istituto Superiore di Sanità

The implementation process needs:

- for Legionella and AMR bacteria the promotion of a network among reference labs, existing and new national and regional laboratories;
- for diphtheria and burdetella there is a need to develop a laboratory network as suggested by ECDC;
- to implement participation within European Networks.

Timescale: October 2010 to April 2012

Surveillance of *Clostridium difficile* infection



- › To analyse and assess the feasibility of different surveillance systems for CDI already implemented at regional and European levels. To describe the epidemiology of CDI in Italy and the circulation of particularly virulent clones. To obtain a comparative analysis of existing Italian experience in evaluating the cost effectiveness of each intervention that has already been implemented. To promote better a CDI diagnostic system and the related scientific research.

Clostridium difficile infections (CDI) represent one of the primary causes of healthcare-acquired infections in many European hospitals, with a growing trend in the last years. A *Clostridium difficile* infection surveillance system is already in operation in many countries and in several Italian regions such as Lombardy or Emilia Romagna, but there is no nationwide system as yet.

Now more than ever, a real-time CDI surveillance system appears necessary.

The aim of the current project is to start up a nationwide real-time CDI surveillance system that can be sustainable in each Italian region to obtain epidemiological data and improve subsequent prevention and control actions.

Timescale: March 2012 to February 2014, extended to August 2014

The owners and organisations involved in the project

- Regional Social and Health Agency of the Emilia Romagna Region
- Istituto Superiore di Sanità
- Lombardy Region
- University of Turin

Healthcare-Acquired Infections (HAI) surveillance



- ▶ To ensure the Italian participation at European surveillance systems for Healthcare acquired infections coordinated by ECDC. To obtain a nationwide HAI epidemiological database, strengthening Italian laboratories networks, sharing data and building dedicated networks.

HAIs are considered to be the most frequent adverse event in healthcare, and their impact has become a Public Health priority. HAI surveillance represents an important instrument to improve the epidemiological trend and to implement improvement actions to manage this issue.

Italy has created an interregional network in recent years aimed at:

- implementing a nationwide SSI surveillance system,
- integrating infection surveillance data from different existing networks.

Italy has been involved in different European networks (such as HALT) for AMR infection surveillance. Several projects have been carried forward for the different healthcare settings:

- Infections in at-risk Surgical units (SNICH Project for SSI Surveillance);
- Intensive Care unit Infections (three networks: a National Database with data from 91 intensive care units, SPIN-uTI project with data from 25 intensive care units, SITIER project with data from 2 intensive care units)
- Hospitals (ECDC promoted a study and Italy participated with data from 49 hospitals)
- Nursing home care.

Timescale: November 2012 to May 2014

The owners and organisations involved in the project

- Regional Social and Health Agency of the Emilia Romagna Region
- Mario Negri Institute
- University of Catania (SPIN-uTI Project-GISIO SItI)

MDR carriage and infections in neonatal intensive care units (NICU)



- To compare epidemiological characteristics and risk factors for the spread of MDR pathogens among some Italian NICUs with different geographical, epidemiological and organisational conditions. To define the key molecular characteristics of these bacteria, with particular regard to MRSA and MDR Gram negative. To check the feasibility and effectiveness of a “network-based” MDR infection real-time surveillance programme, involving all NICUs in Palermo. To define a model and Guideline.

The neonatal intensive care units (NICUs) represent a complex healthcare setting with a high risk of the spread of MDR pathogens, with potential serious consequences for neonates.

The carriage of pathogens represents another risk factor due to the neonatal transfer to NICU from other care settings.

The owners and organisations involved in the project

- Sicily Region
- “La Sapienza” University, Rome
- Istituto Superiore di Sanità
- San Matteo Polyclinic, Pavia

Timescale: April 2015 to April 2017

AMR surveillance for community, food-related, zoonotic infections



- › To implement an AMR surveillance system for multidrug-resistant *Salmonella* and *Campylobacter* strains, causing food-related infections. To implement AMR surveillance for MRSA, causing infection or colonisation, defining the origin (zoonotic, community, nosocomial). To implement surveillance for *E. Coli* with specific AMR and a high morbidity profile. To identify molecular markers for epidemiological analysis.

AMR has a growing impact on Public Health, representing a problem now more than ever in both human and veterinary health. In recent years, food-related infections have become another relevant issue due to antimicrobial resistance against salmonella and campylobacter, the principal food-related zoonotic pathogens. The treatment of MRSA and *E. Coli* infections is often complicated by resistance.

The project has been realised involving other structures of the National Health System.

Timescale: March 2013 to March 2014

The owners and organisations involved in the project

Istituto Superiore di Sanità

NEO-KISS



► **NEO-KISS (nosocomial infection surveillance system for preterm infants on neonatology departments and ICUs) is a mandatory national surveillance system for nosocomial infections in very low birth weight infants in Germany.**

Infection is one of the most important reasons for neonatal morbidity and mortality worldwide. Progress in neonatal intensive care has made it possible to decrease mortality among preterm infants with very low birth weights, but these preterm infants are at especially high risk for developing nosocomial infections. Surveillance has proven itself to be an effective method for reducing the frequency of nosocomial infections.

An important part of the surveillance system is the comparison of infection rates. Nationwide reference data are necessary for comparing infection rates and for evaluating the efficiency of preventative measures. The goal of the NEO-KISS is to make nationwide reference data about the frequency of nosocomial infections among preterm infants more available. It is one module within the Hospital-Infections-Surveillance-System (KISS).

