



Federal Ministry
of Health



G7 GERMANY 2015

Combating Antimicrobial Resistance

Examples of Best-Practices of the G7 Countries

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Dear Readers,



Antimicrobial Resistances (AMR) are an urgent public health threat for both developed and developing countries. They lead to prolonged treatment times, higher mortality, high burden on health systems and high economic impact. Tackling AMR requires a multisectoral approach, encompassing all areas—human and animal health as well as agriculture and the environment. It also needs international efforts as AMR do not stop at borders.

The Global Action Plan of the World Health Organization (WHO) that was adopted by the World Health Assembly in May 2015 takes this One Health approach into account and provides the frame for further action.

Combating AMR is a high priority for Germany. Therefore it was taken up as one of the health topics of the G7-summit in Elmau in June 2015. The G7 strongly support the WHO Global Action Plan and agreed to foster the prudent use of antibiotics and to engage in stimulating basic research. The Global Action Plan calls for the development of National Strategies by all countries within the next two years. The G7 will develop or review, operationalize and share their national action plans.

Following this decision the updated German National Resistance Strategy DART 2020 was released in May 2015. In the implementation of the previous strategy Germany started several activities and projects that as a bundle contribute to the reduction of AMR.

These activities include for instance the set-up and expansion of surveillance systems, measures on infection prevention and the responsible use of antibiotics, the support of research and development and measures to strengthen the One Health approach. The other G7 partner countries have also examples of successful initiatives.

Combating AMR also means to learn from each other and to share experience to strengthen our own efforts in the fight against AMR. This brochure compiles best practice models from all G7-Partners, covering multiple areas. It forms a basis for discussing at the G7-Health Ministers conference in October 2015 in Berlin but is also intended to be used afterwards in the context of the implementation of the WHO Global Action Plan.

A handwritten signature in blue ink, appearing to read 'Hermann Gröhe', written in a cursive style.

Hermann Gröhe MdB
Federal Minister of Health



Dear Readers,

We can only be successful in combating antibiotic resistance if both human and veterinary medicine work closely together. As Germany's Minister of Agriculture, I am therefore only too happy to make my contribution to the topic of 'antibiotic resistance', which the G7 Health Ministers are placing at the centre of their conference. Our joint effort in the spirit of the 'one-health' approach will thus empower us to fulfil our responsibility for human and animal health.

In the area of veterinary medicine, many states, including Germany, were quick to recognise the writing on the wall and put strategies in place to reduce antibiotic resistance. Since 2002, veterinarians in Germany are no longer allowed to dispense or prescribe antibiotics for treatment periods exceeding seven days. The year 2011 saw the introduction of the requirement that the amounts of antibiotics dispensed by veterinarians must be recorded. One important milestone was the launch, in 2014, of the antibiotics minimisation concept for animal husbandry that was legally established in the 2013 Medicinal Products Act.

The Federal Government has been pursuing the 'one-health' approach for quite some time. In the year 2008, for example, we set up the interministerial German Antibiotic Resistance Strategy (DART) that created the foundation for human medicine, veterinary medicine, agriculture and scientific research to work closely together so as to further reduce the use of antibiotics. We are steering the right course here and we will continue to pursue this course consistently with DART 2020.

However, we do not intend to rest on our laurels. Our goal is to limit the use of antibiotic veterinary medicinal products to the minimum and thus continue reducing the risk to the well-being of human beings and animals that is associated with antibiotic resistance. I wish to extend my sincere gratitude to everyone who is contributing to the fulfilment of this demanding task!

A handwritten signature in blue ink, appearing to read 'Christian Schmidt'.

Christian Schmidt MdB
Federal Minister of Food and Agriculture

Dear Readers,



WHO warmly welcomes this G7 joint effort, led by Germany, to combat the rise of antimicrobial resistance. The initiative sets in motion actions recommended in the WHO Global Action Plan on Antimicrobial Resistance, approved by the World Health Assembly in May 2015. It rightly recognizes that combatting antimicrobial resistance must engage society and multiple sectors of government, including veterinary medicine and agriculture, and illustrates how this is being done.

The brochure provides a compendium of best practices in Europe, Canada, Japan, and the USA, and a menu of policy options that can be used by other countries. Options covered include strategies for enhanced surveillance, regulation of the use of antibiotics in veterinary medicine, national campaigns to promote prudent and appropriate use, and initiatives to prevent infections in the first place, especially in intensive care units and surgical wards.

Taking an international approach is imperative. Drug-resistant pathogens are notorious globe-trotters. The growth of medical tourism has accelerated the international spread of hospital-acquired infections that are frequently resistant to multiple drugs.

I cannot overstate the urgency of actions being undertaken by G7 countries. Antimicrobial resistance is now regarded as a major health and medical crisis. Highly resistant “superbugs” haunt emergency rooms and intensive care units around the world. Gonorrhoea is now resistant to multiple classes of drugs. An epidemic of multidrug-resistant typhoid fever is rolling across parts of Asia and Africa. Even with the best of care, only around half of all cases of multidrug-resistant tuberculosis can be cured.

With few new antimicrobials in the pipeline, the world is heading towards a post-antibiotic era when common infections will once again kill. A post-antibiotic era means, in effect, an end to modern medicine as we know it. Some sophisticated interventions, like joint replacements, organ transplantation, cancer chemotherapy, and care of preterm infants, would become far more difficult or even too dangerous to undertake.

Dr Margaret Chan
Director-General of the World Health Organization

Introduction

When Alexander Fleming won the Nobel Prize for the discovery of penicillin and its curative effect in various infectious diseases in 1945, he was already aware that this powerful medical tool could easily become weak. “Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs. X dies,” he explained in his Nobel Lecture. The researcher knew that in the laboratory, it was not difficult to make microbes resistant to penicillin by exposing them to concentrations not sufficient to kill them. “And the same thing has occasionally happened in the body,” he told the audience.

70 years later, antimicrobials still play a crucial role for the current and future success of human and veterinary medicine. However, the number of bacterial pathogens that have become less susceptible or even completely resistant to antibiotics is increasing—essentially due to broad and inappropriate use of antibiotics. Antimicrobial resistance (AMR) has become a major challenge for modern medicine worldwide, affecting humans and animals alike. Each year, hundreds of thousands of people are getting infected with pathogens in connection with inpatient medical treatment worldwide. Too many of them die. Around one third of these infections could be avoided if suitable measures were taken. Resistant pathogens play a particularly important role here, since the treatment options are limited. The current situation shows that the fight against antibiotic resistance is still not being tackled with the necessary urgency worldwide. Awareness of the problem still needs to be improved in various areas.

The Joint Efforts to Combat Antimicrobial Resistance (AMR) formulated in the annex of the Leaders’ Declaration of the G7 Summit in June 2015 summarize the crucial steps to meet this challenge. Among them is the necessity to identify and share best practice examples, providing information on existing programs as well as most successful strategies to prevent avoidable infections and promote the responsible use of antibiotics.

This publication contains best practice examples from G7 countries. It presents some of the existing experience in combating antimicrobial resistance other countries might benefit from. At the World Health Assembly in May 2015 Member States of the WHO committed to develop national action plans on AMR within two years. This best practice brochure aims to contribute to the further development and implementation of the respective national action plans on antimicrobial resistance.

All countries must increase their efforts: They must further develop their concepts and strategies, and expand their measures already in use. The best practice examples presented in this booklet document initial successes for further efforts to build-on. Let us take the opportunity to learn from each other!

The best practice examples are categorized by five subsectors:

1**Strengthening the One Health approach**

Animals and human beings are often infected by the same pathogens, treated with the same antibiotics and thus have a mutual influence on the problems of resistance. All sectors need to work closely together in order to protect the health of both people and animals and to maintain the effectivity of antibiotics.

2**Combating and preventing infections**

by raising awareness of antimicrobial resistance and deepening the knowledge of infection prevention and control—not only among human and animal health professionals but also among the general public.

3**Promote the responsible use of antibiotics**

by committing to use them only for therapeutic reasons after individual diagnosis, and under supervision of health professionals in compliance with legislation. Implementation of stewardship programmes for healthcare professionals as well as livestock producers.

4**Strengthening the surveillance system**

for existing and emerging patterns of antimicrobial resistance and antibiotic use in medical, veterinary and agricultural settings in order to fill knowledge gaps and develop effective strategies to fight AMR.

5**Support of research and development**

by increasing basic research, epidemiological research as well as the development of and access to new antimicrobials, treatment alternatives and rapid diagnostic tools.

CHAPTER **1**

Strengthening the One Health approach

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Pages 12, 20, 21



Page 11



Human, animal and environmental health is inextricably linked. The development of antimicrobial resistance can therefore only be tackled with a cross-sectoral approach: the One Health approach. Building a bridge between public health, health care, animal health and the agricultural sector is essential and has to be improved in all fields (politics, economics, and research) and on all levels (international, national, and local). Setting up national action plans on antimicrobial resistance, for example, requires the collaboration of stakeholders from all relevant areas. Furthermore, research associations should bring together scientists of different sectors by investigating antimicrobial resistance in humans, animals, food and the environment. A common, worldwide approach only can bring about a long-lasting change in the situation.

A world map is shown in a light, semi-transparent style. Three callout boxes are overlaid on the map, each pointing to a specific region. The first callout box, located over Central Europe, contains the text 'Pages 14, 15, 16' and a small German flag. The second callout box, located over Western Europe, contains the text 'Pages 17, 19' and a small European Union flag. The third callout box, located over Southern Europe, contains the text 'Page 18' and a small Italian flag.

Pages 14, 15, 16

Pages 17, 19

Page 18

Federal Framework and Action Plan on AMR



► **The purpose of the Federal Framework is to identify key government of Canada areas of focus and map out a multi-sectoral, coordinated, collaborative approach by federal departments to respond to the threat of AMR. Building on the framework, the Action Plan identifies concrete commitments and activities that will be undertaken by key federal departments.**

In 2013, Government of Canada departments identified the need for better coherence, collaboration and coordination in preventing, limiting and controlling the emergence and spread of AMR in Canada. Specifically, there was a need to bridge between public health, health care, animal health and agri-food sectors for a more integrated approach.

In October 2014, The Government of Canada released Antimicrobial Resistance and Use in Canada: A Federal Framework for Action which takes a One Health approach to antimicrobial use (AMU) and AMR. The Framework maps out surveillance, stewardship and innovation as key areas of focus and identifies the roles and responsibilities of key federal departments in terms of both human and animal health.

The Action Plan released in March 2015 builds on the strategic areas of focus and priority action items outlined in the Framework. It identifies specific actions that will be undertaken by the Public Health Agency of Canada, Health Canada, the Canadian Food Inspection Agency, the Canadian Institutes of Health Research, Agriculture and Agri-Food Canada, the National Research Council, and Industry Canada.

In addition, the Government of Canada is committed to taking a leadership role both nationally and internationally. Leveraging the Federal Framework,

formal governance with provinces and territories, and relationships with human and animal health sectors, it continues to bring together all sectors to take an objective and integrated approach to the development of a pan-Canadian framework on AMR. International efforts include policy discussions with leading countries and partner organizations, and the provision of technical expertise to human and animal health working groups, particularly in the areas of surveillance.

healthycanadians.gc.ca/antibiotics

Timescale: 2015–2019

The owners and organisation involved in the project

Public Health Agency of Canada
Lianne Bellisario
613-863-1588
lianne.bellisario@phac-aspc.gc.ca

2011–2016 National Antimicrobial Alert Plan



› The third plan is a continuation of effective, recognised actions existing in the two previous plans. It stresses the need for good patient care. This requires that the professional have the tool to make the right choices, but also that he/she be trained in the specific aspects of bacterial infections, antibiotic use and resistance phenomena.

In 2002, the French Minister of Health launched a national plan to preserve efficacy of antibiotics, which was renewed from 2007 to 2010, the objectives were to increase awareness of Public and health professionals and to promote good antibiotic prescription.

The 2011–2016 “National Antimicrobial Alert Plan” is pursuing actions initiated under previous plans with the addition of some major new initiatives, in particular a target of reducing antimicrobial prescriptions by 25% over a five-year period, to be nearest of the European average of antibiotic consumption. The other goals of this third plan, are in particular to set up a network of dedicated professionals for helping GPs in order to improve the prescription of antibiotics.

In 2015, Minister Touraine installed a group of experts chaired by Jean Carlet to propose recommendations on the preservation of antibiotics. This report outlined 4 areas of action: establish a national coordination to tackle AMR, encourage research and development in the field of AMR, involve the civil society and promote a specific status for antibiotics.

A specific plan known as Ecoantibio 2012–2017 was drawn up for veterinary medicine. It focuses on: good practices for prescribing antibiotics by veterinarians; information and awareness raising

among veterinarians, farmers and owners of animals on the good use for animals; as for human medicine, there is a quantitative objective to decrease the consumption of antibiotics by 25% in five years; there are also qualitative objectives focused on reducing the use of critical antibiotics in veterinary medicine (focussing on fluoroquinolones, cephalosporins 3–4).

