Responses to the Antimicrobial Resistance Threat

A comparative study of selected national strategies and policies

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PREFACE

Dear Reader,

Over the last 30 years, no major new types of antibiotics have been developed. Without urgent action, we are heading for a post-antibiotics era, in which common infections and minor injuries can once again kill.

Switzerland supports the adoption of the Global Action Plan on antimicrobial resistance by the 68th World Health Assembly this month in Geneva, and co-sponsors the relevant resolution. At national level, Switzerland is currently developing a national strategy to monitor, prevent and combat antibiotic resistance. Linkages across sectors including human and animal health as well as agriculture are important in order to enhance global health security.

Transparency and the exchange of best practices in combatting antimicrobial resistance are key, and Switzerland is committed to participating in international cooperation in this area. Switzerland is sharing this comparative study as a contribution to the Global Health Security Agenda. The purpose of this study is to showcase best practices and present examples of currently applied or developed measures to policy makers who embark on the journey of developing their own national strategy.

We hope you will find this document useful in our common endeavor to fight antimicrobial resistance.

Bern, May 2015
Tania Dussey-Cavassini
Swiss Ambassador for Global Health

EXECUTIVE SUMMARY

The escalating problem of Antimicrobial Resistance is a serious threat to global public health. Treating microorganism infections has become increasingly difficult, clinical outcomes are getting worse, healthcare and social costs continue rising. It has been estimated that resistant bacteria are currently responsible for about 25.000 deaths in Europe and more than 23.000 deaths in the USA each year. WHO has therefore repeatedly called for its member states to develop and implement national AMR strategies and policies.

The overall aim of this study has been to identify key success factors in response to the antimicrobial resistance threat. This study compares the national AMR strategies of a number of European countries with comparable health systems and similar challenges. In addition, the strategies of the USA and South Africa as well as approaches from governments of low and middle-income countries have also been studied.

Many differing measures have been implemented or are being planned by governments and their institutions at both national and local levels. The main areas of work presented in this study include surveillance and monitoring, prescribing practices and regulations, infection prevention and control, awareness and education, research and development, collaboration and coordination mechanisms as well as the preparation of the required framework.

The study demonstrates the complexity of challenges, the diversity of stakeholders involved, and the variety of measures and initiatives in the field of antimicrobial resistances. It also illustrates that a coordinated and harmonized approach at local and national levels as well as at the global level is urgently needed to combat this threat. A *One Health* approach is highly recommendable as AMR is a multifaceted issue at the animal-human-ecosystems interface. Countries need to identify evidence-based solutions suitable to their respective national and local contexts. Setting measurable and achievable targets is essential for securing political commitment and for raising public awareness. Without the exchange of knowledge and experiences between countries the global AMR threat will be very difficult to tackle.

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LIST OF ABBREVIATIONS

ANRESIS	Swiss Centre for Antibiotic Resistances
AMR	Antimicrobial Resistance
ABR	Antibiotic Resistance
ASU	Antibiotic Smart Use Programme
BARDA	Biomedical Advanced Research and Development Authority
BMBF	Federal Ministry of Education and Research (GER)
BMBL	Federal Ministry of Food, Agriculture and Consumer Protection (GER)
BMG	Federal Ministry of Health (GER)
BMU	Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (GER)
CDC	Center for Disease Control (USA)
CRE	Carbapenem-Resistant Enterobacteriaceae
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DART	Deutsche Antibiotika-Resistenz Strategie (Germany)
DEFRA	Department for Environment, Food and Rural Affairs (UK)
DH	Department of Health (UK)
EARS-NET	European AMR Surveillance Network
EB	Executive Board
ECDC	European Center for Disease Control
EFSA	European Food and Safety Authority
EMA	European Medicines Agency

EPRUMA	European Platform for the Responsible Use of Medicines in Animals
ESAC-NET	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-spectrum beta-lactamase
ESPAUR	English Surveillance Programme for antimicrobial utilisation and resistance
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	Federal Drug Administration (USA)
FOPH	Federal Office of Public Health (Switzerland)
GAP	Global Action Plan (WHO)
GARP	Global Antibiotic Resistance Partnership
GHSA	Global Health Security Agenda
GPW	General Program of Work (WHO)
HSLG	Interdepartmental High-level Steering Group (UK)
IHR	International Health Regulations
IPC	Infection Prevention and Control
LMIC	Low- and Middle-Income Countries
MRSA	Methicillin-Resistant Staphylococcus Aureus
NGO	Non-Governmental Organizations
NOIS	Norwegian Surveillance System for Healthcare-associated Infections and Antibiotic Use

NORM-VET	Norwegian surveillance programme for antimicrobial resistance
OIE	World Organization for Animal Health
PHE	Public Health England
SAASP	South African Antibiotic Stewardship Program
SEARO	Regional Office for South East Asia (WHO)
SIDA	Swedish International Development Cooperation Agency
SSI	Statens Serum Institute
SSTF	Start Smart then Focus
STAG-AMR	Strategic and Technical Advisory Group on AMR
STATENS	Statens Serum Institute
STRAMA	Swedish strategic programme against antibiotic resistance
TATFAR	Transatlantic Task Force against AMR
TTT	Technical Task Team (Ghana)
UK	United Kingdom
USA	United States of America
WHA	World Health Assembly
WHO	World Health Organization
WHO/EURO	WHO Regional Office for Europe

This present study explores the national AMR strategies of a number of European countries with comparable health systems and with similar AMR challenges. In addition the AMR strategies of the USA and some approaches from governments of low- and middle-income countries (e.g. South Africa) have also been analysed.

Aim and objectives

The overall aim of this study is to identify best practice solutions in response to the antimicrobial resistance threat. The specific objectives are:

Specific objectives

1. To describe the specific context for the formulation of national strategies
2. To assess which ministries and institutions have been coordinating the national AMR strategy
3. To identify whether the countries have been applying a *One Health* approach for this task
4. To describe the main focus and key areas of the strategies
5. To assess how governments have been trying to reach their stated AMR goals
6. To evaluate the impact of government action through their AMR strategies / policies
7. To identify effective campaigns
8. To highlight the results and key success factors

A mixed-methods study based on an extensive, web-based literature and document review and expert consultation has been carried out to address the objectives stated above, using the most recent national AMR strategies or action plans as core documents. These have been analysed according to the specific objectives and then compared, identifying key success factors and best practice solutions. Wherever it seemed appropriate, previous strategies, policies and activities of the respective country have been included.