A pilot project was started in May 1999. Data collection on a patient-by-patient basis has been underway since January 2000. All children with a birthweight (BW) of less than 1500 g are included until their hospital discharge, death or weight of over 1800 g. Specially developed definitions are used for the diagnosis of the three kinds of infections tracked: pneumonia, primary bloodstream infections, and necrotizing enterocolitis. Stratified incidence density (infections/1000 patient-days) and device-related infection rates per 1000 device-days are calculated by birth weight class (less than 500 g, 501–999 g, and 1000 to 1499 g). Device usage (central venous

catheter, peripheral venous catheter, intubation and continuous positive airway pressure) is taken into account. Data collected for NEO-KISS are put into the database “webKess” decentrally. To perform pathogen surveillance, it is possible to participate in other moduls within KISS.

Timescale: Start: 2006, ongoing

The owners and organisation involved in the project

National Reference Center
for Nosocomial Infection Surveillance
<http://www.nrz-hygiene.de/surveillance/kiss/neo-kiss/>

Canadian Nosocomial Infection Surveillance Program



- ▶ The data collected and analyzed through the Canadian Nosocomial Infection Surveillance Program provides clinicians and decision-makers with evidence-based benchmarks, identifies trends and supports the development of national guidance documents to help reduce the transmission of AMR.

The Canadian Nosocomial Infection Surveillance Program (CNISP) is a collaborative effort between the Public Health Agency of Canada and sentinel acute-care hospitals across Canada which participate as members of the Canadian Hospital Epidemiology Committee (CHEC) of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada.

Established in 1994, the objectives of CNISP are to provide rates and trends of healthcare-associated infections (HAIs) and antimicrobial resistant organisms (AROs) found in Canadian acute care hospitals. The surveillance also provides a measure of the burden of illness, establishes benchmark rates for internal and external comparison, identifies potential risk factors, and allows assessment of specific interventions related to HAIs and AROs.

As of December 2014, CNISP conducted surveillance in 62 major hospitals in 10 provinces across Canada. Current surveillance collects data on healthcare-associated *Clostridium difficile* infection (HA-CDI), methicillin-resistant *Staphylococcus aureus* (MRSA) including healthcare- and community-associated MRSA and MRSA bacteremias, vancomycin-resistant *Enterococci* (VRE), carbapenemase-producing organisms (CPO), carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter* (CRA), and central venous catheter bloodstream infections (CVC-BSI).

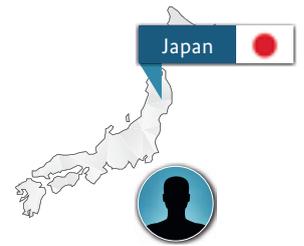
CNISP surveillance provides key information that can be used to measure the quality of patient care, and informs the development of federal, provincial and territorial infection prevention and control programs and policies. Both the surveillance results and the structure to support comprehensive and standard surveillance across jurisdictions will be of interest to countries looking to establish a uniform hospital-based surveillance on AROs.

Timescale: ongoing

The owners and organisation involved in the project

- Public Health Agency of Canada, in collaboration with 62 sentinel acute care hospitals across Canada.
- Surveillance and Epidemiology Division
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Japan Nosocomial Infections Surveillance (JANIS)



► To provide basic information on the incidence and prevalence of nosocomial infections and antimicrobial resistance in medical settings in Japan.

Japan Nosocomial Infections Surveillance (JANIS) is a national surveillance program organized by the Ministry of Health, Labour and Welfare. It is designed to provide basic information on the incidence and prevalence of nosocomial infections and antimicrobial resistance in medical settings in Japan. JANIS was launched in 2000 with three divisions, the clinical laboratory division, the antimicrobial-resistant bacterial infection division, and the intensive care unit division; two more divisions, the surgical site infection division and the neonatal intensive care unit division were added in 2002.

Each of the member hospitals can choose which divisions to join, based on their needs and capacities. Approximately 1,600 hospitals, or 20% of all hospitals in Japan, are participating in JANIS. JANIS is a voluntary program, and there are neither legal obligations nor financial support for participation. The JANIS management office is located in the Department of Bacteriology II in the National Institute of Infectious Diseases. Member hospitals of JANIS submit surveillance data monthly, or once or twice a year, according to the divisions in which they opted.

JANIS produces two types of reports, the Open Report and the Feedback Report. The Open Report, which is available on the JANIS website, aims to provide the national data on the incidence of nosocomial infections and the prevalence of antimicrobial resis-

tance for the public. The Feedback Report includes the analyzed data of each member hospital. It is sent out to each member hospital confidentially, and it is expected to be utilized for evaluation and action planning on infection control measures.

Timescale: established in 2000

The owners and organisation involved in the project

- Ministry of Health, Labour and Welfare
- National Institute of Infectious Diseases
- <http://www.nih-janis.jp/english/index.asp>

Surveillance for anti-biotic consumption and antimicrobial resistance



› The surveillance system for antibiotic consumption and antimicrobial resistance in France relies on several entities, namely the Government, the National Public Health Institute and the National Drug Agency.

Surveillance for antibiotic consumption and antimicrobial resistance.

Antibiotic consumption.

The Government has prepared tools to help professionals calculate antimicrobial consumption.

These tools were aimed at helping GPs and hospitals to monitor their antibiotic consumption. (<http://www.sante.gouv.fr/outils-de-calcul-des-consommations-d-antibiotiques,13616.html>).