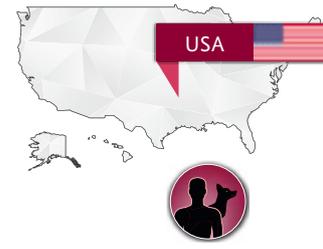
Legislative measures have been taken to reach the goals set in the national plan for veterinary antibiotics, particularly regarding antibiotics of critical importance. When taking all animal species into account, overall exposure to antimicrobials for 2013 fell by 7.3% as compared to 2012.

Timescale: 2012–2017

The owners and organisation involved in the project

- Ministry of Health
- National Drugs Agency
- National health insurance
- ANSES—French Agency for Food, Environmental and Occupational Health & Safety
- Ministry of Agriculture

National Strategy for Combating Antibiotic-Resistant Bacteria (CARB)



- › To prevent, detect, and control illness and death related to infections caused by antibiotic-resistant bacteria, mitigate the emergence and spread of antibiotic resistance, and ensure the continued availability of therapeutics for the treatment of bacterial infections, through domestic and international whole-of-government and whole-of-society approaches.

In December 2013, President Obama called for an assessment of the current and growing threat of antibiotic resistance and the development of a multi-sectoral plan to combat resistant bacteria. Federal Departments and Agencies worked together with input from outside the government to develop practical, evidence-based ways to enhance antibiotic stewardship, strengthen surveillance for antibiotic resistance and use, advance the development of new diagnostics, antibiotics, and novel therapies, and accelerate research and innovation. On September 18, 2014 President Obama launched a comprehensive set of national measures to combat antibiotic-resistant bacteria. These include Executive Order 13676; the National Strategy on Combating Antibiotic-Resistant Bacteria; a \$20 million prize to facilitate the development of rapid diagnostic tests for healthcare providers; and the President's Council of Advisors on Science and Technology report on Combating Antibiotic Resistance. On March 27, 2015 the Administration released the National Action Plan for Combating Antibiotic-Resistant Bacteria, which outlines steps for implementing the National Strategy and addresses recommendations of the PCAST report. In June 2015 White House convened a Forum on Antibiotic Stewardship at which over 150 major food companies, retailers, and human and animal health stakeholders announced commitments to combat antibiotic resistance.

This national effort is already showing successes in preventing the spread of infections, strengthening one health surveillance efforts, developing regulatory pathways to facilitate innovative diagnostics, and accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines. The development of this successful approach required leadership from the White House and wide working level engagement including health, agriculture, policy, economic, defence, foreign relations, and budget experts.

Timescale: Three implementation periods of one, three, and five years.

The owners and organisation involved in the project

- National Strategy for Combating Antibiotic-Resistant Bacteria, Sept. 2014 https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf
- National Action Plan for Combating Antibiotic-Resistant Bacteria

One Health and AMR



- ▶ To slow development and spread of AMR, the UK Government published the 'UK Five Year Antimicrobial Resistance Strategy 2013-2018', in September 2013. The Strategy takes a 'One Health' approach; acknowledging that effective progress can only be achieved by close collaboration between medical, veterinary, food and environment sectors. An update on progress so far and an Implementation Plan setting out activity over the next four years has been published in December 2014. Further progress reports will follow annually.

UK has developed a comprehensive human health surveillance programme (the English surveillance programme for antimicrobial utilisation and resistance or ESPAUR) which tracks prescribing and resistance trends in England. The first report was published in October 2014.

UK veterinary surveillance incorporates antibiotic sensitivity testing of bacteria from healthy animals (since 2014) and from clinical veterinary cases (since 1998), and reports the total quantity of antibiotics sold by veterinary pharmaceutical companies (since 2005). These data have been reported together since 2013 in the annual Veterinary Antibiotic Resistance and Sales Surveillance report, (UK-VARSS). The UK is currently working to establish systems for surveillance of antibiotic consumption in animals.

The UK's One-Health report (<https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals>) brings together and compares the most recently available UK data on antibiotic resistance and antibiotic use in both human and veterinary sectors. It was published for the first time in July 2015 and will be updated every two years.

The UK produced guidance by various British Veterinary Associations and by the Responsible Use of Medicines in Agriculture Alliance (RUMA) to inform their members about responsible prescribing.

The UK is working to develop potential projects in the animal health sector involving AMR standards into day-one-competences (essential competences required for vets students to register as a veterinary surgeon (this is in conjunction with the Royal College of Veterinary Surgeons).

Timescale: ongoing

The owners and organisation involved in the project

Department of Health
 Veterinary Medicines Directorate:
<https://www.gov.uk/government/organisations/veterinary-medicines-directorate>

GERMAP



› GERMAP is a report that provides a summary of data on the consumption of antimicrobials and the extent of resistances against antimicrobials in human and veterinary medicine.

GERMAP is a report that provides a summary of data on the consumption of antimicrobials and every two years the extent of resistances against antimicrobials in human and veterinary medicine. It is compiled by an expert group from human and veterinary medicine and is updated every second year. It is a basis for risk assessment and supports the development of treatment-guidelines for both humans and animals.

Results from the recent report (GERMAP 2012): In human medicine, broad spectrum antimicrobials, especially cephalosporins and fluoroquinolones, still have a large share of the overall consumption of antimicrobials. This applies for ambulatory as well as in-patient treatments. As it is known, both antibiotic classes select for multi-drug resistant bacteria more than most other classes. A reduced use of cephalosporins and fluoroquinolones for therapy in both sectors therefore must be a goal with high priority.

Furthermore the use of antimicrobials can be reduced in prophylaxis, especially when peri-operative prophylaxis continues too long after surgery. In the ambulatory sector the use of antimicrobials against acute respiratory diseases must be reduced. In the veterinary sector reliable data on the sales of antimicrobials in 2011 were available for the first time.

The development of resistances in bacteria pathogenic for animals is characterized by increasing rates of ESBL-producing bacteria and MRSA. The recent

isolation of carbapenemaseproducing bacteria from animals is proof that a transfer of resistant bacteria or resistance genes between humans and animals is possible in both directions.

Timescale: since 2008, ongoing

The owners and organisation involved in the project

- Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienstsitz Berlin
Mauerstraße 39–42, 10117 Berlin
www.bvl.bund.de
- Paul-Ehrlich-Gesellschaft für Chemotherapie e.V.
Campus Hochschule Bonn-Rhein-Sieg
Von-Liebig-Straße 20, 53359 Rheinbach
www.p-e-g.org
- Infektiologie Freiburg
Medizinische Universitätsklinik
Zentrum Infektiologie und Reisemedizin
Hugstetter Straße 55, 79106 Freiburg
- <http://www.p-e-g.org/econtext/germap>

RESET



- › **1. To determine the prevalence of ESBL-producing bacteria in humans (hospital, ambulant, community), animals (livestock, pets), animal food and the environment (wastewater). 2. To identify the respective resistance genes and analyse their transferability between enterobacteriaceae. 3. To compare genetic relationship of bacterial isolates and resistance gene carrying plasmids in different settings (human, animal, environment) to evaluate the transmission pathways of ESBL-resistance.**

The RESET project is funded by the Federal Ministry of Education and Research and its aims are in the scope of the German Antimicrobial Resistance-Strategy DART2020. Ten project partners including public health institutes and universities of human and veterinary medicine as well as hospitals of human medicine and veterinary medicine are involved in the RESET project. In the first period of the project (2011–2013) the project partners conducted different studies to determine the prevalence of fluoroquinolone resistance and cephalosporin resistance (ESBL production) in *Escherichia coli* from humans (hospitalised patients, outpatients, healthy persons), animals (livestock and pets), animal food and environment (wastewater, shed environment). In the second period of the project the genetic relationship of the collected isolates will be compared in detail to evaluate transmission pathways.

Further, special studies e.g. on the risk of infection with ESBL-producing bacteria after previous ESBL-colonization will be conducted. First results showed a high prevalence of ESBL-producing *E. coli* in livestock animals (>50%) and in a certain amount of healthy humans (6%). The vast majority of ESBL-*E. coli* from humans produce CTX-M-15 but in animals this

enzyme type is rare. This indicated a human reservoir and a selection of these resistant bacteria by antibiotic use in human medicine. However, other ESBL-variants, e.g. CTX-M-1 and CTX-M-14, are frequently present in *E. coli* from humans and animals—here a detailed genome-based comparison is in progress to evaluate possible transmission routes between animals, food and humans or to identify potential reservoirs of multidrug-resistant bacteria.

Timescale: 2011–2016

The owners and organisation involved in the project

Institut für Biometrie, Epidemiologie und Informationsverarbeitung
 Prof. Dr. Lothar Kreienbrock
 Stiftung Tierärztliche Hochschule Hannover
 Bünteweg 2
 30559 Hannover
www.reset-verbund.de

MedVet-Staph



- 1. To identify the risk MRSA which emerged in livestock and companion animals pose to humans. 2. To identify the contribution of clinically relevant antibiotic resistance genes contained by staphylococci from animals to antibiotic resistance development in staphylococci of human. 3. To further develop targeted antibiotic resistance surveillance as well as strategies for diagnostics, intervention, and therapy as one health approach.

The MedVetStaph project cluster is funded by the German Ministry of Education and Research and focusses on antibiotic resistance in staphylococci, in particular methicillin resistant *Staphylococcus aureus* (MRSA). The results from this work are translated to the German Antibiotic Resistance Strategy (DART). The cluster consortium consists of 11 partners from human and veterinary medicine in the academia and federal institutions, as well as one company developing tools for rapid diagnostics.

Data from molecular epidemiology based interdisciplinary studies reveal that livestock associated MRSA are able to cause the same kind of infections in humans as *S.aureus* and MRSA in general. They can be introduced to hospitals and cause nosocomial infections there. For this reason screening for MRSA colonization at admittance to hospitals is recommended for farmers and veterinarians with livestock contacts. Although LA-MRSA (> 80%) are multi resistant to several antibiotics there are still sufficient treatment options. Intrahospital dissemination in the absence of sufficient hygiene has only rarely observed for LA-MRSA so far. The proportion of LA-MRSA among all MRSA from nosocomial infections in all Germany is about 3%. This is, however, different in geographical areas with

comparative high density of conventional farms where it amounts up to 10% for MRSA from septicemia and 15% for MRSA from wound infections. This observation should be taken into consideration for future livestock farming and structural planning in rural areas. Comparative genome analysis shows that LA-MRSA have evolved from human adapted methicillin susceptible *S.aureus*, the jump to livestock was obviously associated with several genetic changes. Reversion of them and re-adaptation to humans is currently studied in more detail. It bears a potential health risk and needs tight surveillance and coordinated intervention for which the established network of efficient cooperation is a promising start.

Timescale: 2011–2016

The owners and organisation involved in the project

Institut für Hygiene, Dr. Robin Köck
 Universitätsklinikum Münster
 Robert-Koch-Str. 41, 48149 Münster
www.medvetstaph.net/

European Commission Action Plan on AMR



› Setting out priorities and concrete actions for tackling antimicrobial resistance at EU level, based on a holistic and multi-sectorial approach.

Antimicrobial resistance is a priority for the European Commission with initiatives developed over the past decades in both human and veterinary medicine. To further strengthen its commitment, the Commission launched in November 2011 a 5 year Action Plan against Antimicrobial Resistance, to be implemented in close cooperation with the EU Member States.

The Plan is based on a holistic approach involving all sectors and aspects of antimicrobial resistance (public health, animal health, food safety, consumer safety, research, non-therapeutic use of antimicrobials, etc.). It aims at strengthening the prevention and control of antimicrobial resistance across the sectors and at securing the availability of effective antimicrobial agents. The Action Plan covers seven areas and sets out 12 concrete actions both in the human and veterinary field. Prudent use of antibiotics in human and veterinary medicine, enhanced surveillance systems, development of new antimicrobials and prevention of infections must be pursued in parallel to effectively address AMR. International cooperation is also a key element of the action plan. Collaboration with international organisations such as WHO, FAO and OIE is essential in view of the global nature of AMR.

A progress report on the Action Plan was published in February 2015, showing the state of play of steps taken to address AMR. Moreover, based on the results of an ongoing evaluation of the EC Action Plan, the Commission will decide on possible new or additional policy measures aiming at tackling AMR in the EU and globally in the future.

Timescale: multi-annual

The owners and organisation involved in the project

European Commission,
DG Health and Food Safety
http://ec.europa.eu/health/antimicrobial_resistance/policy/index_en.htm

The Italian National Health System: a longstanding One Health experience



► Coordinated actions among the three levels of the Italian National Health System, the National Health Institute, the national laboratories Network and a specialized Health Police Corp are conducted on the basis of an annual control Plan on the use of antimicrobials in the veterinary and food Sector, aimed to tackle AMR.

The use of antimicrobials in the veterinary and food sector in Italy is monitored by a 3-level system: national (ItMoH, ISS, NAS Command), regional (21 Regions and Autonomous Province) and local (ASLs).

The System adopts annual Plan where Sectors and Matrix to be investigated are identified, on the basis of scientific developments, requests coming from EU Commission and Reference Laboratory, Police investigations etc. The annual Plan takes into account the distinctive production features in the Italian Regions, anyway in a global vision driven by the data collected in the previous years. Test are conducted by the IZS Network.