Choice of countries

The choice of countries for this study has been based on the countries selected for a previous study of the Federal Office of Public Health (FOPH), comparing international strategies on antibiotic resistance with respect to their structure and main content. These countries are the United Kingdom, Sweden, Denmark, Germany, Norway, France and the USA. In addition the proposed strategies of Switzerland and South Africa have also been selected to add additional perspectives.

The key documents of this study are shown in the table below.

Country	Title	Published
United Kingdom	• UK AMR Strategy and Action Plan	2000
	• UK 5 - Year Antimicrobial Resistance Strategy 2013 - 2018	2013
Sweden	• Strategy for coordinated efforts to prevent antibiotic resistance and healthcare-associated infections	2005
	• Swedish Work on the containment of antibiotic resistance, Tools, Methods, Experiences	2014
Denmark	• Risk management of antimicrobial use and resistance from food-producing animals in Denmark	2007
Germany	• DART – German Antimicrobial Resistance Strategy	2008
Norway	• National Strategy for prevention of infections in the health service and antibiotic resistance 2008-2012	2008
France	• Plan national d'alerte sur les antibiotique 2011-2016	2011
USA	• National Strategy for Combating Antibiotic-Resistant Bacteria	2015
Switzerland	• Antibiotic Resistance Strategy (StAR)	2015
South Africa	• Antimicrobial Resistance National Strategy Framework	2015

Limitations

The research methods used in this study are subject to certain limitations. The choice of countries is certainly an important aspect when identifying best practice solutions by analysing national strategies and policies. A further critical aspect is the latency of the implementation of political decisions. Thus results achieved may also be due to many other factors, especially in this very multifaceted AMR field with a high number of different stakeholders. Moreover it is often difficult to distinguish which policy actions have actually been implemented or which rules and regulations have been enforced. This is particularly the case in this kind of multinational study as some countries publish their main strategies and policies in English, while many other official documents, e.g. national laws, are often only published in their national language. Therefore information might be missed or misinterpreted. In summary, possible limitations to this study have been mentioned, although it is rather difficult to estimate what impact these might have.

I. General Introduction

Antimicrobials play an essential role in combatting infectious diseases (e.g. pneumonia or sepsis) in both human and veterinary medicine. Antimicrobial resistance (AMR) develops when microorganisms (bacteria, viruses, fungi or parasites) no longer respond to drugs they were previously sensitive to, leading to treatment and infection-control difficulties, worsening clinical outcomes and increased healthcare and social costs. The main reason for this problem is an excessive and often inappropriate usage of antimicrobial medicines, particularly antibiotics (WHO, 2012).

Dramatically increasing resistances to drugs against tuberculosis and malaria are being observed in low- and middle-income countries, whereas rapidly rising numbers of resistances to antibiotics used for common infections (e.g. urinary tract infections) are being detected worldwide. It has been estimated that resistant bacteria are responsible for about 25.000 deaths in Europe, more than 23.000 deaths in the USA and more than 38.000 deaths in Thailand every year (Norrby et al., 2009; WHO, 2014b). These numbers might appear to be relatively low in comparison to cancer and heart disease mortality rates, but they are constantly on the increase. Although these figures are only estimates, the burden of disease caused by AMR is not only likely to lead to a reduction of options for infectious diseases treatment, chemotherapy, surgery or transplantations but also to a significant impact on health systems and the economies, especially in low- and middle-income countries (WHO, 2012).

Antimicrobial resistance has now become a serious threat to global public health. A coordinated and harmonized approach at local and national levels as well as the global level is urgently needed to combat this threat. At the global level the World Health Organization (WHO) has described AMR as "one of the most significant global threats to public health" (WHO, 2014b) and has been working closely with the World Organization for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO), the European Union (EU) with its European Center for Disease Control (ECDC) and the US Center for Disease Control (CDC) to work out guidelines and schemes to support national governments in developing their AMR strategies (FAO, 2010; WHO, 2012).

Some of these strategies are based on the so-called *One Health* approach, a "collaborative and intersectoral effort of multiple health science professions, together with their related disciplines and institutions – working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants, and our environment." (Gibbs, 2014)

II. World Health Organization and AMR

The mounting problem of Antimicrobial Resistance has become a very serious threat for global public health. The rapid increase of multi-drug resistant and even extremely drug resistant bacteria, e.g. in tuberculosis, is of great concern to both national and international health organizations. The World Health Organization as the leading and coordinating international health authority within the United Nations system is presently at the forefront in the fight against antimicrobial resistances. WHO has been providing technical guidance to its Member States to support their AMR containment and assisting them in the establishment of the necessary infrastructure to support national medicines policy, health services, and surveillance capacities (WHO, 2001).

Already recognizing the rising AMR problem in 1998, the 51st World Health Assembly (WHA) agreed on a resolution urging Member States to become involved in the fight against AMR and encouraged them to develop sustainable systems in order to detect resistant pathogens, to monitor volumes and patterns of use of antimicrobials and of the impact of control measures (WHO, 1998). Following the WHA Resolution, many countries have developed national action plans to address the AMR problem. However even though there had already been strong evidence of the existence of the AMR threat in the late 90's, not much data was available to determine what kind of actions needed to be taken against it and which of these would be most effective.

The 2001 WHO Global Strategy for Containment of Antimicrobial Resistance addressed this challenge and provided a framework of interventions to slow the emergence and reduce the spread of antimicrobial-resistant microorganisms based on (WHO, 2001):

- Reducing the disease burden and the spread of infection
- Improving access to appropriate antimicrobials
- Improving use of antimicrobials
- Strengthening health systems and their surveillance capabilities
- Enforcing regulations and legislation
- Encouraging the development of appropriate new drugs and vaccines

World Health Day 2011

In 2011 the WHO's World Health Day was held under the theme "Antimicrobial resistance: no action today, no cure tomorrow" to bring international attention to this growing threat to public health. WHO's Director General, Margaret Chan, stated, "The message on this World Health Day is loud and clear. The world is on the brink of losing these miracle cures. In the absence of urgent corrective and protective actions, the world is heading towards a post-antibiotic era, in which many common infections will no longer have a cure and, once again, kill unabated." (Chan, 2011)