The French Drug Agency is in charge of collecting data on antimicrobial consumption, and publishes an annual report detailing the consumption of antibiotics in France. A specific network is in charge of collecting data on antibiotic consumption from hospitals regarding antimicrobial resistance. The French Institute for Public Health Surveillance collects the data coming from voluntary French labs and from monitoring networks.

As per EPC, a specific surveillance exists, and the result of this surveillance is published online by the French Institute for Public Health.

Surveillance is also organised by specific interregional networks, with specific reports being drafted on multi-resistant bacteria. There is a specific tool for hospitals, as well as a tool for GPs which helps to monitor resistances for *E. coli* and *S. aureus*.

For veterinary medicine, antibiotic consumption and antimicrobial resistance are followed specifically.

The ANSES publishes its assessment of the risks of emergence of antimicrobial resistance related to patterns of antibiotic use in animal health.

The owners and organisations involved in the project

- Ministry of Health
- Regional Health Agencies
- ANSES-National Drugs Agency
- National Institute of Public Health Surveillance

Surveillance of antibiotic consumption



- **The objective of the project is to provide an electronic automated system for the collection, analysis and reporting of antibiotic consumption data in the hospital sector. It aims to support the hospitals in the conduct of antibiotic consumption surveillance and local antibiotic stewardship efforts and to build up a national database as a basis for the provision of reference data.**

The national public health institute (Robert Koch Institute, RKI) in cooperation with the National Reference Center for the Surveillance of Nosocomial Infections, has built up an electronic system for collection, calculation and reporting of antibiotic consumption data in the hospital sector. Aims of the project are to support the hospitals in the implementation and conduct of antibiotic consumption surveillance, to contribute to local antibiotic stewardship activities, to build up a national data base and to provide reference data to the medical public.

For saving resources, an already existing web-based data portal, which serves for the collection of data in the German Hospital Infection Surveillance System has been extended in order to allow for the entry of antibiotic consumption data and the consecutive transfer to the RKI. In addition, this construct paves the way for future crosslinking of data from the different surveillance systems.

The data flow can be divided into three major steps:

1. Preparation und upload of the data via a web-based tool ("webKess") and consecutive transfer to the RKI.
2. Data analysis and generation of feedback reports.
3. Retrieval of individual reports by the hospital via an interactive database, which allows a specification and tailoring of the request according to the needs

and preferences of the user. The system offers different types of reports supporting various forms of interpretation (e.g. analysis of trends, benchmarking).

In summary, a fully operational electronic platform for a superordinate surveillance of antibiotic consumption has been developed. The system supports an effective and resource-sparing monitoring of antibiotic consumption on the level of the individual hospital and as well allows the establishment of a national database.

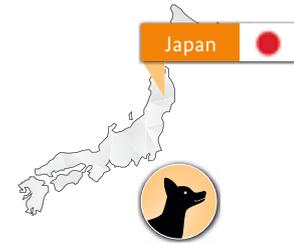
Timescale: Start of the project: 2013.

Pilotphase: 08–12, 2014. Routine phase: since 2015

The owners and organisation involved in the project

Robert Koch Institute, Dep. 3, FG37
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www.rki.de
 Webside project: <https://avs.rki.de>

Japanese Veterinary Antimicrobial Resistance Monitoring System



► The objectives of Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM) are to monitor the occurrence of antimicrobial resistance in bacteria in food-producing animals, and to monitor the quantities of antimicrobials used in animal. JVARM allows the efficacy of antimicrobials in food-producing animals to be determined, prudent use of such antimicrobials to be encouraged, and the effect on public health to be ascertained.

The Codex Alimentarius Commission (CAC), specified as the international standard setting body in the WTO' SPS Agreement, established the code of practice and guidelines on AMR issue which recommend application of risk analysis to AMR issues. CAC also developed a number of recommendations and working principles on risk analysis. In Japan, the Government follows the risk analysis framework. In practice, FSC conducts risk assessment of individual antimicrobial agents used in livestock sector, while MAFF conducts risk management measures based on the risk assessment results in order to reduce the risk caused by antimicrobial resistant bacteria.

JVARM was established in 1999 to implement risk management measures effectively, in response to international concern about the impact of antimicrobial resistance on public health. JVARM consists of (1) monitoring of antimicrobial resistance in zoonotic bacteria, indicator bacteria and animal pathogenic bacteria and (2) monitoring quantities of antimicrobials used in animals.

Following bacteria are monitored for antimicrobial resistance: Salmonella, Campylobacter, Escherichia coli, Enterococcus, Staphylococcus and the others. NVAL acts as the reference laboratory of JVARM and collaborates with prefectural governments and

Food and Agricultural Materials Inspection Center. Concerning monitoring quantities of antimicrobial use, the marketing authorization holders report the sales amount of veterinary antimicrobials to the NVAL annually. NVAL subsequently collates and evaluate these data and estimates the quantities of use from the sales amount. The annual report of JVARM is officially published through the scientific journals and NVAL website as JVARM report. The data of JVARM have been utilized for Risk assessment of antimicrobials by the FSC and Risk management by MAFF.

JVARM has started collaboration with JANIS (Japan Nosocomial Infectious Surveillance: AMR surveillance for human health sector).