The main driving force of this system is the One Health approach. Veterinary, food safety and human health Authorities are represented and work together at the 3 Level of the NHS. So, any issue is faced in a coordinated and integrated way. Since the establishment of MoH (1958) and of the NHS (1978), veterinarians, prevention and public health experts, scientists and doctors are represented in the different bodies (ItMoH, ISS, Regions, ASLs' Departm. of health).

Controls are made on animals (bovine, swine, birds, etc.) and on their products or derivatives (meats, milk, honey, etc...).

The results are collected through web system at the ItMoH, analysed by ISS and published yearly. Starting from them, the Authorities adopt decisions on interventions in the veterinary, food and/or human field, working together in a Coordination table at the Directorate General for food safety/ItMoH.

The efficacy of this One Health approach is confirmed by the number of test for year, exceeding the legal obligation (more than 11000 per year), and by the very small number of non conformities (0.037%).

Timescale: 2006—ongoing

The owners and organisations involved in the project

- Ministry of Health (ItMoH)
- Regional Health Authorities
- Local Health Authorities (Asl)
- Istituto Superiore di Sanità (ISS)
- Istituti Zooprofilattici Sperimentali (IZS)
- Health Police Corp (NAS)

EU support to One-Health research



- › Support research on AMR that follows a holistic One-Health approach, addressing AMR in human health, animal health as well as in the environment.

The European Commission is strengthening research that follows a holistic One-Health approach and addresses AMR in human health, animal health as well as in the environment. The supported research includes the EvoTAR project that has already characterized a large number of resistance genes and has provided more insight into the dynamics of resistance within hosts as well as between different reservoirs of resistance (human, animal, and environment). Furthermore, the EFFORT project aims to provide scientific evidence to inform decision makers, the scientific community and other stakeholders about the consequences of AMR in the food chain. The project is studying the relationship between farming practises, antimicrobial usage, animal health and resistance and reaches out to policy makers world-wide via webinars.

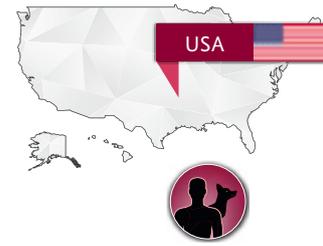
Early 2016, the Joint Programming Initiative on Anti-microbial Resistance (JPIAMR) will launch a transnational research call that will be co-funded by the European Commission via an ERA-net, welcoming proposals focussing on the dynamics of AMR at genetic, bacterial, animal, human, societal and environmental levels, in order to design and evaluate preventive and intervention measures for controlling resistance.

Timescale: multi-annual

The owners and organisation involved in the project

European Commission,
DG Research & Innovation
e.g. <http://www.evotar.eu/>;
<http://www.effort-against-amr.eu/>;
www.jpiamr.eu

Get Smart: Know When Antibiotics Work



› Antibiotic resistance is a growing problem and the main cause of this problem is misuse of antibiotics. CDC’s Get Smart: Know When Antibiotics Work program works to make sure antibiotics are prescribed only when they are needed and used as they should. The Get Smart program focuses on common illnesses that account for most of the antibiotic prescriptions written for children and adults in doctors’ offices and other outpatient settings.

The Get Smart: Know When Antibiotics Work program focuses on educating healthcare providers and patients on the appropriate use of antibiotics in the outpatient setting and promoting outpatient antibiotic stewardship programs and interventions. Outpatient stewardship refers to coordinated efforts to promote appropriate prescribing of antibiotics for non-hospitalized patients in clinics, offices, and emergency rooms.

Programs can range in size and scope and can be implemented by a variety of stakeholders. Regardless of the clinical setting, the overarching goal is to promote adherence to clinical practice guidelines to provide the best standard of care and to minimize the spread of antibiotic-resistant bacteria. The program works closely with partners to reach this goal.

Additionally, the program coordinates Get Smart About Antibiotics Week, an annual observance to raise awareness of the threat of antibiotic resistance and the importance of using antibiotics appropriately. The observance is a key component of CDC’s efforts to improve antibiotic stewardship in communities, in healthcare facilities, and on the farm in collaboration with state-based programs, nonprofit partners, and for-profit partners.

The observance is an international collaboration, coinciding with many other countries and organizations activities during the week.

Timescale: ongoing

The owners and organisation involved in the project

Lauri Hicks, DO
 Director, Office of Antibiotic Stewardship
 Centers for Disease Control and Prevention, DHQP
 404-639-3630, LHicks@cdc.gov
www.cdc.gov/getsmart/community

FDA Approach to Judicious Antibiotic Use in Animals



- ▶ Working through public-private partnerships, to promote judicious antibiotic use in food animals, the U.S. Food and Drug Administration (FDA) developed a collaborative approach to help ensure medically important antimicrobial drugs in food producing animals are limited to uses necessary for assuring animal health and include veterinary oversight.

Working through public-private partnerships, the U.S. Food and Drug Administration (FDA) developed a collaborative approach to help ensure medically important antimicrobial drugs in food-producing animals are limited to uses necessary for assuring animal health and include veterinary oversight. This voluntary effort represents a significant change in how these products have been used for decades and has proved to be considerably faster to implement than a mandatory approach.

A mandatory withdrawal of individual approved drugs can involve protracted legal proceedings and is subject to challenge. In contrast, FDA sought broad public input over a number of years on plans to work with pharmaceutical companies to voluntarily withdraw production uses and require veterinary oversight of remaining therapeutic uses of medically important antimicrobials approved for use in feed or water of food producing animals. All 25 pharmaceutical companies with affected products agreed to fully adopt the FDA's judicious use approach, withdrew 30 drugs from the market, and began implementing some of the recommended changes prior to the 3 year target.

The value of this approach was confirmed at a June 2015 White House Antibiotic Stewardship Forum where participants highlighted voluntary commit-

ments to stewardship. In addition to aligning their products with FDA's guidance, pharmaceutical companies are investing in vaccines, on-farm hygiene, and innovations to benefit animal health. Food producers are voluntarily setting standards to phase out affected products, providing responsible use guidelines to meat suppliers, and funding research for antibiotic alternatives. Feed industry organizations and farmers are educating producers about the FDA changes. Veterinary and agriculture associations are developing stewardship guidelines and conducting regional workshops on the new policies. Non-government organizations are developing standards and verification programs.

Timescale: ongoing

The owners and organisation involved in the project

U.S. Food and Drug Administration
<http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm216939.htm>

CHAPTER **2**

Combating and preventing infections

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Page 25



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Human Health



Animal Health



Human and Animal Health



There is a whole range of interventions that help prevent and control infections and the spread of antimicrobial resistant bacteria. Hand hygiene, for example, is particularly important. Measures like these need to be accompanied by the development and implementation of guidelines and training for healthcare-professionals. The establishment of networks including hospitals, ambulatory care, nursing homes, laboratories and public health institutions contributes to the implementation of interventions across all health sectors. With the help of quality indicators assessing the performance of healthcare-providers, infection prevention and control efforts can be compared among hospitals. Apart from that, developing and implementation of novel antimicrobial drugs or alternatives for humans and animals could help reduce antibiotic use and thus also influence the emergence of antimicrobial resistance.

A world map is shown in a light grey tone. Three callout boxes are overlaid on the map, each pointing to a specific country. The first callout box, located over Germany, is blue and contains the text 'Page 26' and a small German flag. The second callout box, also over Germany, is orange and contains the text 'Page 36' and a small German flag. The third callout box, located over Japan, is blue and contains the text 'Pages 28, 35' and a small Japanese flag. A fourth callout box, located over Italy, is blue and contains the text 'Pages 30, 31, 32, 33' and a small Italian flag.

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Pages 30, 31, 32, 33

National Action Plan to Prevent Healthcare-Associated Infections (PROPIAS)



› The national plan on HAI is in line with the national plan on antibiotics 2011–2016, the national programme on patient safety 2013–2017 and the national health strategy. It is clearly prevention-focused and patient-centred, as it aims to impact the daily practice of health professionals in the patient management.

Prevention and control of healthcare-associated infections—the 2015 National Action Plan to Prevent Healthcare-Associated Infections (Propias) aims to

1. Enhance the prevention of HAI across the continuum of settings in which health care is delivered (acute care and long-term facilities, out-patient treatment),
2. Reinforce control of antibiotic resistance, and
3. Reduce the risks of HAI with regard to invasive procedures.

A target is drafted for each action and the source of measurement defined. Propias is available at: <http://www.sante.gouv.fr/programme-national-d-actions-de-prevention-des-infections-associees-aux-soins-propias.html>

Timescale: 2015–2020

The owners and organisations involved in the project

- Ministry of Health
- Regional Health Agencies
- National Drugs Agency
- Social Security
- French Institute for Public Health Surveillance

Improvements in combating infections



- › The UK continues to support quality improvement standards for IPC at a national level to reduce the risk of harm from healthcare-associated infections for patients, staff and visitors; and to reduce the costs associated with preventable infection.

The UK is developing an integrated indicator (to come into effect from April 2016) which will assess the performance of acute care facilities on infection prevention and control. The indicator will provide a more comprehensive picture of prescribing and resistance trends set out against each healthcare provider. This information will be in addition to current surveillance provisions covering rates of bloodstream infections: MRSA; E. coli; MSSA and C. difficile infections.

The UK has strengthened the Code of Practice on the prevention and control of infection and related guidance (The Code), linked to the Health and Social Care Act 2008. The changes strengthen the infection prevention and control requirements and antimicrobial stewardship framework for healthcare providers. We have also engaged with the Care Quality Commission to explore how infection prevention and control and antimicrobial stewardship aspects can be built into the key lines of enquiry used in their inspections of healthcare providers.

The National Institute for Health and Care Excellence (NICE) published guidance on medicines optimisation in March 2015 and on antimicrobial stewardship in August 2015 to drive best practice across the health-care system. Other guidance related to AMR and IPC is included on the NICE work programme including a suite of short infection syndrome guidelines.

Public Health England is working with the Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare-Associated Infections to develop an overarching national framework to optimise prescribing by end of 2016/17. The framework will address diversity in prescribing and monitoring of its effect on patient outcomes enabling the safe delivery of year on year reductions in infections.

Scotland has a National Infection Prevention and Control Manual adopted by all NHS Boards and considered best practice in all non-National Health Service settings.

Timescale: ongoing

The owners and organisation involved in the project

Department of Health/NHS England/
Public Health England

“Aktion Saubere Hände” (Clean Hands)



- › Hand hygiene is of particular importance for infection prevention. “Aktion Saubere Hände” (Clean Hands) is a national campaign for improvement of compliance to hand disinfection in German healthcare facilities based on the WHO campaign “Clean Care is Safer Care” that started in 2005. It supports implementation of multimodal infection control interventions.

The Clean Hands project “Aktion Saubere Hände” (ASH) supports implementation of multimodal infection control interventions in healthcare institutions (HCI), for example by providing training material and video tutorials for health care workers. The contents of the campaign were adapted to the different medical situations and the modular structure allows application not only to hospitals, but also to residential and nursing homes and outpatient treatment. In addition information for patients and relatives are available for improvement of patient safety. On a voluntary basis 1900 health care institutions are participating, including almost 50% of the approximately 2000 German hospitals (June 2015).

Another core objective of ASH is to collect data from healthcare institutions to monitor the effectiveness of interventions over the campaign period. Since 2008 the evaluation of alcohol-based hand rub consumption data was established as a surrogate parameter for hand hygiene performance. The latest data records further progress as, over a period of eight years, the hospital-wide hand rub consumption increased by 84%.

In 2015 ASH presented for the first time the compliance data collected by direct observation of Health Care Workers for benchmark analysis in Germany.

The overall mean for hand hygiene compliance is 72%. The reference data reports the current state and the distribution of hand hygiene compliance and stimulates further improvements for patient safety.

Timescale: 2008—ongoing

The owners and organisation involved in the project

- German National Reference Center for Surveillance of Nosocomial Infections: <http://www.nrz-hygiene.de/>
- Coalition for Patient Safety: <http://www.aktionsbuendnis-patientensicherheit.de/>

Infection Prevention and Control Guideline Series



- › This project provides healthcare professionals with infection prevention and control guidance for health care settings. The series includes two foundation documents: hand hygiene practices in health care settings (2012) and routine practices and additional precautions for preventing the transmission of infection in healthcare settings (2013), along with more concise guidance targeting specific organisms such as *Clostridium difficile*.

Developing and implementing effective infection prevention and control measures reduces the risk of transmission of pathogens by interrupting the epidemiological chain of infection (altering host, organism, environment, transmission route/risk) in both healthcare and community settings.

To help reduce, minimize or prevent the occurrence of infection, the Public Health Agency of Canada (the Agency) produces a series of infection prevention and control guidelines for healthcare professionals in the healthcare setting.

The Agency works with a group of external technical experts to draft evidence-informed guidance and collaborates with stakeholders, professional associations and organizations, and provinces and territories to share information and identify best practices.

The Agency's guidance informs practitioners of essential infection prevention and control practices. In addition, Routine Practices and Additional Precautions Assessment and Educational Tools includes a summary of the elements of routine practice, an algorithm for a point of care risk assessment for personal protective equipment, and case scenarios.