Although there was already an awareness of the more essential strategic interventions needed to control antimicrobial resistance, both national and global responses had been inadequate so far, recommended policy changes hadn't been followed, and overall efforts had often been only fragmented and not comprehensive enough. This unsatisfying situation led WHO and its Member States in 2011 to work out policy packages for combatting antimicrobial resistance, defining six priority areas for action. These packages involved the following:

WHO - Priority areas for action (2011)
- Committing to a comprehensive, financed national plan with accountability and civil society engagement
- Strengthening surveillance and laboratory capacity
- Ensuring uninterrupted access to essential medicines of assured quality
- Regulating and promoting rational use of medicines including in animal husbandry, and ensuring proper patient care
- Enhancing infection prevention and control (IPC)
- Fostering innovations and research and development for new tools

In addition a Strategic and Technical Advisory Group on AMR (STAG–AMR) was set up in September 2013 to advise the WHO Director-General on WHO's strategic plan and on priority activities in tackling AMR, on major issues and challenges to be addressed by WHO with respect to achieving the strategic goals for AMR and on the engagement of partners and outreach efforts to tackle AMR. The STAG-AMR has been working closely with the Secretariat and technical teams from each of WHO's Regional Offices as well as with representatives and observers from a broad range of partner organizations. (WHO, 2013b)

Reporting to the WHO Executive Board (EB) in December 2013 the Secretariat highly emphasized the need for global action again. WHO and the STAG-AMR experts have called for an urgent renewal and expansion of the action being taken to tackle this growing public health threat. In their report it was also stated that only 32% (29 of 92) of WHO's Member States covered by a survey already had a comprehensive national action plan in place (60% of high income countries and less than 20% of low- and middle-income countries) (WHO, 2013a). During the following EB meeting in January 2014 it was noted that "awareness of the broad scope and urgency of the threat posed has been limited and that previous resolutions of the Health Assembly and WHO's strategies for the containment of antimicrobial resistance have not yet been widely implemented." (WHO, 2014c)

In March 2014 WHO published its first Global Report on Surveillance of Antimicrobial Resistance with data from 114 countries providing a comprehensive picture of the magnitude of AMR and the current state of worldwide surveillance. The report shows clearly that resistance to common bacteria has reached worrying levels in many regions of the world, even limiting available treatment options for common infections in some settings. In addition the report reveals that AMR surveillance is still inadequately coordinated, including a lack of standard methodology and data sharing, and that there are still many information and research gaps which need to be addressed. Strengthening global AMR surveillance is described as an essential factor in monitoring the effectiveness of interventions and in detecting new developments and threats (WHO, 2014b).

World Health Assembly Resolution 2014

In May 2014 the World Health Assembly, recognizing WHO's leadership role in the containment of antimicrobial resistance, issued a new AMR resolution, welcoming the establishment of the WHO Strategic and Technical Advisory Group on AMR and the tripartite collaboration between WHO, FAO and OIE (WHO, 2014a). This resolution urges Member States and regional economic integration organizations (e.g. European Union):

1. to increase political awareness, engagement and leadership concerning the AMR threat
2. to take urgent action at national, regional and local levels to strengthen infection prevention and control
3. to develop or strengthen national plans and strategies and international collaboration for the containment of AMR
4. to mobilize human and financial resources for the implementation of these plans
5. to strengthen overall pharmaceutical management systems and laboratory infrastructure
6. to monitor the use of antibiotics and the extent of AMR in all relevant sectors (human health, veterinary health and agriculture)
7. to improve, among all relevant care providers, the public and other sectors and stakeholders, awareness of (i) the threat posed by antimicrobial resistance, (ii) the need for responsible use of antibiotics and (iii) the importance of infection prevention and control measures
8. to encourage and support research and development, including by academia and through new collaborative and financial models
9. to collaborate with the Secretariat in developing and implementing a draft global action plan to combat antimicrobial resistance
10. to develop antimicrobial resistance surveillance systems in all sectors involved

In June 2014 a two-day Ministerial Conference on Antibiotic Resistance (ABR) in The Hague, Netherlands, was co-hosted by the Dutch government and WHO under the theme *Joining Forces for Future Health* (Netherlands, 2014). Ministers and senior officials from more than 20 countries and delegates from key partners (e.g. FAO, OIC, EC, World Bank) called for intensified international political action, strongly supporting the development of the WHO AMR Global Action Plan and many other specific actions, especially a cross-governmental approach to AMR at the national level led by health ministers. In addition they emphasized the need for new and next generation antibiotics as well as the development and use of rapid point-of-need diagnostics.

Draft Global Action Plan on Antimicrobial Resistance

In October 2014, following the new WHA Resolution on AMR, the WHO held an informal Member State consultation on the development of a Global Action Plan (GAP) for tackling antimicrobial resistance in Geneva. Preceding this Member State consultation all interested organizations, institutions, networks and civil society groups were invited by WHO to take part in a web-based consultation in order to include additional perspectives from the relevant sectors into the discussions on the GAP draft document. The overall aim of the Global Action Plan is "to ensure, for as long as possible, continuity of treatment and prevention of infectious diseases with effective and safe medicines that are of appropriate quality, used in a responsible way, and accessible to all who need them". The following measures of outcome and impact have been proposed to monitor the effectiveness of the GAP (WHO, 2014d):

WHO Global Action Plan - Proposed measures of outcome and impact

- A reduction in the prevalence of AMR, based on data collected through integrated AMR surveillance programs and specific infectious disease control programs in all countries
- A reduction in the mortality attributable to AMR
- A reduction (to zero) in the number of serious infectious diseases that cannot be prevented or treated
- A reduction in the prevalence of selected infectious diseases, and in particular preventable infections (achieved through effective IPC measures)
- An increase in the number of organisms for which specific rapid diagnostic tests are available (including for use in LMIC)
- Increase in the number of new medicines entering phase II clinical studies, and for which mechanisms are in place to ensure preservation, and access in low and middle-income countries.
- A reduction in global human consumption of antibiotics, recognizing the need for improved access in some settings
- A reduction in the consumption of antibiotics used in food production and reduction in the veterinary use of antibiotics critically important for human health.
- Progressive reduction (to zero) in the use of medical and veterinary antimicrobials for applications other than human and animal health

Detailed actions are described in the draft GAP to enable the achievement and measurement of these targets. The draft GAP is based on six guiding principles and is structured around five strategic objectives:

Guiding principles

1. Whole-of-society engagement
Antimicrobial resistance affects everyone, regardless of where they live, their health or economic circumstances, lifestyles or behaviors. It has an impact on sectors beyond human health, such as agriculture, food security and economic development. Everyone – from all sectors and disciplines – should therefore be involved in the implementation of this action plan on a personal, societal or professional basis.