Timescale: since 1999

The owners and organisation involved in the project

- National Veterinary Assay Laboratory (NVAL)
- Ministry of Agriculture, Forestry and Fisheries (MAFF)
- <http://www.maff.go.jp/nval/english/>

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)



- › CIPARS monitors trends in antimicrobial use and resistance in selected bacterial organisms from human, animal and food sources across Canada. This information supports the creation of evidence-based policies to control antimicrobial use in hospital, community, and agricultural settings and thus prolong the effectiveness of these drugs; and the identification of appropriate measures to contain the emergence and spread of resistant bacteria between animals, food, and people.

Created by the Public Health Agency of Canada in 2002, the Canadian Integrated Program for Antimicrobial Surveillance (CIPARS) is a national program dedicated to the collection, integration, analysis, and communication of trends in antimicrobial use (AMU) and antimicrobial resistance (AMR) in selected bacteria from humans, animals, and animal-derived food sources across Canada.

Analysis is conducted for AMR and AMU components individually, then findings integrated across surveillance components, over time and regions, and across host/bacterial species. Components include humans, retail meat, healthy animals at slaughter, healthy animals on farm, sick animals, and isolates from animal feed. Animal species include cattle, pigs, broiler chickens and retail meat includes beef, chicken, pork and turkey. Bacterial species monitored in animal components are *Salmonella*, *Campylobacter*, and *E. coli*. For humans, *Salmonella* is currently monitored. AMU surveillance in humans involves antimicrobial dispensing from community pharmacies, hospital antimicrobial purchases, and sampled physician diaries. AMU surveillance in animals involves voluntary provision of distribution data from manufacturers of antimicrobial agents intended for use in animals, and surveys of AMU

on sentinel grower-finisher pig and broiler chicken farms. The value of this surveillance is demonstrated through the strong correlation identified between ceftiofur resistance in *Salmonella heidelberg* from human infections and retail poultry in two Canadian provinces (2003 data released in early 2005). Hatcheries voluntarily withdrew ceftiofur for disease prophylaxis, followed by a marked reduction in the proportion of resistant *S. heidelberg* from humans and retail chickens. Select CIPARS data are now being integrated into the Canadian Antimicrobial Resistance Surveillance System (CARSS) reports to support more integrated reporting of AMU and AMR.

Timescale: ongoing

The owners and organisation involved in the project

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<http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php>

QS Quality scheme for food: The food industry's own antibiotics monitoring



› Reducing the number of antibiotic treatments in livestock to the inevitable minimum. Strengthening prudent use.

In Germany the pig and poultry sector have implemented a monitoring system for antibiotics in 2012 (<https://www.q-s.de/veterinarians/antibiotics-monitoring-veterinarians.html>).

The comprehensive database on the use of antibiotics in livestock is a prerequisite for its optimisation and thus mitigating the threats of resistant bacteria. In the q-s system, veterinarians have to enter all relevant data for each single antibiotic treatment of livestock into the q-s database. All details on this are described in specific guidelines, which are published in the internet. For this, veterinarians have to register in the q-s-system. The analysis of this data by q-s enables veterinarians and livestock keepers to compare the antibiotic treatments with the average of all farms in the q-s system.

If necessary, specific measures can be implemented to reduce the use on antibiotics on a given farm.

Timescale: continuing since 2013

The owners and organisation involved in the project

QS GmbH

<https://www.q-s.de/veterinarians/antibiotics-monitoring-veterinarians.html>

National Animal Health Monitoring System



- ▶ To measure management practices (including antimicrobial drug use) and antimicrobial resistance on-farm by production class to evaluate changes over time in the context of on-farm conditions.

USDA's Animal and Plant Health Inspection Service's National Animal Health Monitoring System (NAHMS) commodity studies distribute questionnaires to U.S. livestock, poultry, and aquaculture farmers to establish nationally representative estimates of management practices and operation/animal characteristics.

NAHMS performs a study in each major commodity at 5- to 7-year intervals. With regard to antimicrobial resistance, in recent years NAHMS studies gather information about general farm policy and management practices related to reasons for use, antimicrobial class, and delivery route. Surveys participation is voluntary. In some cases information collected is protected by Title 7, U.S. Code, Section 2276 and the Confidential Information Protection and Statistical Efficiency Act which prohibits public disclosure of individual information. Also, personal data, including reported data, is protected from legal subpoena and Freedom of Information Act requests. Through confidentiality protections and collection of animal health data shared with producers, NAHMS usually gains enough volunteer participation to generate estimates reflecting at least 70% of the Industry.

NAHMS studies incorporate collection of biological samples from animals or their environment and may collect individual animal data. For many years, fecal samples were collected to isolate important pathogens/commensal bacteria to determine the

presence of antibiotic resistance. The repeated nature of NAHMS studies has allowed an examination of patterns over time. Finally, NAHMS studies evaluate preserving animal health on farms, which may reduce the need to use antibiotic drugs to prevent, control, or treat disease.

Furthermore, the data allow direct evaluation of associations between management practices (including antibiotic drug use) and AMR as well as animal health observed in the farm setting. Such information is important in identifying potential strategies to be employed in stewardship programs.

Timescale: ongoing

The owners and organisation involved in the project

United States Department of Agriculture
http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth/sa_monitoring_and_surveillance/sa_nahms/

Determining the AMR profile of foodborne pathogens by genome sequencing



- ▶ This project seeks to determine various genetic features such as typing, virulence and AMR markers through real time whole genome sequencing of food pathogens, coupled to bioinformatic pipelines. A standardized genomic analysis report detailing the genetic profile of the isolate will be produced for risk assessment and surveillance purposes.