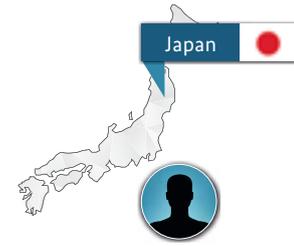
These tools may assist other jurisdictions that have not yet developed similar guidance. The external advisory approach may also be a model that could be used to leverage expertise not available within governments.

Timescale: ongoing

The owners and organisation involved in the project

Public Health Agency of Canada,
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margaret.galerowe@phac-aspc.gc.ca
<http://www.phac-aspc.gc.ca/nois-sinp/guide/pubs-eng.php>

Area network for infection control



› **Area network for infection control involves not only advanced hospitals but also small hospitals, clinics and nursing care facilities. They share their best practices and educate each other through mutual site visits to promote infection control.**

In Japan's healthcare system, tertiary hospitals are considered to be a "hub" of the area network for infection control. Within the networks, tertiary hospitals and other facilities including secondary hospitals, nursing homes and clinics learn their best practices and educate each other through mutual site visits to promote infection control.

Hospitals receive additional reimbursement from insurers to hospitals, if they meet the criteria, such as designating full time certified infection control nurse or infection control doctor, holding medical area meetings four times per year or more, and promote the prudent use of broad-spectrum antibiotics and anti-MRSA drugs. Through the area networks, hospitals share surveillance data on antimicrobial resistance (AMR) rates and incidence of infections.

Addressing the infection control by a single healthcare facility alone is not enough, because a patient may often receive health care at multiple facilities including nursing homes. In addition, the number of infection control specialists is still not enough to cover all health care facilities. Therefore, shared awareness of issues and collective activities within the area are necessary to tackle AMR. Education provision is also an important role of the network, such as hand hygiene, surveillance method and epidemiological data of the local infections. The networks contribute to enhancing preparedness to AMR in the area building "herd immunity" to AMR.

The area networks also contribute to outbreak response. When a nosocomial infection outbreak occurs, each hospital takes the primary responsibility to contain it in compliance with the law. However, if the hospital fails to control, it asks the network for support. Response to outbreaks includes active surveillance, environmental screening, re-education of healthcare workers, special sterilization (i.e. vapor hydrogen peroxide) and special testing (i.e. pulsed-field gel electrophoresis, gene tests).

Timescale: The governmental support on nosocomial infection control area network project started in 2004. Reimbursement from insurers started in 2012.

The owners and organisation involved in the project

Ministry of Health, Labour and Welfare

NHSN Antimicrobial Use and Resistance Module



- › The National Healthcare Safety Network (NHSN) Antimicrobial Use and Resistance (AUR) Module enables hospitals to report, track, and respond to antimicrobial use and antimicrobial resistance data and enables CDC to use the data for national benchmarks and analyses. As a result, the AUR data can be used to measure and improve the use of antimicrobials in U.S. hospitals and lessen the burden of antibiotic resistant infections.

CDC's National Healthcare Safety Network (NHSN) is the most widely used healthcare-associated infection (HAI) tracking system within the U.S. NHSN provides facilities, states, regions, and the nation with data needed to identify problem areas, measure progress of prevention efforts, and ultimately eliminate healthcare-associated infections. The goal of the NHSN AUR Module is to provide a mechanism for facilities to report and analyze antimicrobial use and/or resistance as part of local or regional efforts to reduce AR infections through antimicrobial stewardship efforts or interruption of transmission of resistant pathogens at their facility. The AUR Module only allows for electronic reporting, with microbiology and pharmacy data captured and reported electronically from Electronic Medication Administration Record (eMAR) or Bar Coding Medication Administration (BCMA) systems in hospitals.

The AU reporting option provides a mechanism for facilities to report and analyze antimicrobial usage as part of antimicrobial stewardship efforts at their facility. CDC has developed a measure based on this data to help facilities compare antimicrobial use that the hospitals report with expected antimicrobial use based on national data. The measure is comprised of a discrete set of ratios, Standardized Anti-

microbial Administration Ratios (SAARs) that summarize observed-to-predicted antimicrobial use based on the antibiotic and patient location. The SAARs are designed to serve as indicators for antimicrobial stewardship programs (ASPs), revealing possible overuse, underuse, or inappropriate use of antimicrobials; track improvements to antimicrobial prescribing; and evaluate impact of antimicrobial stewardship programs. The AR reporting option facilitates the evaluation of AR data using a standardized approach while providing facilities with an improved awareness of AR issues within their hospital to aid in clinical decision making and prioritize prevention efforts.

Timescale: ongoing

The owners and organisation involved in the project

Daniel Pollock, MD
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 404-639-4237, DPollock@cdc.gov
<http://www.cdc.gov/nhsn/acute-care-hospital/aur/>

Risk analysis for the control of HAI in Intensive care and Surgery



- To perform a risk analysis for the control of HAI in Intensive care and Surgery Units, identifying the main preventable risk factors. To evaluate the effectiveness of the prevention measures identified, their implementation and related compliance level. To describe the epidemiology of some alert pathogens, defining an effectiveness assessment of PH interventions. To develop an educational programme and a set of indicators. To estimate the costs of surveillance and preventive interventions.

HAIs are considered to be the most frequent adverse event in healthcare, and their impact has become a Public Health priority. HAIs are a focus point for the development and spread of AMR.

There is a need to identify the risk factors related to these infections in order to define specific interventions reducing subsequent risks. Epidemiological surveillance represents an important instrument of hospitals' quality management.

Timescale: November 2012–May 2015

The owners and organisations involved in the project

- University of Milan
- University of Marche
- University of Sassari
- University of Catania
- University of Udine
- University of Bari
- University of Parma
- University of Verona

Proposal of a risk analysis model for HAI in Intensive Care Units (ICU)



- To perform risk analysis for HAIs in intensive care units. To identify and apply effective practices and guidelines. To assess the effectiveness of the actions carried out.

HAIs are considered an important Public Health issue due to related morbidity and mortality and the associated AMR infections. In Intensive Care Units patients are exposed to greater HAI risks due to their clinical conditions, invasive procedures, undergoing multiple strong antimicrobial therapies.

In particular, as supported by scientific literature, the antimicrobial resistance rate in ICUs is significantly higher than in other units. Even if these considerations highlight the importance of AMR surveillance in ICUs, a more integrated approach is needed to obtain better results.

Timescale: October 2012 to April 2014 extended April 2015

The owners and organisations involved in the project

- University of Cagliari
- Brotzu Hospital, Cagliari
- Giovanni Paolo II Hospital, Olbia
- San Raffaele Hospital, Milan
- Verona Polyclinic
- Padua Hospital

Integrated approach for SSI prevention in joint replacement surgery



- › Assessment of adherence to the recommendations on procedures for antibiotic prophylaxis and the level of microbiological contamination of the air during clean hip and knee operations, as well as evaluating the cost effectiveness and the impact on health outcomes that different ventilation systems have on SSI related to joint replacement, taking into account a previous evaluation of anti-microbial prophylaxis and the characteristics of operating rooms.

Joint replacement surgery in Italy is characterised by a volume of more than 120,000 interventions per year, entailing considerable costs for our National Health System. Surgical site infections are common avoidable complications of this surgery. Antibiotic prophylaxis, a better ventilation system in operating rooms and the application of international guidelines have improved the complication rate in recent years.

Many studies highlight the role played by ventilation systems, prophylaxis and guideline adherence to obtain a microbiological environmental quality improvement. Integration of different actors (surgeons, public health medical doctors, biomedical engineers, infectivologists) involved in infection surveillance and the different procedures focused on avoiding SSI represents the strategic key of the project.

Timescale: March 2010 to May 2012

The owners and organisations involved in the project

- University of Milan
- University of Parma
- University of Sassari
- University of Catania
- University of Rome “La Sapienza”

MDR pathogens colonization assessment in Residential Health Care



- To describe the circulation of AMR pathogens of public health concern among the elderly population in nursing home care. To evaluate the prevalence of AMR strains of E. Coli, K. pneumonia, MRSA, Clostridium difficile, with particular regard to Enterobacteriaceae-producing carbapenemases. To perform data analysis to identify the main risk factors related to the colonisation of specific AMR pathogens.

There are more than 13,000 nursing homes in Italy providing assistance to more than 400,000 patients, 75% of whom are elderly. Infections represent a major cause of mortality among this population.

In these settings, outbreaks represent a possible risk with high costs for the health system, and the same assistance setting can be considered a reservoir for AMR infections given the frequent hospitalisation of the guest population.

A nationwide analysis of MR enterobacterias, MRSA, MR Clostridium difficile strains in the context of Nursing Home Care represents a priority in the field of Public Health.

Timescale: February 2014 to December 2016

The owners and organisation involved in the project

- ISS
- Emilia Romagna Regional Social and Health Agency
- Papa Giovanni XXIII Hospital, Bergamo
- Campo di Marte Hospital, Lucca
- Spirito Santo Hospital, Pescara
- Agostino-Estense-Baggiovara Hospital, Modena

U.S. Department of Veterans Affairs MRSA Prevention Initiative



› The Veteran’s Administration targeted potentially life-threatening staph infections in hospitalized patients to reduce rates of health care-associated infection with MRSA. The initiative serves as important confirmation that multifaceted intervention strategies can achieve effective and sustained control of MRSA in U.S. hospitals.

A Department of Veterans Affairs (VA) initiative targeting potentially life-threatening staph infections in hospitalized patients has produced significant results. VA’s success in substantially reducing rates of healthcare-associated infection with methicillin-resistant *Staphylococcus aureus* (MRSA) serves as important confirmation that multifaceted intervention strategies can achieve effective and sustained control of MRSA in U.S. hospitals.

Among VA patients in intensive care units (ICU) between 2007 and 2012, healthcare-associated infection (HAI) rates with MRSA dropped 72%—from 1.64 to 0.46 per 1,000 patient days. Infection rates dropped 66%—from 0.47 to 0.16 per 1,000 patient days—for patients treated in non-ICU hospital units.

The MRSA Prevention Initiative consists of a bundle of interventions that have been associated with reductions in MRSA HAIs. These are active surveillance screening programs for MRSA, contact precautions for hospitalized patients found to have MRSA, and emphasis on hand hygiene in common areas, patient wards, and specialty clinics throughout medical centers. Online training, frequent measurement, and continual feedback to medical staff reinforce such practices.

Additionally, VA created a culture that promotes infection prevention and control as everyone’s responsibility. A major part of that commitment is a dedicated employee at each VA medical center, the MDRO Prevention Coordinator, to monitor compliance with MRSA bundle prevention practices, educate staff, and work with Veteran patients and families.

Implementation of elements of the same core prevention strategies in VA’s long-term care facilities, spinal cord injury units, and outpatient clinics provides a coordinated strategy for MRSA control in all venues where patients receive care.

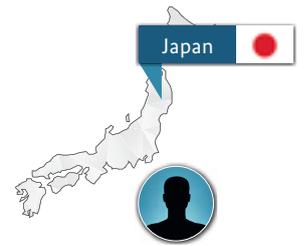
VA operates the largest integrated health care delivery system in the U.S. (8 million Veterans) and these results reflect a large-scale, organized prevention program with documented impact.

Timescale: 2007—present

The owners and organisation involved in the project

<http://www.va.gov/health/>

DOTS in Japan



› **DOTS (Directly Observed Treatment Short-course) prevent development of drug resistant tuberculosis. Due to the comprehensive DOTS program, the proportion of multi-drug resistant TB cases remains quite low at 0.7% among culture-positive cases in Japan.**

In Japan, medical treatment for patients with tuberculosis (TB) is provided by hospitals, clinics and public health centers (PHC) in the prefectural governments. DOTS in Japan is a TB management package of (1) physician's notification, (2) public health nurse's (PHN) visit, (3) inpatient DOTS, (4) outpatient DOTS and (5) coordination through DOTS conferences. Due to the comprehensive DOTS program, the proportion of multi-drug (isoniazid and rifampicin) resistant TB cases, which was reported through the routine surveillance in 2014, remains quite low at 0.7% among culture-positive cases in Japan.

Physicians must report to PHC on the day of a TB diagnosis. Upon receipt of the notification, a PHN visits the patient to inform treatment regimens and laboratory results and collect information on possible contacts. Smear-positive patients are hospitalized at TB hospitals for 2 months and they are treated under daily direct observation as inpatient DOTS. Before being discharged, patient's treatment regimens and problems are communicated with a PHN at the DOTS conference, which is held monthly so that the PHN can closely engage with the patient management.

For non-hospitalized patients, including those with latent TB infection and discharged patients, a PHC coordinates with various actors in the community, such as pharmacists, visiting nurses and the family

to lead patients to continue the treatment under observation as outpatient DOTS. The frequency of PHN's visit depends on the risk of defaulting. Drug intake is assured daily, weekly or monthly by several methods such as direct observation at patient's home, checking the patient's notes and confirming empty blisters.

Several times a year, PHC holds a cohort meeting and discuss the treatment outcomes of all patients in the PHC's responsible area. The discussion records are reported to the hospitals.

Timescale: 2000—present

The owners and organisation involved in the project

- Ministry of Health, Labour and Welfare, Japan
- Local prefectural governments in Japan
- Japan Anti-Tuberculosis Association

German Antimicrobial Resistance Strategy— veterinary issues



- Reducing the number of antibiotic treatments of fattening animals to the inevitable minimum by improving animal health and strengthening prudent use through legal requirements.