2. Actions based on best available knowledge and evidence
The actions and investment needed to address AMR must be supported wherever possible by clear and compelling evidence of risk analysis, or rationale for their benefit and cost-effectiveness.

3. Prevention first
Every infection prevented (without use of antimicrobial medicines) is one that needs no treatment. Many interventions for the prevention of infection are cost-effective and can be implemented in all resource settings and sectors.

4. Access not excess
The overall goal is to preserve the ability to treat serious infections. Actions to address AMR need to take into account the need to maintain equitable access to, and appropriate use of, existing and new antimicrobial medicines.

5. Sustainability
Actions are more likely to be sustainable where they are integral to health systems or practices in other sectors, and where there is evidence of continuing health and economic benefit. Action will be more sustainable if all parties accept accountability for implementation and report regularly against agreed targets.

6. Incremental targets for implementation
All countries and other stakeholders need to be able to demonstrate progress towards implementation of the global action plan, and achievement of action plan objectives and goals, whatever their current status. A step-wise approach to targets and performance indicators for implementation of the plan, based on a series of "building-blocks", would allow for the differing priorities and capacities of Member States and other stakeholders.

WHO Global Action Plan - Strategic objectives

1. Improve awareness and understanding of AMR through effective communication, education and training

2. Strengthen the knowledge and evidence base through research and surveillance

3. Reduce the incidence of infection through effective hygiene and infection prevention measures

4. Optimize the use of antimicrobial medicines in human and animal health

5. Develop the business case for sustainable investment that takes account of the needs of all countries, as well as the need for investment in new medicines, diagnostic tools, vaccines and other interventions

To further develop the WHO Global Action Plan an international consultation on "Commitments to responsible use of antimicrobials in humans" was held in Oslo, Norway, in November 2014 (NIPH, 2014a). This consultation focused on concrete strategies, especially for the national and regional levels, taking the many differences in health systems, culture, ecology, epidemiology and economic status into account. These strategies together with a strong political will and an international collective effort, including the full use and application of the core capacities of the International Health Regulations (WHO, 2008) under the guidance of WHO were identified as the key factors for the success of the proposed Global Action Plan to combat AMR. Every nation should develop and implement national AMR action plans, based on a multi-sectoral One Health approach using practical and appropriate, evidence-based solutions.

A special meeting to discuss local and global action to raise awareness and commitment to the development and early implementation of a global program for surveillance of antimicrobial resistance in human health was held in Stockholm, Sweden, in December 2014. Among the main goals of this meeting were the promotion of a coherent multilateral and multi-sectorial approach, reaching an agreement on a roadmap for the development of a global AMR surveillance program and the launching of an international collaboration in order to begin an early implementation phase to test the feasibility of collecting and sharing data according to the proposed surveillance standards. These activities and programs are to be included into the draft of the WHO Global Action Plan, which will be further discussed during the meeting of the WHO Executive Board in January 2015 (PHAS, 2014).

WHO's Regional Offices have also been working on specific regional strategies against AMR. In 2010 the "Regional Strategy on Prevention and Containment of Antimicrobial Resistance 2010-2015" was published by SEARO (Regional Office for South East Asia) (SEARO, 2010). In addition to this the health ministers of all SEARO Member States adopted the "Jaipur Declaration on Antimicrobial Resistance" in 2011. Acknowledging the growing AMR threat for public and global health, the declaration emphasized the urgency for national governments to "preserve the efficacy of antibiotics in the fight against microbial diseases." (SEARO, 2011)

In 2011 the WHO Regional Office for Europe (WHO/EURO) presented a "European strategic action plan on antibiotic resistance 2011–2016" urging its Member States to ensure political commitment and resources for their national AMR strategies, to strengthen AMR surveillance and monitoring of antibiotic consumption and resistance and to establish means for multisectoral coordination and cooperation and for raising public awareness (WHO/EURO, 2010). WHO/EURO has been providing strategic leadership and supporting its Member States in implementing their national action plans and has been working closely with many regional partners, such as the European Commission (EC).

III. European Union and AMR

The European Commission (EC) and its European Center for Disease Control (ECDC) have also developed a number of EU-wide policies and initiatives to tackle the increasing AMR threat. In 2001 the EC presented a first, comprehensive *Community Strategy against AMR* calling for EU-wide initiatives concerning prevention, research, surveillance and international cooperation and leading to further EU-wide recommendations and guidelines against AMR including the implementation of a European AMR surveillance system and the prohibition of the use of antimicrobials for growth promotion in animals in 2006 (Bronzwaer et al., 2004).

The EC and its European Center for Diseases Control launched the first European Antibiotic Awareness Day in 2008 to increase public awareness and to promote sensible use of antimicrobial agents (ECDC, 2008). The EU has been cooperating closely with multilateral organizations, such as FAO, OIE and WHO to strengthen international cooperation against the AMR threat and in 2009 also set up the Transatlantic Task Force against AMR (TATFAR), a bilateral cooperation with the United States of America (TATFAR, 2011). In November 2011 the EC presented its new 5-year A*ction Plan against the rising threats from Antimicrobial Resistance 2011-2016*. This plan was based on a multisectoral approach following the *One Health* concept and incorporated all the important areas, including public health, veterinary health, food safety and environmental aspects. The plan contained 12 concrete key actions for implementation in EU member states and categorized 7 different focal areas, both in the human and the veterinary fields (EC, 2011).

The actions put forward in this Action Plan aim at:

- Mitigating the risk of developing AMR in humans from the use of antimicrobials both in humans and animals by effectively ensuring their appropriate use across the EU, and promoting microbiological diagnosis as the means to determine, as far as possible, the actual need for antimicrobials.

- Putting in place effective ways of preventing microbial infections and their spread.

- Developing effective antimicrobials or alternatives for treatment of both human and animal infections.

- Joining forces with international partners to contain the risks of spreading AMR through international trade and travel and via the environment.