The Canadian Food Inspection Agency (CFIA) food microbiology testing programs are implementing whole genome sequencing (WGS) as an alternative to traditional procedures to identify and characterize bacterial isolates recovered from food inspection samples. WGS provides a “one test fits all” approach for the high-resolution characterization of bacteria which can replace current biochemical, serological and molecular techniques. The analysis of WGS data yields critical information for risk assessment and surveillance purposes, such as determination of typing, virulence and AMR marker profiles.

The CFIA has developed practical WGS procedures that can be completed within the timeframe of a food safety investigation to provide critical laboratory evidence supporting regulatory actions. A key output is a standardized report of genomic analysis (ROGA) which presents analytical information in a user-friendly format for ease of use by risk assessors and recall specialists. The ROGA provides a convenient means of transmitting and archiving essential information pertaining to foodborne bacterial isolates. The AMR marker data will be a valuable contribution to national public health surveillance programs seeking to close the gaps in identifying the role of the food production continuum in the emergence of clinically significant AMR bacteria.

The genetic profiles and the standardized report would be useful to other jurisdictions in expediting the analysis and reporting of AMR pathogens in food isolates during outbreaks.

Timescale: 2015–2017

The owners and organisation involved in the project

Canadian Food Inspection Agency,
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Enhancing Food Safety AMR Surveillance



- › The surveillance program will provide bacterial isolates from food safety surveillance to complement national AMR surveillance in the agri-food sector.

The Canadian Food Inspection Agency (CFIA) tests foods for pathogens that are considered to have the greatest potential for health risks and indicator organisms. The isolates recovered from tested fresh fruits and vegetables by the CFIA are further analysed for AMR studies by the Public Health Agency of Canada laboratories.

Under the Pathogen Reduction Initiative, national microbiological baseline studies are conducted for the presence and levels of select pathogens highly important to human health and indicator organisms in poultry and meat at different stages along the agri-food supply. These isolates are tested for AMR and further characterized at the molecular level to enhance food safety AMR surveillance at the national level. In identifying pathogens demonstrating, or at risk of demonstrating AMR, actions could be taken to mitigate the risk. The baseline studies and results of AMR testing of food isolates could be used by other jurisdictions to support a better understanding of AMR in food.

Timescale: ongoing

The owners and organisation involved in the project

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CHAPTER **5**

Support of research and development



- Human Health 
- Animal Health 
- Human and Animal Health 

Research will remain one key strategy to combat the spread and impact of antimicrobial resistance. Antimicrobial resistance resembles a global challenge; likewise, research efforts should be internationally concerted. Fostering exchange among international research groups in the field of AMR will strengthen synergies and avoid duplications of research efforts. In addition, interdisciplinary cooperation between human and veterinary medicine is warranted. The development of novel antimicrobial drugs or alternatives is equally important as research to better understand the emergence of resistance, and its spread across species. Finally, integrated research also needs to address best practices for education and stewardship in a scientific, evidence-based manner.



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EU support to anti-microbial drug development and alternatives



- › The EU is providing financial support to the development of antimicrobial drugs and alternatives through several research programmes, such as the “New Drugs for Bad Bugs” initiative.

In 2012 the “New Drugs for Bad Bugs” (ND4BB) programme was launched within the Innovative Medicines Initiative (IMI)—a Joint Undertaking between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). This has brought together partners from academia, small and medium enterprises (SMEs), regulators, patient organisations and large industry, creating a new model for open innovation in the pharmaceutical research area. ND4BB now funds seven projects with a total committed budget of more than € 650 million.

In 2013, 15 new AMR research projects with a cumulative budget of more than € 90 million were funded by the EU’s Seventh Framework Programme for Research and Technological Development. Seven of the new projects aim to develop novel antibiotics, vaccines or alternative treatments (such as phage therapy) for drug-resistant microbial infections.

In 2015 the European Investment Bank and the European Commission have launched InnovFin Infectious Diseases that will ensure that new drugs, vaccines and medical and diagnostic devices are made available faster to people who need them. These financial products allow projects with a higher risk factor to receive loans. € 150 million has been allocated initially to kick-start the initiative (http://www.eib.org/attachments/documents/innovfin_infectious_diseases_flysheet_en.pdf).

Timescale: multi-annual

The owners and organisation involved in the project

European Commission,
 DG Research & Innovation
 e.g. http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/index_en.html
<http://www.imi.europa.eu/content/nd4bb>

Promoting innovative drug development by the US Government



► **New therapeutics, vaccines, and diagnostics are urgently needed to combat emerging and reemerging antibiotic-resistant pathogens. In response, the United States Government has accelerated efforts to support innovative drug development through new grants and contracts, through public private partnerships.**

The United States Government has accelerated efforts to advance the discovery and development of novel tools to address antibiotic resistance, with special attention to treatment of multidrug-resistant Gram-negative bacteria, as well as tuberculosis (drug sensitive and drug resistant strains). The U.S. is supporting innovators exploring ways to develop new classes of antibiotics as well as new therapies that could potentially replace the use of antibiotics in agriculture and humans. For example:

NIH has been funding the discovery and development of new antibiotics for many years. Recently, NIH-funded researchers discovered Teixobactin, a powerful new candidate antibiotic with a novel mechanism of action that seems to be less likely to promote resistance. This exciting new discovery was made possible by an innovative screening technology that provides access to chemicals produced by organisms found in nature that previously could not be grown in the laboratory. Teixobactin is now undergoing preclinical development at a biotechnology and additional NIH-funded projects are working to extend this screening technology to discover new antibiotic candidates for other problematic resistant bacteria.