The strategy to minimize the use of antibiotics in animal husbandry implemented with the 16. Revision of the German Drug Law aims at improving animal husbandry and thus, by improving animal health reducing the need for antibiotic treatment.

http://www.bmel.de/SharedDocs/Downloads/EN/Agriculture/AnimalProtection/MedicinalProductsAct-AMG.pdf?__blob=publicationFile

See §§ 58ff of the German medicinal products act:
http://www.bmel.de/SharedDocs/Downloads/EN/Agriculture/AnimalProtection/MedicinalProductsAct-AMG.pdf?__blob=publicationFile

Timescale: Came into force April 1, 2014

The owners and organisation involved in the project

Legislator

Advancing Vaccine Research, Innovation and Development



- › Government of Canada departments and agencies are working together to strengthen security and protection against vaccine-preventable diseases and biological threats, and expand investment and commercialization opportunities for Canada's vaccine industry and research community.

Canada is advancing vaccine research, innovation and development by bringing together 13 federal departments and agencies with interests and responsibilities relevant to these three areas. Most recently, this group established national vaccine priorities for humans and animals that will bring focus to research and development activities.

The priorities were established by assessing the risks for human and animal health, the burden of disease, impacts on immune-compromised individuals, and antimicrobial resistance (AMR). A One Health approach is being taken with both human and animal vaccine priorities identified.

The Government of Canada is encouraging the development of new and/or improved vaccines that target AMR pathogens, such as *Clostridium difficile* and Group A *Streptococcus*. In reducing the overall incidence of the disease and the available reservoir in which the microbe can mutate, the use of antibiotic medications will be reduced, thereby reducing the emergence of AMR.

Ultimately, working toward common vaccine priorities will foster greater coordination of Government of Canada vaccine research and development efforts. This will increase collaboration amongst Canadian researchers, creating an environment that promotes and fosters research

and innovation in Canada leading to new understanding and discoveries in disease prevention and public health.

Timescale: ongoing

The owners and organisation involved in the project

13 federal departments with responsibilities relevant to vaccine development, research and innovation.

Contact: Rhonda Kropp,
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rhonda.kropp@phac-aspc.gc.ca
<http://healthycanadians.gc.ca/healthy-living-vie-saine/immunization-immunisation/va>

CHAPTER **3**

Promote the responsible use of antibiotics

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Human Health



Animal Health



Human and Animal Health



International studies show that up to 50 per cent of antibiotic treatments in healthcare settings are unnecessary or inappropriate. Apart from posing risks for the individual patient, antibiotic (mis-)use is associated with increasing the pathogens' resistance to antibiotics. Antibiotic stewardship (ABS) programmes tackle these problems by fostering the appropriate use of antibiotics in humans and animals. By means of evidence-based recommendations and guidelines for diagnosis and treatment, Antibiotic stewardship programmes improve patient outcomes and slow down the development of resistance. However, awareness and knowledge about antibiotics has to be increased as well—not only among healthcare professionals but also among the general public. Improvement of animal health will contribute to the reduction of antibiotic treatment in food production.



Pages 47, 51

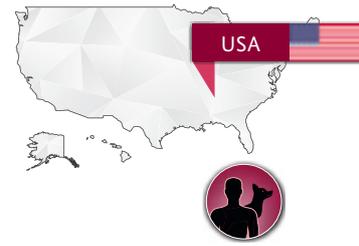
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White House Forum on Antibiotic Stewardship



► To bring together key human and animal health constituencies involved in the development, promotion, and implementation of activities to ensure the responsible use of antibiotics.

At the event, over 150 major food companies, retailers, and human and animal health stakeholders announced commitments to implement changes over a five year period to slow the emergence of resistant bacteria and prevent the spread of resistant infections. One commitment was for clinical societies to identify best practices and practical guidance for antibiotic stewardship efforts in their field. For example, a program developed by the Association of American Medical Colleges (AAMC), Wake Forest School of Medicine, in collaboration with the Centers for Disease Control and Prevention (CDC) to increase understanding of antimicrobial resistance prevention and control among medical students. <http://www.wakehealth.edu/School/CAUSE/Get-Smart-About-Antibiotics.htm> has resulted in an improved curriculum to address best practices in antimicrobial resistance.

Hospitals, health systems, long-term care facilities and pharmacies made commitments to reducing errors in prescribing antibiotics and working to protect the current antibiotics for future use. This includes many agreeing to adopt the Centers for Disease Control's (CDC) Core Elements of Hospital Antibiotic Stewardship Programs, and submit antibiotic use and resistance data to CDC.

Animal pharmaceutical companies committed to aligning their products with Food and Drug Administration policy changes, and investing in vaccines, on-farm hygiene, and innovations

to benefit animal health. Food producers are voluntarily setting standards to phase out affected products, providing responsible use guidelines to meat suppliers, and funding research for antibiotic alternatives. Feed industry organizations and farmers are educating producers about the FDA changes. Veterinary and agriculture associations are developing stewardship guidelines and conducting regional workshops on the new policies. Non-government organizations are developing standards and verification programs for responsible antibiotic use.

Timescale: held June 2, 2015

The owners and organisation involved in the project

<https://www.whitehouse.gov/the-press-office/2015/06/02/fact-sheet-over-150-animal-and-health-stakeholders-join-white-house-effo>

Public Campaigns on responsible use of antibiotics



- **The first national plan on antibiotics in 2002 aimed to raise awareness of the prudent use of antibiotics among the general public. Nationwide mass media campaigns were launched. Global antibiotic consumption fell by 10.7% between 2000 and 2013.**

The National Health Insurance launched several campaigns:

- 2002–2006: to break the reflex “common diseases = antibiotics”. Slogan used: “antibiotics are not automatic”.
- 2007–2009: a focus on a new idea “viral disease = antibiotic cannot heal”. The same slogan was used.
- 2010: focus on good practice, illustrated by diseases for which unnecessary antibiotic prescriptions are common (tonsillitis, bronchitis). New slogan for public awareness raising: “antibiotics, if you use them incorrectly, they will be less strong”.

The public campaigns used a range of tools, including TV and radio spots, information booklets for parents of young children, for a larger public, an exhibition entitled “micro-organisms in questions” touring around France, and press releases giving advice on good antibiotic use for those likely to use them more (young mothers, young workers, old people...).

Several tools were promoted for physicians:

- Guidelines on treating infectious diseases, leaflets on respiratory diseases, specific website with all guidelines ...
- Streptotests: free of charge for physicians (since 2002), but currently hardly used (18% of GPs used them regularly).

- Visits to GPs by local members of the national health insurance, with information on which drugs, and especially antibiotics, the GP has prescribed, compared to the average in the geographic area.

At hospital level, each hospital must have a person responsible for antibiotic treatment (help with prescriptions, distribution of guidelines, follow up, ...). Moreover, guidelines and tools are available online to help count antibiotics. Tools for paediatric professionals were also created and distributed to nursery nurses, and to directors of crèches. These measures led to a decrease in antibiotic consumption in the community: Global antibiotic consumption fell by 10.7% between 2000 and 2013. A 5.9% increase in antibiotic consumption has been observed since 2010.

Timescale: 2002–2013

The owners and organisations involved in the project

- Ministry of Health
- Regional Health Agencies
- National Drugs Agency
- National Health Insurance
- National Institute of Surveillance

Antibiotic Resistance Awareness Campaign



- ▶ This campaign aims to raise awareness and knowledge of AMR among Canadian parents of children aged 0–12 years in order to promote appropriate use of antibiotics, and to support health professionals in discussing antibiotic use with their patients.

healthycanadians.gc.ca/antibiotics

The Public Health Agency of Canada implemented a pilot multi-media campaign to raise awareness of AMR. Pre-campaign research indicated that Canadians have low levels of understanding about when antibiotics should and should not be used, and the risks posed by AMR. The campaign materials focused on increasing awareness and knowledge of antibiotic use and AMR among Canadian parents of children aged 0-12 years, and supporting health professionals in discussing antibiotic use and resistance with their patients.

Key organizations contributed to the development of campaign materials and their distribution to healthcare professionals. Campaign messages tailored to audiences were promoted using print, electronic and social media. The Public Health Agency of Canada also collaborated in the November 2014 ECDC-led Global Twitter Chat. The Agency continues to host AMR-related webinars to promote knowledge and awareness products, surveillance reports, guidance and policy documents to healthcare professionals.

The campaign video was shown on 4,483 medical and pharmacy waiting room screens in November 2014, delivering a total of 10,660,626 impressions, and was watched online 108,643 times. A total of

956,407 brochures and 20,871 posters were distributed to family physicians, general practitioners, paediatricians and pharmacists across Canada.

Building on the results of the pilot, the Public Health Agency of Canada plans to develop additional knowledge products in 2015. Effective collaboration and partnerships with key Canadian and international organizations optimized campaign resources, while expanding campaign reach. The pre and post campaign evaluations and the campaign materials may be of use to other jurisdictions wishing to launch similar initiatives.

Timescale: November 2014–March 2015
(pilot campaign)

The owners and organisation involved in the project

Public Health Agency of Canada
Marsha Hay Snyder
marsha.haysnider@phac-aspc.gc.ca

Do Bugs Need Drugs?



- › “Do Bugs Need Drugs?” is a community education program designed to address antibiotic resistance by promoting handwashing, increasing awareness of the differences between viruses and bacteria, and advocating appropriate use of antibiotics.

“Do Bugs Need Drugs?” is an educational program for the community and for healthcare professionals, designed to address AMR by decreasing the inappropriate use of antibiotics. Resources are available for physicians, pharmacists, nurses and the public, including children, their parents and caregivers, teachers, employers and workers and long-term care facilities. Most are available in English and French and are posted on-line. Arising from a pilot project in one community in 1997, it is being used in two of Canada’s largest provinces: Alberta and British Columbia.

There are four key strategies: consistent messaging (e.g. handwashing is the best way to stop the spread of infections); networking (through dedicated committee members who have engaged government ministries, professional organizations, health care organizations, academia, industry and businesses, and community groups); aligning interests (e.g. engaging nursing and medical students to deliver a program on AMR to Grade 2 students as part of their community health curriculum); and containing costs (e.g. partnering with other organizations for distribution of materials and sharing administrative and printing costs between the Do Bugs Need Drugs programs in the two participating provinces).

The success of the program is linked to an increased willingness in the scientific and medical community to discuss the risks associated with antibiotic use and

of growing public awareness that AMR is linked to misuse and overuse of antibiotics. British Columbia has seen reductions in the rate of community prescribing at the population level, especially for respiratory tract infections in children, the major early target of the program. In Alberta, consistent reductions in antibiotic prescribing in long-term care facilities have been achieved with implementation of an antimicrobial stewardship strategy that includes education for staff and feedback on antibiotic prescribing rates.

Timescale: ongoing since 1997

The owners and organisation involved in the project

- Alberta Health Services
mary.carson@albertahealthservices.ca
- www.dobugsneeddrugs.org
- www.francais.dobugsneeddrugs.org
- British Columbia Centre for Disease Control

Antibiotic awareness



► **The UK has made use of the latest research to deliver change in prescriber and public behaviours. It has developed a programme of interventions, awareness raising activity and the development of tools and guidance.**

The UK has shown a sustained commitment to increasing public and professional awareness and knowledge of antimicrobial resistance (AMR). In September 2014, Public Health England, in partnership with the Devolved Administrations and professional organisations, launched the Antibiotic Guardian campaign as part of activities to support European Antibiotic Awareness Day.

The purpose of the campaign is to encourage behaviour change strategies to encourage both healthcare professionals and the public to make better use of antibiotics, helping to conserve these vital medicines and to ensure that they are used for the right infection, at the right dose and at the right time.

The UK has also held clinical leaders and diagnostics workshops (November 2014 and July 2015 respectively) to spread the message on AMR to key clinicians and microbiologists.

Public Health England has collaborated with the Royal College of General Practitioners to develop the TARGET Antibiotics Toolkit. The toolkit aims to help influence prescribers' and patients' personal attitudes, social norms and perceived barriers to optimal antibiotic prescribing. It includes a range of resources that can each be used to support prescribers' and patients' responsible antibiotic use, helping to fulfil continuing professional development (CPD) and revalidation requirements.

TARGET has been updated following recent evaluation, and includes the development of a clinical e-learning module to support implementation. (TARGET stands for: Treat Antibiotics Responsibly, Guidance, Education, Tools).

In 2013, the Scottish Reduction of Antimicrobial Prescribing programme launched an educational intervention for changing prescribing behaviours across primary care. Education resources have been developed to support secondary care healthcare staff in delivering stewardship—most recently an electronic workbook specifically aimed at nurses and midwives.

Timescale: ongoing

The owners and organisation involved in the project

Department of Health and Public Health England

Choosing Wisely Canada



› **Choosing Wisely Canada is a physician-led campaign designed to engage physicians and patients in conversations about overuse of unnecessary tests, treatments and procedures. The goal is to improve the quality of health care and to prevent harm from unnecessary care. One of the key recommendations of the campaign is to decrease the use of unnecessary antibiotics.**

Unnecessary tests, treatments and procedures take away from care by potentially exposing patients to harm, leading to more testing to investigate false positives and contributing to stress for patients. It also creates increased strain on the resources of the health care system.