- Reinforcing research to develop the scientific basis and innovative means for combatting AMR.

The European Commission has also published a detailed road map for this action plan setting milestones and deadlines for each of the planned activities (EC, 2014).

The European Commission has implemented a special AMR working group to improve harmonization and coordination. This group has been working closely on all related to AMR with the ECDC, the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA). The ECDC has been running various AMR related programs and has hosted the European AMR Surveillance Network (EARS-NET) and the European Surveillance of Antimicrobial Consumption Network (ESAC-NET) (ECDC, 2012).

EFSA is in charge of risk assessment regarding food and feed safety at the EU-level, providing independent, scientific advice on "the emergence, spread and transfer to humans and animals of AMR through the food chain" (EFSA, 2014). The European Medicines Agency has an essential role in the authorisation of new antimicrobial medications and has been coordinating a program on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) (EMA, 2014).

The European Commission has also been funding many transnational collaborative AMR research projects. Over the past 15 years almost € 950 million have been spent for AMR-related research projects in the areas of human health, veterinary health, food and environment, showing the EC's holistic approach toward the AMR threat based on the *One Health* Concept (O'Neill, 2014).

The European Commission published a progress report on the AMR Action Plan in February 2015, showing the state of steps taken to address AMR and concluding that AMR will remain of high priority in the EU beyond 2016 (EC, 2015).

Figure 1: Proportion of Methicillin Resistant Staphylococcus Aureus (MRSA) isolates in selected countries 2013
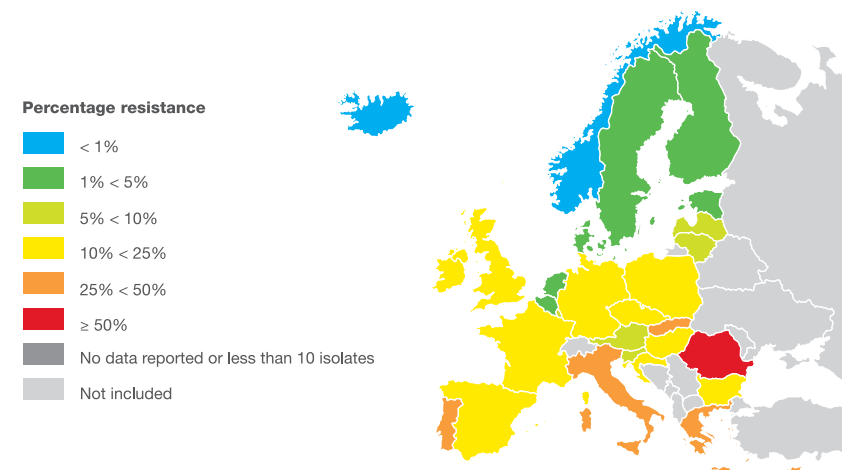
Source: European Center for Disease Control 2013

IV. One Health concept and Tripartite Collaboration

The *One Health* approach addresses issues of infectious diseases and their control at the interface between human health, animal health, food, agriculture and the ecosystem, recognizing that infectious organisms often cross species in ways both known and unknown.

The *One Health* approach has not yet been clearly defined. The One Health Commission defines the concept as "the collaborative effort of multiple health science professions, together with their related disciplines and institutions – working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants and our environment." In comparison to this the Food and Agriculture Organization of the United Nations (FAO) describes One Health as "a collaborative, international, cross-sectoral, multidisciplinary mechanism to address threats and reduce risks of detrimental infectious diseases at the animal-human-ecosystem interface." (Gibbs, 2014)
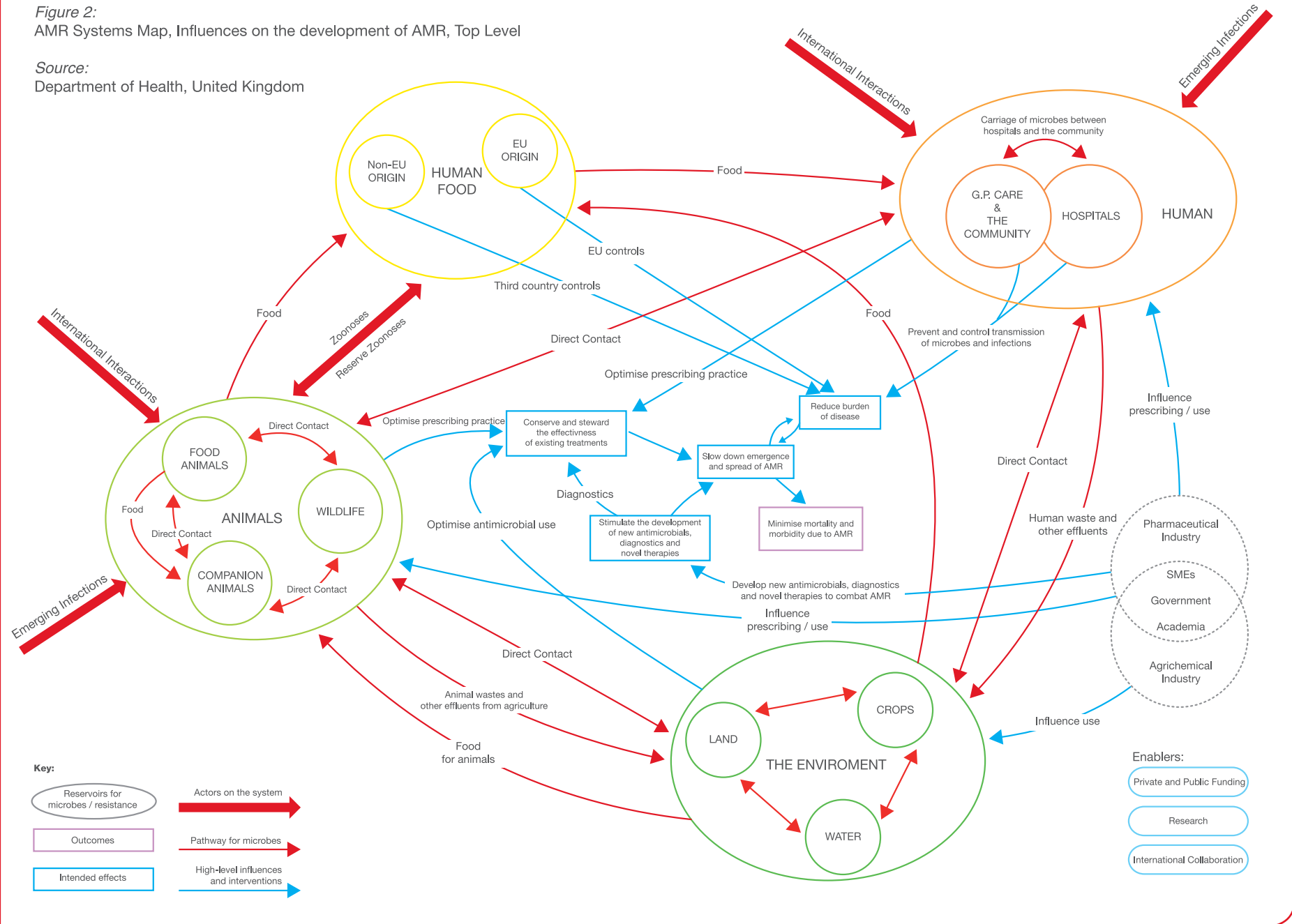
The latter definition is most probably based on the fact that the *One Health* concept arose from the great concern that a zoonotic disease (in this case: the 2004 H5N1 virus outbreak) could lead to a global human pandemic worse than the Spanish Influenza pandemic in the early 20th century. Since then there has been a wider global recognition among governments and scientists that greater interdisciplinary collaboration (incl. physicians, veterinarians, environmentalist, anthropologist and others) is essential for the prevention and control of zoonotic diseases such as avian influenza or rabies (Gibbs, 2014).