The Defense Threat Reduction Agency (DTRA), an agency within the United States Department of

Defense is funding Emergent BioSolutions which has acquired a portfolio of broad spectrum antibiotics including a molecule being developed for use against *B. pseudomallei*.

The Biomedical Advanced Research and Development Authority at Health and Human Services is home to the Broad Spectrum Antimicrobials (BSA) Program which funds public-private partnerships for antibiotic development research.

Timescale: ongoing

The owners and organisation involved in the project

- https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf
- <http://directorsblog.nih.gov/tag/teixobactin/>
- <http://www.phe.gov/ASPRBlog/Lists>

Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)



► JPIAMR pools national research efforts of 17 European countries, Israel and Canada in order to make better use of public R&D resources to address the global challenge of AMR.

As AMR is a global problem which requires consolidation of otherwise fragmented research activities, JPIAMR has been set up, bringing together 17 European countries, Israel and Canada to coordinate their research, in order to allow greater impact and avoid duplication. This initiative that is expanding globally (e.g. in February 2015 Argentina joined as an observer) provides a good basis for developing a global research initiative on AMR, and its Strategic Research Agenda provides an initial framework for a global research agenda to be developed in cooperation with WHO.

JPIAMR has already launched two transnational research calls with a total budget of € 23.5 million to fund research projects that aim to revive neglected and disused antibiotics, improve infection prevention, develop therapies and antimicrobial drugs, and study pharmacokinetics. Additional calls are under development.

Timescale: multi-annual

The owners and organisation involved in the project

European Commission,
DG Research & Innovation
<http://www.jpiamr.eu/>

Research and innovation on the fight against Anti-microbial Resistance



► In front of the current situation, it's essential to provide better structures and to coordinate research and development efforts on AMR.

A research policy dedicated to AMR must take in account to understand and to control. It must structure and coordinate efforts for research, development and innovation on AMR and its consequences, and strengthen research efforts and innovation.

One important measure of France's research programme on antimicrobial resistance is the European Joint Programming Initiative on AntiMicrobial Resistance (JPI-AMR). A wider programme focuses on 'One Health' according to the French Strategic Research Agenda published in March 2015. According to this new policy, the French Strategic Research Agenda published in March 2015 promotes multidisciplinary projects, including the environment, ecosystems, and a holistic approach towards health. Scientific sectors dedicated to health, biology, the environment and human sciences have already published a joint document entitled "Initiative française pour la recherche en environnement et santé" (French environmental and health research initiative).

The Ministry of Research also promotes contributions from scientific teams to:

- JPI-Water (strategic research agenda October 2014), aiming at identifying antibiotic life cycles in the environment.
- One Health zoonose emerging threats European Joint Program (in preparation for 2018)
- EJP Human Biomonitoring Initiative (EHBMI), in preparation for 2017.

Timescale: 2015

The owners and organisation involved in the project

- Ministry of Health
- Regional of Research
- ANSES-National Drugs Agency

Research Area “Anti-microbial Resistance and Nosocomial Infections”



› Supporting research and development is one goal of the German Antimicrobial Resistance Strategy “DART 2020”. The research area “Antimicrobial Resistance, Hygiene and Nosocomial Infections” supports its implementation.

Based on the recommendations of the Joint Scientific Council, the Federal Ministry of Health has established a research area “Antimicrobial Resistance, Hygiene and Nosocomial Infections”. Within this activity 11 projects out of four thematic areas were funded over a period of three years. The projects include results-based intervention studies, the training of specialist staff, model projects for inter-sectoral health care, and the further development of quality assurance.

These projects were an important element in the implementation of the first German Antimicrobial Resistance Strategy “DART”. It is planned to continue the research based on a needs analysis with different projects within the implementation of the further developed DART 2020.

Timescale: 2012–2015

The owners and organisation involved in the project

German Federal Ministry of Health
<http://www.bmg.bund.de/themen/praevention/krankenhausinfektionen/antibiotika-resistenzstrategie.html>

Improving AMR research capability



- › The UK's priority has been to establish new mechanisms to improve collaboration between research bodies with expertise on AMR and to fund new research spanning both human and animal health.

The UK has established a new AMR Research Funders Forum, led by the UK Medical Research Council, bringing together major research funders and government departments to promote joint action to better understand the relationship between AMR in animals and humans. The Funders Forum, which is convened by the UK Medical Research Council has an investment of approximated £27.5m currently.

The purpose of the Forum is to provide a strategic overview of the UK AMR research base with an understanding of its output, skill base, resources and impact to create a common vision for the future of AMR research and its implementation; to add value to existing programmes of work through coordination, synergy of activities and gap awareness; to coordinate and/or support the initiation of unilateral, bilateral or multilateral funding and delivery programmes, and to raise the understanding and profile of AMR research base in the UK and internationally through proactive communication with all stakeholders.

The UK has established two National Institute for Health Research (NIHR) Health Protection research Units (HPRUs) with a focus on Healthcare Associated Infections (HCAIs) and AMR, to lead on research to support the development of effective approaches to combat AMR. Of equal magnitude and size the Scottish Government has established SHAIPi (Scottish HAI Prevention Institute) to develop new interventions to reduce healthcare associated infections and AMR.