Representing a broad spectrum of physicians, Canadian national specialty societies participating in the campaign have been asked to develop lists of “Five Things Physicians and Patients Should Question.” These lists identify tests, treatments or procedures commonly used in each specialty which are not supported by evidence, and/or could expose patients to unnecessary harm.

Modelled after the Choosing Wisely® campaign in the United States, Choosing Wisely Canada recognizes the importance of educating and engaging patients so that they can make informed choices about their care. It has created patient-friendly materials to help patients learn about the tests, treatments or procedures in question, when they are necessary and when they are not, and what patients can do to improve their health.

Choosing Wisely Canada is working with various stakeholder groups to disseminate the patient materials widely, and with medical schools to

introduce new content into the undergraduate, postgraduate and continuing medical education curricula.

While Choosing Wisely began in North America it has spread to over 17 countries in Europe, Asia and South America. Collaboration with the Organization for Economic Development is beginning to measure the extent of overuse in multiple countries and the use of antibiotics is one of the key indicators.

Timescale: ongoing

The owners and organisation involved in the project

1-416-864-6060 x 77548

info@choosingwiselycanada.org

<http://www.choosingwiselycanada.org/>

Good practices in anti-microbial resistance surveillance and control



► To promote already existing best practices in the field of antimicrobial-resistance surveillance and control. To transfer good practices to all contexts through the production and the implementation of guidelines at regional and national level.

AMR represents a threat to public health as well as a growing concern all over the world in both human and veterinary health. In Italy for example, the rate of carbapenem-resistant *K. pneumoniae* rose to 35% in 2013. Different Italian regions started up programmes to combat AMR through the creation of AMR and antimicrobial use surveillance networks based on sharing laboratory and drug consumption data. Common strategies and interventions are still needed to better face the problem.

To increase the general capability level, it is necessary:

- to define, highlight and share regional and national best practices in AMR surveillance, antimicrobial use monitoring, guideline implementation, etc.,
- to identify joint minimum standards to make the impact analysis of different contexts easier,
- to streamline the existing national AMR surveillance systems,
- to promote the implementation of common guidelines,
- to implement communication strategies on this topic,
- to foster the relationship between regional and national institutions and all stakeholders involved in the process.

Timescale: July 2015–July 2017

The owners and organisations involved in the project

- Emilia Romagna Region
- Istituto Superiore di Sanità
- Toscana Region
- Campania Region
- Lombardia Region
- INMI L. Spallanzani
- Bambino Gesù Hospital, Rome
- University of Turin
- Mater Domini Hospital, Catanzaro

Hospital antibiotic stewardship (ABS) expert training and network initiative



- To increase the number of physicians and pharmacists with knowledge and skills in rational prescribing and strategic antibiotic stewardship activities in acute care hospitals. To establish a stewardship expert network for exchange of experience, for continuous education, and as forum for cooperative quality improvement projects

In order to increase knowledge and skills in antimicrobial prescriptions at the bedside, we designed a training programme open to hospital physicians and hospital pharmacists. The training curriculum includes 4 training modules (each lasting one week in interdisciplinary groups not exceeding 30 participants) with intensified training in pharmacology and microbiology (module “Basics”), infectious disease practice guidelines (“Fellow”), antibiotic policy, stewardship activities and quality management (“Advanced”) and practical problems and implementation (“Expert”). Each participant must present methods and results of a practical ABS project in her/his hospital and defend it in front of their peers. After completion of the course, the participant is considered a “certified ABS expert”.

During the first 4 years (2010–2013), the programme was financially supported (50%) by the German Ministry of Health and produced >200 certified ABS experts (a total of 46 weekly courses were held). The evaluation of the courses by the participants yielded consistently scores of <2 (scores 1–5, 1=best).

In the second period (2014–2017 another 400 ABS experts will be certified (current number of experts [as of 31 July 2015]: 356). The ABS expert network was set up through an independent website (providing online chat and materials) and annual educational

network meetings (on the European Antibiotic Awareness Day in November) with special working groups on: pharmacoepidemiology & surveillance, stewardship tools and quality indicators.

The network has been discussing, evaluating and formally consenting ABS quality indicators (see Thern et al. *Infection* 2014) and facilitating a study assessing the feasibility of using selected process of care quality indicators in the field of antimicrobial prescriptions and stewardship (publication in preparation).

Timescale: 2010–2013 and 2014–2017

The owners and organisation involved in the project

- Abteilung Infektiologie, Universitätsklinikum Freiburg
- Abteilung Infektiologie, Universitätsklinikum Dresden
- DGI
www.dgi-net.de
- ABS-Expertennetzwerk
www.antibiotic-stewardship.de

Antimicrobial Stewardship Program— Province of Ontario



- › The objective is to optimize the appropriate use of antimicrobials in the hospital setting and standardize data collected in the provincial critical-care information system.

Mount Sinai Hospital and University Health Network, two academic health science centres in Toronto, Ontario, jointly established a robust, well-resourced antimicrobial stewardship program (ASP). Over the course of four years, the program was expanded to five intensive care units (ICUs), effective change management practices were identified and the successes of the ICU project were leveraged to other areas of the hospitals. Overall, strong leadership with clear accountability, and valid, reliable data to monitor progress were identified as the two critical success factors.

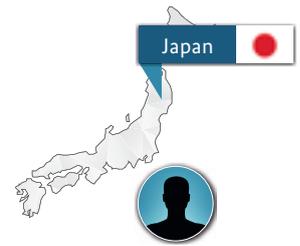
The program has since expanded to 14 academic hospital ICUs, and more recently was leveraged to help community hospitals without in-house infectious diseases specialists to implement ASPs. Three new data fields were introduced into the provincial critical care information system—days of antibacterial therapy, days of antifungal therapy, and ICU-onset *C. difficile*—which will help standardize data collection moving forward. This model—starting with academic health sciences centres, and antimicrobial stewardship experts and leaders who then mentor and develop new experts and leaders—could be copied in other jurisdictions both within and outside of Canada.

Timescale: Since 2009 at Mount Sinai Hospital, and expanding into academic hospitals in the province of Ontario since 2011.

The owners and organisation involved in the project

Dr. Andrew Morris
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Network
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Antimicrobial Stewardship



► **Objective:** In the Japanese national fee schedule, incentives are given to promote prudent use of antibiotics. Also, many professional societies have their own certification programmes which contribute to antimicrobial stewardship and human resource development.

A national fee schedule is used to give incentives for prudent use of antibiotics in Japan: healthcare providers must promote the prudent use of broad spectrum of antibiotics and anti-MRSA drugs in order to receive additional reimbursement from insurers. The promotion includes permission for use or notification to an antimicrobial stewardship team or infection control team in each hospital when using antibiotics.

Japan has dedicated the last decade to human resource development to promote antimicrobial stewardship. It is characterised by its interprofessional approach: good collaboration between health professionals is a key to its successful implementation. Pharmacists play an essential role in the stewardship; hence the Japanese Society of Pharmacists started a certification programme and the Japanese Society of Chemotherapy has its own board to train pharmacists.

As for other professionals, the Japanese Society for Clinical Microbiology launched a certification program for “infection control by microbiological technologists.” Infection control doctors and infection control nurses play important roles, too.

An expert panel comprised of members from the government and the Executive Council for Nosocomial Infection issued the “Recommendation on AMR” on April 1st, 2015. It aims at providing

knowledge on AMR to the general public, healthcare providers and policy makers and support the expansion of the stewardship throughout the country. The Japanese government will continue to prevent the proliferation of antimicrobial resistance (AMR).

Timescale: Reimbursement from insurers started in 2012. The establishment of the certification programmes differs among the professional societies.

The owners and organisation involved in the project

- Ministry of Health, Labour and Welfare
- Professional societies

NHSN Patient Safety Component Annual Hospital Survey—Antibiotic Stewardship Practices



- › The National Healthcare Safety Network (NHSN) Patient Safety Component Annual Hospital Survey must be completed by all hospitals upon enrollment and at the beginning of each year. Starting with the 2014 survey, hospitals must answer questions regarding their antibiotic stewardship program. CDC will use this information to better understand the stewardship policies and practices currently used in U.S. hospitals and compare them to CDC’s Core Elements of Hospital Antibiotic Stewardship Programs.**

CDC’s National Healthcare Safety Network (NHSN) is the most widely used healthcare-associated infection (HAI) tracking system within the U.S. NHSN provides facilities, states, regions, and the nation with data needed to identify problem areas, measure progress of prevention efforts, and ultimately eliminate healthcare-associated infections. The NHSN Patient Safety Component Annual Hospital Survey must be completed by all hospitals upon enrollment into NHSN and/or activation of an NHSN component and at the beginning of each calendar year. The survey includes questions designed to gain additional insight on the hospital, including the patient population, size, laboratory practices and capabilities, and infection control practices. This additional information is used by CDC to analyze data reported from the hospital within NHSN in the previous year by estimating the risk of HAIs.

Beginning with the 2014 NHSN Patient Safety Component Annual Hospital Survey completed in early 2015, in an effort to improve antibiotic stewardship practices, U.S. hospitals are also required to answer questions regarding their antibiotic stewardship program. These questions are designed to gain an understanding of the antibiotic stewardship policies

and practices currently used in U.S. hospitals and compare them to CDC’s Core Elements of Hospital Antibiotic Stewardship Programs (<http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>). CDC plans to continue gathering data from future annual surveys to track the improvement of antibiotic stewardship practices over time.

Timescale: annual survey, ongoing

The owners and organisation involved in the project

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http://www.cdc.gov/nhsn/forms/57.103_PSHospSurv_BLANK.pdf

MRSA-Net and Regional MRSA/MDR Networks (Germany)



- **Reduction of MRS (MDR) load in the ambulatory, hospital and nursing home setting by increasing the implementation of guidelines and communication in stakeholder networks.**

MRSA-Net: As MRSA in hospitals and in the community can be a problem in cross-border health care, the European Union-funded EUREGIO MRSA-net project was established in the bordering regions of Twente/Achterhoek, Netherlands, and Münsterland, Germany. The main aim of the project is the creation of a network of major health care providers in the EUREGIO and the surveillance and prevention of MRSA infections. A spa-typing network was established in order to understand the regional and cross-border dissemination of epidemic and potentially highly virulent MRSA genotypes. As the reduction of differences in health care quality is an important prerequisite for cross-border health care, a transnational quality group comprising hospitals, general practitioners, public health authorities, laboratories, and insurance companies has been established since 2005 to harmonise the quality criteria for the control of MRSA on both sides of the border.

Regional Networks: MRSA-Net served as a model for the establishment of networks in all German regions since 2008. Beside MRSA, they consider other multi-resistant pathogens. Under the coordination of the public health service partners from all sectors (hospitals, practitioners, nursing-homes etc.) in a region aim to agree on consistent measures in the prevention and control of resistant pathogens. In addition, quality seals make the efforts of participating hospitals transparent. Regular Network meetings ensure an exchange of experience.

Timescale: since 2005

The owners and organisation involved in the project

- regional and local health offices
- MRSA-Net
<http://www.mrsa-net.nl/de/>
- Regional MRSA/ MDR Networks (Germany)
http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Netzwerke/Netzwerke_node.htm

German Antimicrobial Resistance Strategy— veterinary issues



- › Reducing the number of antibiotic treatments for fattening animals to the inevitable minimum by improving animal health.
Strengthening prudent use through legal requirements.

The strategy to minimise the use of antibiotics in animal husbandry, implemented through the 16th revision of the German Drug Law, aims at improving animal husbandry and reducing the need for antibiotic treatment by improving animal health.

http://www.bmel.de/SharedDocs/Downloads/EN/Agriculture/AnimalProtection/MedicinalProductsAct-AMG.pdf?__blob=publicationFile

See §§ 58ff of the German medicinal products act http://www.bmel.de/SharedDocs/Downloads/EN/Agriculture/AnimalProtection/MedicinalProductsAct-AMG.pdf?__blob=publicationFile

Timescale: coming into force April 2014

The owners and organisation involved in the project

Legislator

Guidelines— Veterinary Medicine



› Reducing the number of antibiotic treatments for fattening animals to the inevitable minimum by improving animal health. Strengthening prudent use through legal requirements.

In Germany, Guidelines for the prudent use of veterinary antimicrobial drugs have been established in 2000 and revised in 2010 and 2014 (http://www.bundestieraerztekammer.de/downloads/btk/leitlinien/Antibiotika-Leitlinien_01-2015.pdf). They describe the ideal approach for using antibiotics. A deviation from this approach should only be considered in rare, well-justified cases. In any event, the legal provisions have to be respected. These guidelines are meant to be concise recommendations for veterinary practitioners on the prudent use of antibiotics in the treatment of sick animals.

Farmers are addressed by a booklet which deals with the drug law for farmers (<http://shop.aid.de/1575/Arzneimittelrecht-fuer-Nutztierhalter>). It provides answers to all relevant question related to veterinary medical devices, covering definitions, approval requirements, directions for use and documentation obligations for livestock owners. It also addresses the legal provisions for the dispersion of drugs by veterinarians and storage of drugs on the farms.