The introduction of the *One Health* initiative has provided an opportunity for international agencies to strengthen their inter-institutional and interdisciplinary collaboration to address the threat of emerging zoonotic diseases. The most prominent example of this is the tripartite collaboration between the FAO, OIE and WHO (FAO/OIE/WHO, 2010). These three organizations have aimed at "sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces" by improving their communication and coordination as well as by identifying new synergies (including normative work, capacity building, pathogen detection, risk assessment etc.). In recent years this tripartite collaboration has become increasingly active in the field of Antimicrobial Resistance.

A *One Health* approach to combatting AMR would be certainly beneficial, because AMR is a very complex issue at the animal-human-ecosystems interface. This was also one of the key points made at a Ministerial conference on Antibiotic Resistance in The Hague, Netherlands, in June 2014, where ministers and high-level representatives from more than 20 countries and many international organizations (incl. WHO, OIE, FAO, World Bank, European Commission and others) met with the objective of accelerating political commitment in the fight against antibiotic resistance and of raising awareness to this rapidly increasing multi-level threat. In addition a cross-governmental approach to AMR and measurable targets to be included in the WHO Global Action Plan were suggested (WHO, 2014e).

Figure 2:
AMR Systems Map, Influences on the development of AMR, Top Level

Source:
Department of Health, United Kingdom

International Interactions

Emerging Infections

HUMAN FOOD

Non-EU ORIGIN

EU ORIGIN

Carriage of microbes between hospitals and the community

G.P. CARE & THE COMMUNITY

HOSPITALS

HUMAN

Food

EU controls

Third country controls

Food

Food

International Interactions

Zoonoses

Reserve Zoonoses

Direct Contact

Prevent and control transmission of microbes and infections

Optimise prescribing practice

Reduce burden of disease

Optimise prescribing practice

Conserve and steward the effectivness of existing treatments

Slow down emergence and spread of AMR

Influence prescribing / use

FOOD ANIMALS

Direct Contact

WILDLIFE

ANIMALS

Food

Direct Contact

COMPANION ANIMALS

Direct Contact

Diagnostics

Optimise antimicrobial use

Stimulate the development of new antimicrobials, diagnostics and novel therapies

Minimise mortality and morbidity due to AMR

Develop new antimicrobials, diagnostics and novel therapies to combat AMR

Human waste and other effluents

Direct Contact

Pharmaceutical Industry

SMEs

Government

Academia

Agrichemical Industry

Emerging Infections

Influence prescribing / use

Direct Contact

Animal wastes and other effluents from agriculture

Food for animals

LAND

CROPS

THE ENVIROMENT

WATER

Influence use

Enablers:

Private and Public Funding

Research

International Collaboration

Key:

Reservoirs for microbes / resistance

Actors on the system

Outcomes

Pathway for microbes

Intended effects

High-level influences and interventions

20

UNITED KINGDOM

1.1 Context

The rapid spread of multi-resistant microorganisms and the lack of effective antimicrobials to treat infections caused by these organisms pose an increasing challenge to both human and animal health. Since 2000 the United Kingdom has had a programme tackling antimicrobial resistance (AMR) with an initial focus on bacteria and antibiotic resistance in human and animal health sectors. However a comprehensive and concerted effort is still urgently needed to minimize further harm, reduce the risk of cross-infection and improve patient safety, animal health and welfare.

The *UK Five Year Antimicrobial Resistance Strategy 2013 – 2018* (UK GOV, 2013c) builds on the output of the first *UK AMR Strategy and Action Plan* (UK GOV, 2000), published in 2000, bringing together a number of existing, new and planned actions. It sets out to address those challenges by taking into account the *Chief Medical Officer's Annual Report 2011* (Davies, 2011) as well as developments at EU and international level, including the 2011 *EU Strategic Action Plan* (EC, 2011) and the 2012 *EU Council Conclusions* (EU Council, 2012). The AMR Strategy also aims at providing a framework to improve coordination and information sharing between different stakeholders.