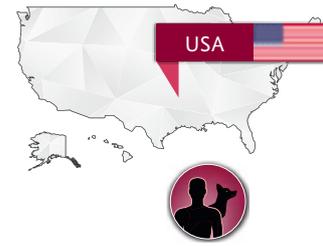
In the veterinary sector, Defra (UK ministry of agriculture) and the Veterinary Medicines Directorate funds research on AMR in animals, as well as contributing to the Research Funders Forum.

Timescale: ongoing

The owners and organisation involved in the project

UK Department of Health & Medical Research Council

International S&T Collaboration



› Through international collaboration on s&t, improve domestic and global capacity to implement evidence-based, contextually adapted interactions to combat the emergence and spread of antimicrobial resistance.

International Collaboration: Collaboration between nations and among all stakeholders is foundational to successful advancement in addressing the research and development needs to combat the emergence and spread of antimicrobial resistance. Examples of effective U.S. approaches to research collaboration across nations include:

Scientist to Scientist Research Collaborations: U.S. Departments and Agencies participate in and/or support international research partnerships. Examples include

- USDA Agriculture Research Service International Research Partnerships:
<http://www.ars.usda.gov/Research/docs.htm?docid=22827>
- National Institute of Allergy and Infectious Diseases' Antimicrobial Resistance Program:
<http://www.niaid.nih.gov/topics/antimicrobialresistance/Pages/default.aspx>

Multilateral Research Efforts:

- The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) to promote information exchange, coordination and co-operation to address urgent AMR issues through enhanced dialogue.
<http://www.cdc.gov/drugresistance/tatfar/>

Science Policy Advocacy and Coordination. The U.S. incorporates AMR into dialogues on implementation of binding bilateral and multilateral Science and

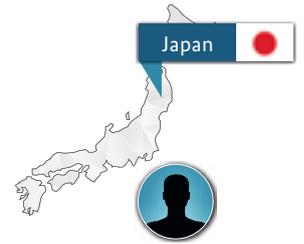
Technology Agreements as well as science policy dialogues with partner countries and organizations. Advocacy for AMR research through these policy forums helps to raise the priority of AMR research and improve S&T coordination and collaboration.

Timescale: ongoing

The owners and organisation involved in the project

Multiple Federal Departments and Agencies

Research Program on Emerging and Re-emerging Infectious Diseases



- › The objective is to protect both Japanese citizens and people worldwide from infectious diseases including drug-resistant bacteria. The Japanese Government will strengthen measures to combat infectious diseases by promoting research based on collaboration among various ministries, and will ensure more efficient and effective linkages of these results into the development of therapeutic drugs, diagnostics, and vaccines.

The committee for innovation and development of novel antimicrobials was established in 2013. The members of the committee consist of researchers from the academia, government officials and pharmaceutical company employees. The Japanese Society of Chemotherapy, one of the main bodies that launched the committee, the Japanese Association for Infectious Diseases, the Japanese Society for Clinical Microbiology, the Japanese Society for Infection Prevention and Control, the Japanese Society for Bacteriology, and the Pharmaceutical Society of Japan published a proposal for the development of new antimicrobials in 2014. In this proposal, the six societies clearly stated the way for Japan to proceed to the development of new antimicrobial agents.

Specifically, it has called the public for understanding about the need for new therapeutic agents for infectious diseases. It also asked the Japanese Government to execute measures to promote development of antimicrobial agents. For the pharmaceutical companies, it recommended that they establish a system of coordination of companies, academic societies, the government, and universities, united as “ALL JAPAN”, to promote the development of antimicrobials. To universities and research institutions, it called for the promotion of research to search for candidates for novel antimicrobials.

Currently, the Ministry of Health, Labour and Welfare, the Ministry of Education, Culture, Sports, Science and Technology, and the Japan Agency for Medical Research and Development are conducting a collaborative research project to construct a whole-genome database for drug-resistant bacteria and aim to identify drug target sites and develop new therapeutics and rapid diagnostics.

Timescale: Started in April 2015

The owners and organisation involved in the project

- Ministry of Health, Labour and Welfare Japan (MHLW)
- Ministry of Education, Culture, Sports, Science and Technology Japan (MEXT)
- Japan Agency for Medical Research and Development (AMED)

Antimicrobial Resistance Research



› Conserving the effectiveness of existing treatments through research, infection prevention and control guidelines, education and awareness, regulations and oversight.

Antimicrobial resistance (AMR) is a top research priority for the Government of Canada. The Canadian Institutes of Health Research (CIHR) has invested \$93.8M(CAD) from 2009 to 2014 in research on AMR with additional funding confirmed in the 2015 Government of Canada's budget.

The Government of Canada, through CIHR, holds an international leadership role, as a member of the Joint Programming Initiative on AMR (JPIAMR), working with 20 countries from across the globe to define strategic and scientific priorities benefiting from collaboration and national funds to achieve long-term reductions in AMR levels. In April 2015, CIHR announced an investment of \$4 million (CAD) to support Canadian researchers working with international partners on six JPI AMR projects that focus on identifying new targets for AMR drug development, new approaches to treating drug-resistant bacterial infections, and methods for preserving the effectiveness of existing antibiotics. Canada is the largest funder of the call.