The manual for the oral administration of veterinary medicines in the livestock sector through feed or drinking water has been revised in 2014 (http://www.bmel.de/SharedDocs/Downloads/EN/Agriculture/AnimalProtection/Leitfaden-Orale-Medikation.pdf?__blob=publicationFile). It describes the requirements for facilities that need to be met for the administration of drugs to livestock by food or drinking water and provides a corresponding checklist.

A manual on the control of bovine mastitis was published by the German Association for Veterinary Medicine (Deutsche Veterinärmedizinische Gesellschaft, DVG).

It describes all steps from taking milk samples via the lab analyses to the treatment options for bovine mastitis (<http://www.dvg.net/index.php?id=1286>).

Timescale: recently updated publications

The owners and organisation involved in the project

Federal Ministry of Food and Agriculture and stakeholders

Beef Quality Assurance Guide for Judicious Use



› The BQA program promotes the responsible use of antimicrobial drugs in beef cattle and develops robust antimicrobial stewardship practices while working to minimize the development of antimicrobial resistance.

The Beef Quality Assurance (BQA) Program (<http://www.bqa.org/>), funded by the Beef Checkoff, is a nationally coordinated, state-specific, voluntary program that provides guidelines for beef cattle production practices, helping every segment of the industry to implement proper cattle management techniques and demonstrates a commitment to quality. An area of ongoing focus within BQA is antimicrobial stewardship. In 1987, cattle farmers and ranchers created the Beef Producers Guide for Judicious Use of Antimicrobials in Cattle and this document has evolved as changes in scientific thinking occurred over the years. The current document contains 14 guidelines for judicious antimicrobial use and can be found at: <http://www.bqa.org/CMDocs/bqa/JudiciousMicrobials.pdf>.

Antimicrobial stewards seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, work to manage their animals to prevent infections, and limit the selection for antimicrobial resistant strains. BQA influences the management practices of more than 90% of the cattle on feed in the U.S.

The most recent Checkoff-funded 2011 National Beef Quality Audit (performed every 5 years to provide benchmarks for the U.S. beef industry) demonstrated that 9 out of 10 of the respondents reported a working relationship with a veterinarian. Moreover, 74% of the respondents (overall) reported that they always/

usually use written records to track animals that have been given an animal health product. Over 93% of cattlemen within each sector of the cattle industry reported that they always/usually verify withdrawal times for cattle that have received an animal health product. BQA continues to educate cattlemen and women on the judicious use of antimicrobial drugs and directs initiatives to improve antimicrobial stewardship practices.

Timescale: Initiated in 1987 with the development of the Beef Producers Guide for Judicious Use of Antimicrobials in Cattle, BQA antibiotic stewardship represents an ongoing quality assurance component of the larger BQA program for the U.S. beef industry.

The owners and organisation involved in the project

National Cattlemen's Beef Association and the Beef Checkoff

Guidelines of responsible and prudent use of antimicrobials in the livestock sector



- To reduce selection of antimicrobial resistant bacteria or resistance determinants because of use of antimicrobials in livestock animals. To minimize transmission of antimicrobial resistant bacteria or resistance determinants from livestock animals to humans. To preserve the effectiveness of antimicrobials for livestock animals and humans.

The Codex Alimentarius Commission (CAC), set up as the international standard setting body in the WTO' SPS Agreement, established the code of practice and guidelines on AMR issues which recommend the 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, the Food Safety Commission conducts risk assessment of individual antimicrobial agents used in the livestock sector, while the Ministry of Agriculture, Forestry and Fisheries (MAFF) implements risk management measures based on the risk assessment results in order to reduce the risk caused by antimicrobial resistant bacteria.

One of the risk management measures is the prudent use of antimicrobials. MAFF published the Prudent Use Guidelines to achieve the objectives mentioned above. The Guidelines point out the following:

1. To keep animals healthy by observing the standards of rearing hygiene management based on the Animal Infectious Diseases Control Law and to prevent infectious diseases by vaccinations or other means.
2. To determine treatment measures based on an appropriate diagnosis by veterinarians including identification of pathogenic bacteria.

3. To choose appropriate antimicrobials with the help of a microbial sensitivity test.
4. To use critically important antimicrobials such as fluoroquinolones only when the primary treatment has been ineffective.
5. To evaluate the efficacy of the antimicrobial treatment within an appropriate period of time and to change antimicrobials if necessary.
6. To share information regarding antimicrobial resistance among all stakeholders.

Timescale: since 2013

The owners and organisation involved in the project

Ministry of Agriculture, Forestry and Fisheries (MAFF)
http://www.maff.go.jp/j/syouan/tikusui/yakuzi/pdf/prudent_use.pdf
 (Available in Japanese)

National Chicken Council Judicious Use of Antibiotics



► **The objective of the national chicken council’s statement is to provide a unified position on the judicious use of antibiotics in the United States broiler chicken industry.**

The National Chicken Council (NCC), based in Washington, D.C., is the national, non-profit trade association representing the U.S. chicken industry. Our members, consisting of chicken processors, poultry distributors, and allied industry firms, provide approximately 95 percent of the chickens produced in the United States. The chicken industry shares the concern and desire to preserve antibiotics’ effectiveness in both humans and animals. The National Chicken Council supports FDA Guidances #209 and #213, and recognises the responsibility of the industry to implement the recommendations to phase out the use of medically important antibiotics in food animals for growth promotion.

Use of antibiotics in poultry production is low, with administration focused primarily on disease prevention and treatment. One-third of broiler chicken companies currently produce “No-Antibiotics Ever” and/or organic chicken products. All companies are eliminating the use of antibiotics for growth promotion, and most have already voluntarily eliminated antibiotics for this use. Companies are additionally investing in research and development of antibiotic alternatives and husbandry methods to further mitigate antibiotic use on farms.

NCC also supports the FDA’s Veterinary Feed Directive, which will ensure that all antibiotics administered to food producing animals are only done so under the care and prescription of

a licensed veterinarian. Proper animal care is under the stewardship of the producer and the veterinarian whom together share the responsibility to carefully protect the effectiveness of all antibiotics. Our core principles are based upon responsible use, transparency, and validation of treatment practices to assure consumers that the greatest care is taken in raising and producing broiler chickens.

Timescale: 3 years (End date: December 2016)

The owners and organisation involved in the project

National Chicken Council
www.nationalchickencouncil.org

TM Drug Residue Avoidance and Best Practice Guide



- › The milk and dairy beef residue avoidance manual is a concise resource to review those antibiotics approved for dairy animals and is also an educational tool and resource for farm managers as they develop their on-farm best management practices necessary to assure responsible and judicious use of antibiotics. Dairy farmers use this manual with their veterinarians and employees to assure antibiotic stewardship as their responsibility to combat antimicrobial resistance.

The National Milk Producers Federation (NMPF), based in Arlington, VA, develops and carries out policies that advance the well-being of dairy producers and the cooperatives they own. The members of NMPF's cooperatives produce the majority of the U.S. milk supply, making NMPF the voice of more than 32,000 dairy producers on Capitol Hill and with government agencies.

Among the measures available to treat and prevent the outbreak and spread of animal diseases among the nation's dairy cattle, the judicious and responsible use of antimicrobial drugs has a positive impact on animal health and well-being while maintaining a safe milk supply for the public.

For more than 20 years, the U.S. dairy industry has focused educational efforts on the judicious use of antimicrobial drugs through the annual publication of a Best Practices Manual. The 2015 edition of the National Dairy FARM Program: Farmers Assuring Responsible Management™ Milk and Dairy Beef Drug Residue Prevention Manual (published in October 2014) developed by NMPF is the primary educational tool for dairy farm managers throughout the country on the judicious and responsible use of antibiotics including avoidance of drug residues in milk and meat. Additionally, the 2015 edition of

the Residue Prevention Manual provides dairy farm managers guidance about the implementation of the federal Food and Drug Administration Guidances for Industry #209 and #213 and the revised Veterinary Feed Directive Rule.

Through the 2016 edition of the Residue Prevention Manual (to be published October 2015), NMPF and the U.S. dairy industry will continue our commitment to the judicious and responsible use of antimicrobials. Additionally, the 2016 edition will include a focus on antimicrobial stewardship.

Timescale: ongoing

The owners and organisation involved in the project

- National Milk Producers Federation
2101 Wilson Blvd, Suite 400
Arlington, VA 22201
www.nmpf.org
- National Dairy FARM Program
www.nationaldairyfarm.com

National Pork Board Antibiotic Stewardship Plan



› The pork industry will continue to support stewardship outreach to our pork producers, veterinarians and consumers to augment our Pork Quality Assurance® Plus program; we will continue to define additional methods to maintain the highest swine herd health status possible to minimize the need for antibiotic use; we will measure success through conducting new research and collecting data to improve our understanding of the optimum role of antibiotics in raising a safe and healthy pork supply.

1. EDUCATION—The National Pork Board will collaborate with allied partners to develop educational materials about the new FDA regulations and antibiotic stewardship. The Pork Board will revise and give added emphasis to antibiotic stewardship in the industry's Pork Quality Assurance® Plus program. This action will ensure that America's pork producers understand the importance of the veterinarian-client-patient relationship and are prepared to implement the FDA regulations.

2. RESEARCH—The Pork Board will make antibiotic use and resistance a top research priority. Since 2000, the Pork Checkoff has invested \$5.3 million in research on the epidemiology of antibiotic resistance, as well as efforts to define alternatives to antibiotic use. The board will invest close to a million dollars of new money in additional research and educational programming in 2016. The Pork Board will work with an advisory group of subject matter experts to objectively review and provide recommendations on Pork Checkoff policies and programs in the area of antibiotic use and resistance. The Pork Board will continue to work closely with federal agencies and other commodity group partners to research and identify models and metrics that will provide value to the pork industry for continual improvement of antibiotic use.

3. COMMUNICATION OUTREACH—Communication regarding antibiotics to all segments of the pork chain will continue to be a main emphasis for the Pork Board, with special emphasis on pig farmers and the new FDA rules. Collaboration with all state pork associations, the American Association of Swine Veterinarians, the National Pork Producers Council, the American Feed Industry Association, land-grant universities and others will coordinate and amplify the National Pork Board's communications efforts.

Timescale: The work coincides with our 5 year strategic plan of which we are now nearing the end of the first year under this plan.

The owners and organisation involved in the project

National Pork Board
 Phone: (515) 223-2600
 Email: info@pork.org
 Web: <http://www.pork.org>
<http://www.pork.org/antibiotics>

Use of Antibiotics in Animals Training Module



- ▶ To promote education and outreach on judicious use of antibiotics in animals through supporting training requirements for accredited veterinarians.

USDA's Animal and Plant Health Inspection (APHIS) Service undertook the creation of a training module, Use of Antibiotics in Animals, through a cooperative agreement with Iowa State University's Center for Food Security and Public Health (CFSPH) in FY 2011 to support training requirements for accredited veterinarians. USDA assembled a broad range of contributors/reviewers from multiple areas of the veterinary and public health world to collaborate on the online and PowerPoint training module.

The objectives of the module include describing how antimicrobial drugs are currently used and providing resources on responsible antimicrobial drug use available to veterinarians. To date, 6,465 hours of training have been logged for accredited veterinarians since 2012 with the module being completed 10,208 times online since 2012. Of USDA's suite of 25 training modules, Use of Antibiotics in Animals is the 8th most popular module. All of USDA's training modules are open to the public without a user name or password, and according to Google Analytics the traffic the online module sustains exceeds that which can be attributed to accredited veterinarians alone.

The module is available at <http://aast.cfsph.iastate.edu/ABX/index.htm> as well as through PowerPoint presentations conducted at multiple veterinary meetings each year. A thumb-drive pdf version of the module is also available for purchase by accredited veterinarians from Iowa State University's Center for Food Security and Public Health (CFSPH) for a nominal cost of production and shipping.

Timescale: ongoing

The owners and organisation involved in the project

USDA

http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth?urlile=wcm%3apath%3a%2Faphis_content_library%2Fsa_our_focus%2Fsa_animal_health%2Fsa_vet_accreditation%2Fct_aast

Rules for oral medication of livestock



- › **Strengthening prudent use through legal requirements. In 2015, provisions of the manual for the oral administration of veterinary medicines in the livestock sector through feed or drinking water have become legally binding.**

A recently adopted regulation obliges farmers to ensure that only sick animals are treated with oral medication. Technical dosing devices have to be technically up to current standard and placed as closely as possible to the animals being treated. After the treatment, all technical installations involved in the treatment have to be cleaned.

With the adoption of this regulation the above-mentioned provisions, which are part of the manual for the oral administration of veterinary drugs in the livestock sector through feed or drinking water, have become legally binding.

Timescale: coming into force July 2015

The owners and organisation involved in the project

Legislator

Prescription only for antibiotics in veterinary medicine



- › Reducing the amount of antibiotic treatment of fattening animals to the inevitable minimum by improving animal health. Strengthening prudent use through legal requirements.

In Germany, all antimicrobial veterinary medicinal products are available only on prescription by a veterinary surgeon who in turn is only permitted to hand out prescriptions to owners of animals under his or her care. Over-the-counter sale is prohibited.