1.2 Coordination

The Department of Health (DH) has overall responsibility for delivery of the strategy. Public Health England (PHE) leads the implementation of the AMR Strategy across the health and care sector in England and the Department for Environment, Food and Rural Affairs (Defra) has responsibility for coordinating cross- sector activities relating to the delivery of the animal health, agriculture, food and environmental aspects of the AMR programme. Strategy implementation and progress are overseen and monitored on an ongoing basis by an interdepartmental High-level Steering Group (HLSG). The Devolved Administrations (Scotland, Wales and Northern Ireland) are represented on the HLSG and have developed their own strategies and action plans, these contribute to delivery of the wider UK Strategy. The strategy coordinates a multi-sectoral AMR approach involving practitioners and users as well as researchers in both human and animal health sectors at local, national and global levels.
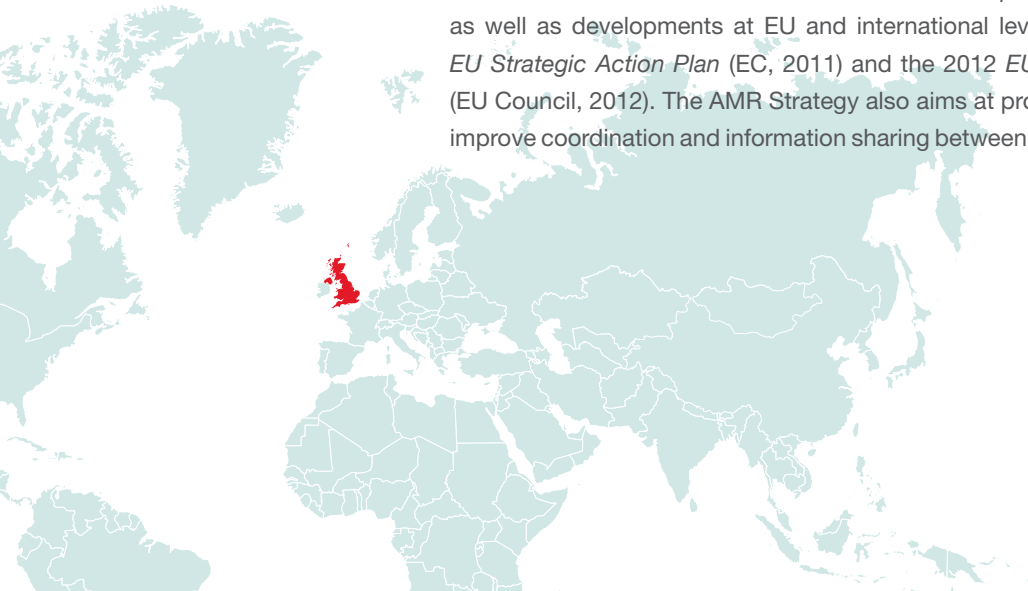
1.3   One Health integration

The strategy aims to slow the development and spread of resistance by taking an integrated *One Health* approach, facilitating collaborative multi-disciplinary work at all levels to realize optimal health for people and animals and to conserve the environment.

1.4   Focus

The *UK Five Year Antimicrobial Resistance Strategy 2013 – 2018* focuses on the following three strategic aims:

1. **Improve knowledge and understanding of AMR** through better information, intelligence, supporting data and developing more effective early warning systems to improve health security

2. **Conserve and steward the effectiveness of existing treatments** through improving infection prevention and control and development of resources to facilitate optimal use of antibiotics in both humans and animals

3. **Stimulate the development of new antibiotics, diagnostics and novel therapies** by promoting innovation and investment in the development of new drugs and ensuring that new therapeutics reach the market quickly

1.5   Approach

These three strategic aims are underpinned by actions in seven **key areas:**

1. Improving infection prevention and control practices
in human and animal health, both through enhanced dissemination and implementation of best practice and better use of data and diagnostics

2. Optimising prescribing practice
through implementation of antimicrobial stewardship programmes that promote rational prescribing and better use of existing and new rapid diagnostics

3. Improving professional education, training and public engagement
to improve clinical practice and promote wider understanding of the need for more sustainable use of antibiotics

4. Developing new drugs, treatments and diagnostics
through better collaboration between research councils, academia, industry and others; and by encouraging greater public-private investment in the discovery and development of a sustainable supply of effective new antimicrobials, rapid diagnostics, and complementary tools for use in health, social care, and veterinary systems

5. Better access to and use of surveillance data
in human and animal sectors through new arrangements that facilitate greater consistency and standardisation of the data collected across the system and encourage improved data linkage

6. Better identification and prioritisation of AMR research needs
to focus activity and inform our understanding of AMR. This may identify alternative treatments to new drugs as well as new or improved rapid or point-of-care diagnostic tests for humans and animals

7. Strengthening international collaboration
working with and through a wide range of governmental and non-governmental organisations, international regulatory bodies and others to influence opinion, galvanise support, and mobilise action to deliver the scale of change needed globally

A wide range of public and private sector bodies in the following areas have been identified to deliver the overarching actions:

- Human health and social care sector
- Livestock, food retail and veterinary sectors
- Research councils, other research funders and academics
- Pharmaceutical industry (including bio-pharmaceutical and diagnostics manufacturers)
- Other organisations, including local governments, Royal Colleges, professional bodies and learned societies and expert scientific advisory committees.

As part of the UK strategy a number of initiatives promote responsible veterinary use of antibiotics:

- Inclusion of responsible use of antimicrobials as a requirement within the Code of Professional Conduct for Veterinary Surgeons
- Government liaison with non-governmental organisations such as the Responsible Use of Medicines in Agriculture Alliance (RUMA)
- Publication of general and species specific prescribing guidelines by the British Veterinary Association, the British Equine Veterinary Association and the British Small Animal Veterinary Association
- Provision of lectures to veterinary students highlighting the principles of responsible prescribing
- Production of leaflets on responsible use for vets and for the general public
- A voluntary ban by the British Poultry Council on the use of certain critically important antibiotics for human medicine in day old chicks.

Around 20% of the over 200,000 farms in the UK are expected to review their antimicrobial stewardship programmes and introduce Farm Health Plans and biosecurity measures. Annual sales of critically important antimicrobials are expected to drop as a result of this. The UK AMR strategy aims to reach a point where:

- Good infection prevention and control measures help prevent infections occurring become the norm in all sectors of human and animal health
- Infections can be diagnosed quickly and the right treatment used to maximise the effect
- There is a sustainable supply of new and effective antimicrobials
- Patients and animal keepers fully understand the importance of antibiotic treatment regimens and adhere to them
- Surveillance is in place, which quickly identifies new threats or changing patterns in resistance

The strategy uses a multi-disciplinary approach to improve antibiotic stewardship and aims to prevent infections from occurring in the first place, reduce the current and future prevalence of AMR and any increase over time. While difficult to quantify or monetise, the effects are only likely to be felt in the long run.