Further, in 2013–2014, CIHR invested \$1M(CAD) in stewardship projects and that amount has been steadily increasing every year over the last 5 years. CIHR is funding and will continue to fund various projects that aim at evaluating or improving current practices in the prescribing of antimicrobials. Examples of funded projects are: 1) dissemination of AMR Stewardship Programs implemented in hospitals and reporting early outcomes and results

of the intervention; 2) Café Scientifique which put together a panel of experts to stimulate discussion regarding the impact of widespread antibiotic use on the health of Canadians and local agricultural practices; 3) dissemination of knowledge on prevention and treatment of community-acquired methicillin-resistant *Staphylococcus aureus* and skin and soft tissue infections.

Timescale: 2015 and ongoing

The owners and organisation involved in the project

Canadian Institutes of Health Research (CIHR)

AMR and animal health related research



› Research to optimize animal husbandry, monitoring and feedback, diagnostics and targeted treatment with antibiotics. Approaches for agricultural livestock farming to reduce the occurrence of resistant bacteria.

There are two major approaches for agricultural livestock farming to reduce the exposure of consumers to resistant bacteria and their resistance characteristics from livestock farming:

1. Reducing the occurrence of resistant bacteria in livestock farming through preventive measures to maintain the health of animal stocks without antibiotics
2. Preventing the transmission of resistant bacteria along the food chain.

Examples on research addressing approach 1 are:

- Examining the influence of improved farming systems and animal breeding measures on animal health and thus on the use of drugs in livestock farming
- Examining the dynamic of resistances in the microbiome of farm animals within different age and production type groups
- Examining the influence of different treatment methods in diseased animals on the development of resistance in treated animals and the other animals in the stock
- Further developing vaccines and vaccination programmes to maintain the health of animal stocks and control infections which acts as pacesetters for secondary bacterial infections
- Developing additional benchmarking systems to assess animal health in livestock in the sense of an animal health index which supplements the system of recording the frequency of treatment.

Examples on research addressing approach 2 are:

- Developing improved measures to prevent the transmission of zoonotic pathogens and other resistant bacteria in food production and processing
- Examining the particular significance of cross-border trading within the scope of international commodity chains for food and animal feed for the spread of resistant pathogens and resistance characteristics
- Examining possible positive effects of bacteriophages and other substances to reduce or eliminate bacteria on carcasses as a supplement to process hygiene.

See also next steps in veterinary medicine and agriculture under Goals 3 and 6 of DART 2020: <http://www.bmel.de/SharedDocs/Downloads/EN/Publications/DART2020.html>

Timescale: next 5 years

The owners and organisation involved in the project

Federal Ministry of Food and Agriculture and stakeholders

USDA-NIFA Agriculture and Food Research Initiative (AFRI) program



- ▶ The National Institute for Food and Agriculture funds integrated research, education, and extension grants focusing on science that dictates action in the field of AMR addressing key problems of national, regional, and multi-state importance in sustaining all components of agriculture.

USDA's National Institute of Food and Agriculture (NIFA)'s flagship competitive Agriculture and Food Research Initiative (AFRI) program is charged with funding integrated research, education, and extension grants that address key problems of national, regional, and multi-state importance in sustaining all components of agriculture.

AFRI identifies programmatic challenges such as Food Safety where the antimicrobial resistance (AMR) program resides. AFRI solicits applications across the country through publicly released Request for Applications (RFAs). All applications are subjected to a competitive peer review process to select the most competitive projects. For the AMR program, projects must address any combination of the agricultural missions: research, education and extension/outreach. The best project proposals will include a team of scientists including social and behavioral, are multi-disciplinary in nature and may include international and private/public sector collaborations.

AFRI's AMR program goes where the latest and best science dictates action, for example, it covers the entire food continuum, from primary producers to primary consumers to include crops and food animals. USDA's AFRI program supports international workshops/conferences to facilitate professional interactions and dialogue among the best and the brightest scientists in order to facilitate, advance

and enhance the reach of outcomes, outputs and impacts. Peer reviewers are drawn from various sectors of society including public, private, and government. Stakeholder input is solicited in each RFA. Input can be submitted at any time through one-on-one interactions with agency personnel or electronic submissions to an established mail box. Funded projects for the FY 2014 AMR program can be found at:

<http://nifa.usda.gov/press-release/usda-awards-36-food-safety-grants-including-67-million-antimicrobial-resistance>.

Timescale: ongoing

The owners and organisation involved in the project

United States Department of Agriculture
<http://nifa.usda.gov/program/afri-food-safety-challenge-area>

Antimicrobial resistance beef safety research



- › The National Cattlemen’s Beef Association as a contractor to the Beef Checkoff through contracts with various universities, USDA-ARS laboratories and private research companies fund research to better understand factors that influence resistance formation and mechanisms to prevent it across bacterial species linked to food safety.

Research conducted over last 10+ years has produced over 60 project reports. The beef producers have allocated over \$17 million to fund beef safety research in this time. These projects on antimicrobial resistance represent over 30% of all research funds available for beef safety during this time (other research conducted addressed other industry needs like E. coli O157:H7, other shiga-toxin producing E. coli and Salmonella reductions).

Please see www.beefresearch.org and the beef safety section. Search for “antimicrobial resistance” for links to project summaries on this topic.

Timescale: Research conducted over last 10+ years

The owners and organisation involved in the project

National Cattlemen’s Beef Association as a contractor to the Beef Checkoff (www.beefresearch.org) through contracts with various universities, USDA-ARS laboratories and private research companies.

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