The details are laid down in section 56 (medicated feed), section 56a (prescription, dispersion and administration by veterinarians) and section 57 (acquisition and possession by animal owners) of the German drug law (http://www.gesetze-im-internet.de/englisch_amg/medicinal_products_act.pdf) and in the Regulation on veterinary pharmacies (http://www.gesetze-im-internet.de/bundesrecht/t_hav/gesamt.pdf). These legal provisions also refer to the guidelines for the prudent use of veterinary antimicrobial drugs. In short, drugs can only be prescribed for animal species and indications for which they have been approved. Off-label use is possible within the legal provisions.

There is an EU-wide ban on the use of antimicrobial veterinary medicinal products as growth promoters since 2006. Their use as routine prophylaxis when bringing in new animals is not considered as state of the art.

Timescale: ongoing since many years

The owners and organisation involved in the project

Legislator

CHAPTER **4**

Strengthening the surveillance system

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Human Health



Animal Health



Human and Animal Health



When addressing specific interventions of infection prevention and control, it is essential to know the extent of antimicrobial resistance as well as how it emerges and spreads. Surveillance systems have been set up in many (industrialized) countries, monitoring antibiotic resistance and antibiotic use, nosocomial infections, and animal health. The data show the dimension of the problem. Together with detailed information obtained by national reference centers, the data also permit an early detection of resistant strains that might pose a threat to public health, and timely interventions. Strengthening these surveillance systems and enabling them to provide timely, accurate, representative and comparable data are a major step in combating AMR.

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Surveillance



› **The UK has made significant progress in improving the quality of the available data to better measure antibiotic use and trends in resistance across the health sector. In 2014, Public Health England Published prescribing data for both secondary and primary care in England for the very first time.**

Building on the adoption of the Global Action Plan on AMR, the UK announced the establishment of the Fleming Fund, a £195m Fund to support the development of surveillance networks and laboratory capacity in low and middle income countries.

The work includes the provision of £3m funding for WHO to sustain and develop momentum around AMR as a global health threat, support countries to develop high quality action plans; develop norms and standards for AMR; and links with agriculture and animal husbandry.

The UK has also strengthened surveillance through a comprehensive surveillance programme in England—the English surveillance programme for antimicrobial utilisation and resistance or ESPAUR, and the Electronic Communication of Surveillance in Scotland (ECOSS)) which tracks prescribing and resistance trends in UK agreed drug/bug combinations and publishes the results.

In the veterinary sector, a report which combines veterinary antimicrobial sales and antibiotic susceptibility of veterinary pathogens was first published in November 2013: the UK Veterinary Antibiotic Resistance and Sales Surveillance report, (UK-VARSS). It is updated and published annually in November. Sales data give an indication of the pattern of use of veterinary antimicrobial

products in the UK and have been published since 1993; Resistance data provides an estimate of the level of resistance in both veterinary and zoonotic pathogens since they have been added to the report in 2013.

UK veterinary surveillance incorporates antibiotic sensitivity testing of bacteria from healthy animals (since 2014) and from clinical veterinary cases (since 1998), and reports the total quantity of antibiotics sold by veterinary pharmaceutical companies (since 2005). These data have been reported together since 2013 in the annual Veterinary Antibiotic Resistance and Sales Surveillance report, (UK-VARSS). The UK is currently working to establish systems for surveillance of antibiotic consumption in animals.

Timescale: Some of the work has been completed. Ongoing work is indicated.

The owners and organisation involved in the project

Department of Health/Public Health England/
Veterinary Medicines Directorate

Canadian Antimicrobial Resistance Surveillance System (CARSS)



- ▶ **CARSS will strengthen the coordination and reporting of AMR and AMU data from animal, agri-food, human health care and community settings to support informed decisions and concrete action on the prudent use of antimicrobials to mitigate diseases.**

The Canadian Antimicrobial Resistance Surveillance System (CARSS) was established by the Public Health Agency of Canada in 2014 to provide a national picture on AMU and AMR and strengthen the coordination of AMR/AMU activities and information on animal and human health held by many stakeholders. Building on existing animal and human health surveillance systems, CARSS represents an important step in the evolution of AMR/AMU surveillance that will use accurate, relevant and timely data to provide an annual, comprehensive, integrated picture of AMR in Canada.

The first CARSS report released in March 2015 included human health data and animal and food AMR/AMU data that is currently produced through the Public Health Agency of Canada's surveillance systems. The second report to be released in March 2016 will enhance the analysis and knowledge translation, while over time more comprehensive animal surveillance information will be incorporated to better reflect a One Health approach.

From a system perspective, the first phase of CARSS focuses on incorporating comprehensive AMR/AMU human health information, while the second phase will incorporate more comprehensive animal AMR/AMU surveillance information. In addition to reporting on the state of AMR and AMU in Canada, CARSS reports will inform the expansion of

surveillance activities to areas of greatest need, and provide useful and relevant information to stakeholders and the public in support of antimicrobial stewardship interventions to further protect the health of Canadians.

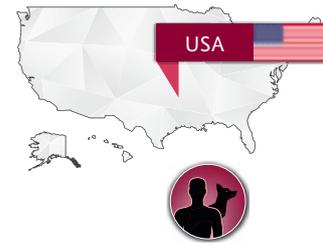
This integrated approach requires significant internal and external review, consultation and planning in order to arrive at a system that reflects valid and credible data to provide an accurate national picture. The work being done by the Public Health Agency of Canada in this area can inform other jurisdictions wishing to enhance AMR and AMU surveillance over multiple sectors.

Timescale: 2014–2017

The owners and organisation involved in the project

Lead: Public Health Agency of Canada,
Dr. Chris Archibald
carss-scsra@phac-aspc.gc.ca
<http://healthycanadians.gc.ca/publications/drugs-products-medi>

The National Anti-microbial Resistance Monitoring System



- ▶ To provide meaningful data to help identify antimicrobial drug resistance in humans and animals, and to provide timely updates to veterinarians and physicians on patterns of resistance, in part through monitoring trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals.

The National Antimicrobial Resistance Monitoring System (NARMS) was established in 1996. NARMS is a collaborative project of state and local public health departments, the FDA, the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA). This national public health surveillance system tracks changes in the antimicrobial susceptibility of enteric (intestinal) bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA) in the United States.

The NARMS program helps promote and protect public health by providing information about emerging bacterial resistance, how resistant infections differ from susceptible infections, and the impact of interventions designed to limit the spread of resistance. NARMS monitors antibiotic resistance among the following four major foodborne bacteria: Salmonella, Campylobacter, Escherichia coli, and Enterococcus. NARMS data are used by FDA to make regulatory decisions designed to preserve the effectiveness of antibiotics for humans and animals. This provides a one health approach to surveillance resulting in information critical for the assessment of resistant bacteria in humans and the food supply.

In December 2013, the FDA announced plans to end the long-term practice of administering medically

important antibiotics to food producing animals for promoting animal growth and increasing feed efficiency, practices based on economic efficiency rather than medical necessity. This judicious use strategy is part of the agency's multipronged approach to preserving the power of antibiotics for treating infectious diseases in humans and animals. By tracking resistance to the antimicrobial compounds affected by this policy, NARMS will play a role in measuring the strategy's impact on overall resistance in foodborne bacteria.

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/>
<http://www.cdc.gov/narms/>

Timescale: ongoing

The owners and organisation involved in the project

State and local public health departments, the FDA, CDC, and the USDA

EU surveillance of AMR in bacteria from humans and animals



- › The European Union legislation on AMR in the food chain ensures harmonised monitoring systems in the EU, fosters comparability between the member states and facilitates the monitoring of patterns of multi-drug resistance. Through coordination with surveillance in human health, it allows for comparisons between the human and veterinary sectors.**

EU Surveillance of AMR in bacteria from humans:
The European Antimicrobial Resistance Network (EARS-Net) is an EU-wide network of national surveillance systems coordinated by the European Centre for Disease Prevention and Control (ECDC). AMR data in 7 bacterial pathogens are collected by national networks from 900 public-health laboratories serving over 1,400 hospitals. Publication is via an interactive database with maps, graphs and tables, and an annual report. The Food and Waterborne Diseases and Zoonoses Network (FWD-Net) coordinated by ECDC collects data on AMR in Salmonella and Campylobacter infections in humans. Results are presented in the annual “EU Summary Report on AMR in zoonotic and indicator bacteria from humans, animals and food” published by the European Food Safety Authority (EFSA) and ECDC.

EU Surveillance of AMR in bacteria from farmed animals and food:
A revised union legislation, which entered into force on 1 Jan. 2014, lays down minimum requirements for harmonised monitoring of AMR from a public health perspective, combinations of bacterial species/food producing animal populations/food and includes rules for sampling, analysis of the isolates and interpretations of the results. The legislation also includes requirements for harmonised monitoring

and reporting of ESBL-, AmpC- and carbapenemase-producing bacteria in certain animal populations and food types. Reliable and comparable data are essential to assess the sources of AMR, conduct risk assessments and evaluate the impact of the mitigation measures in place. They provide EU reference data on AMR for public health purposes. The network is coordinated by EFSA and results published in the “EU Summary Report”.

Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA):
In 2015, ECDC, EFSA and the European Medicines Agency (EMA) published the first integrated analysis of EU data combined with data on antimicrobial use in animals and humans.

Timescale: multi-annual

The owners and organisation involved in the project

European Commission, DG Health and Food Safety
<http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013D0652>

Antimicrobial Resistance Surveillance (ARS)



› Antimicrobial Resistance Surveillance (ARS) is a laboratory-based sentinel surveillance system with continuous collection of data on antimicrobial resistance for the entire spectrum of clinically relevant bacterial pathogens for both inpatient and outpatient care at national level. The major objective is to provide reference data for public use and specific feedback for participating laboratories.

Antimicrobial Resistance Surveillance (ARS) was established in 2008 by the Robert Koch Institute (RKI) with funding of the MoH; since 2010 it is a permanent task of the RKI. As a national surveillance system, ARS takes part in the European Antimicrobial Resistance Surveillance Network (EARS-Net).

ARS was designed as a laboratory-based sentinel surveillance system with continuous data collection. Laboratories conducting microbiology testing of samples from medical care institutions participate voluntarily in ARS. They forward results of susceptibility testing as performed during routine diagnostics in standardized format via an electronic interface to the RKI where, after plausibility testing, they are stored in a central database. For participating laboratories ARS provides feedback for individual hospitals as well as an alert system for rare resistance phenotypes.

Proportions of resistance for the 16 most common and clinically relevant bacteria are computed on a yearly basis and made accessible to the public on the ARS website via an interactive database. These data can and should be used as reference data for evaluation on local, regional and national level.

Since 2008 the number of laboratories participating in ARS has increased every year resulting in growing

numbers of healthcare institutions under surveillance (coverage 2014: 346 hospitals which corresponds to 17 percent of all German hospitals; approx. 7,000 practices corresponding to 8.5 practices per 100,000 inhabitants). Participation is voluntary.

The innovative feature of ARS is the completely electronic data flow from laboratory to the central database and widely automated data processing that reduces workload in the laboratory and at the RKI thus allowing for large numbers of participants which is crucial for a country with thousands of health care institutions that should be monitored.

Timescale: ongoing

The owners and organisation involved in the project

Robert Koch Institute
<https://ars.rki.de/>

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
 Contact: Dr. Michael Mulvey, Federal Co-Chair
michael.mulvey@phac-aspc.gc.ca
<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).

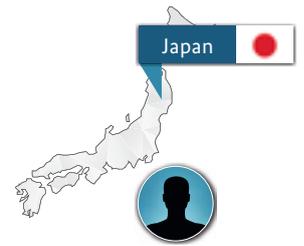
CNISP surveillance provides key information that can be used to measure the quality of patient care, and informs the development of federal, provincial and territorial infection prevention and control programs and policies. Both the surveillance results and the structure to support comprehensive and 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
cnisp-pcsin@phac-aspc.gc.ca

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.

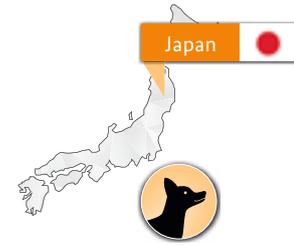
Timescale: Start of the project: 2013.

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

The owners and organisation involved in the project

Robert Koch Institute, Dep. 3, FG37
Seestr. 10, D-13353 Berlin
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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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

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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.jpjamr.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.

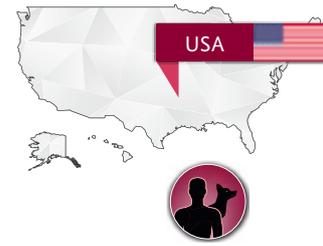
In the veterinary sector, Defra (UK ministry of agriculture) and the Veterinary Medicines Directorate funds research on AMR in animals, as well as contributing to the Research Funders Forum.

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

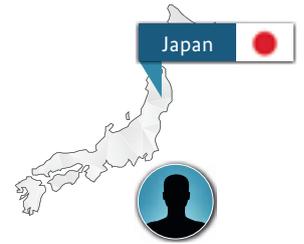
Technology Agreements as well as science policy dialogues with partner countries and organizations. Advocacy for AMR research through these policy forums helps to raise the priority of AMR research and improve S&T coordination and collaboration.

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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Gemeinsam handeln.*