1.6   Campaigns

The UK government believes that the publication of the strategy itself has helped to raise awareness of already existing programmes. Furthermore it has used the 2015 National Risk Register (NRR) for Civil Emergencies, to highlight AMR as a particularly serious longer-term issue and, to give AMR a higher priority at a local, national and international level (UK GOV, 2013c). Some of UK's recent AMR-related campaigns are listed below:

Remember, antibiotics won't help your defences against a cold
The European Antibiotic Awareness Day held every November 18 since 2008, has proven to be a cost-effective way to raise awareness of AMR, appropriate prescribing and drive behavioural changes. In 2014 PHE established the *Antibiotic Guardian pledge campaign*, encouraging everyone to pledge to make better use of antibiotics. (PHE, 2014a)

The main purpose of the *Antibiotic Guardian pledge campaign 2014* was to:
1. Increase people's (public, health professionals and students) engagement with the rising threat of AMR
2. Help people feel that they have taken concrete personal and collective action to help keep antibiotics active
3. Provide a system to measure behavior change

Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) & Stemming the Tide of Antibiotic Resistance (STAR)
TARGET and *STAR* are a web-based toolkit and an educational programme to support general practioners (GPs) prescribing in England and Scotland respectively. Reportedly it has helped to deliver changes in local prescription practice reducing unnecessary antibiotic use. Prior analyses expect 50% of GPs to consult the website leading to improved quality of prescribing in primary care. (RCGP, 2009; UK_MRC, 2005)

Start Smart then Focus: Right Drug, Right Dose, Right Time, Right Duration, Every Patient
Launched in England in 2011, *Start Smart then Focus* (SSTF) has provided guidance on antibiotic stewardship in the secondary healthcare setting (UK_GOV, 2011). In 2015 PHE updated SSTF in line with newly published evidence and user feedback. A PHE led national survey in 2014 indicated that 94% of responding Acute Trusts had a dedicated AMS committee and 85% had established the recommended governance structure recommended for AMS (UK_GOV, 2015). In 2013, a survey of the 48-hour post prescription review recommended by SSTF revealed that hospital antibiotic policies relied heavily on broad-spectrum penicillins (particularly penicillin/inhibitor combinations) and prolonged courses (7 days or more). Evaluation of SSTF has shown that NHS prescribers are "starting smart" by using broad spectrum agents empirically; however this may have the potential unintended consequence of increasing the use of broad-spectrum antibiotics (PHE, 2014b). An ESCMID-ISC survey on antimicrobial stewardship showed that among those hospitals that had conducted a formal review of their antimicrobial stewardship programme following SSTF, over 75% had seen a reduction in inappropriate prescribing. 10% had also shown reduced length of stay. Provisional evidence from the UK CPA survey shows that nearly 25% of hospitals have already observed a reduction in antimicrobial resistance in their settings.(UK_GOV, 2013a)

1.7   Performance measurement

In June 2014 the High-level Steering Group published the outcome measures against which the UK will assess progress (UK GOV, 2013b) These outcome measures are being kept under review:

1. **Trends in resistance**

    by monitoring

- Key bacterial human infections and the current levels of resistance in specific microbe-drug combinations

Resistance trends in the animal health sector with a particular focus on the key zoonotic bacteria affecting humans, Salmonella sp., commensal E.coli and Campylobacter jejuni. In addition, there is an extensive programme of passive surveillance which tests over 5000 animal bacterial pathogens a year for antibiotic susceptibility; isolates tested include pathogens of importance to animal health as well as zoonotic pathogens (UK GOV, 2013d).

2. **Trends in prescribing**

    by measuring

- Total antibiotic consumption in primary and secondary health care
- The proportion of antibiotics prescribed from the cephalosporin and fluoroquinolone classes in primary care
- Total carbapenem antibiotics consumption in secondary health care
- Total weight of antibiotic sold for use in the veterinary sector and the proportion of each antibiotic class (a data-hub to facilitate the collection of species specific usage data to measuring more accurately the consumption of veterinary antibiotics is in development).

3. **Quality of public and professional antibiotic stewardship**

    by monitoring

- Public awareness and behavior through a survey amongst adults
- Uptake of TARGET antibiotic toolkit and *Start Smart Then Focus* toolkit
- Impact of European Antibiotic Awareness Day activities

4. **Strengthening global security**

    by achieving a series of milestones relating to the contribution of the UK in ensuring global alignment in addressing AMR.

1.8   Results

In the *Annual progress report and implementation plan 2014* (UK GOV, 2014b) the UK government has described the good progress made during the first year of the new strategy. Developments marking a step change in the first year include: strengthened collection of data from which antibiotic prescribing and trends in antibiotic resistance can be monitored; development of a strong AMR research infrastructure to address knowledge gaps and promote collaboration. The UK has also taken a lead role in garnering support for coordinated action and advocating the need for a *One Health* approach internationally and contributing significantly to the development of the WHA resolution, the *WHO Global Action Plan* and the AMR action package as part of the Global Health Security Agenda. The HLSG has been considering outputs from PHE's *English Surveillance Programme for Antimicrobial Utilisation and Resistance* (ESPAUR), to identify areas where intervention is most needed. A comprehensive description of the developments in the UK in the areas of antibiotic resistance, antibiotic consumption and stewardship was presented in the first annual report of ESPAUR, published by Public Health England in September 2014 (PHE, 2014b).

Antibiotic resistance
Resistance and use data were collected on several indicator bacteria causing bloodstream infections and combinations of drugs used to treat them, between 2010 and 2013. The antibiotic resistance level of the detected Escherichia coli, Klebsiella pneumoniae or Streptococcus pneumoniae bacteria that were resistant to antibiotics was stable within this period and is comparable to levels in other European countries. However as the number of infections caused by these organisms increased over the period the rate of antibiotic resistance increased. As this data was mainly based on voluntary reporting and as the observation period was relatively short, the authors of the report stated that these results needed to be interpreted cautiously.

A report from the Department of Health AMR Strategy Analytical Group, published in December 2014, has described the observed UK AMR resistance trends as being heterogeneous. While significant decreases have been observed in the number of reported Methicillin-resistant Staphylococcus aureus (MRSA) cases (nearly 80% decrease between 2007/8 and 2012/13), a very worrying increase has been observed in the number of infections with extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae. The report has emphasized the difficulties involved in data interpretation due to heterogeneity and many other factors influencing data collection and reporting. (UK GOV, 2014a)

Antibiotic consumption
In the period 2010 - 2013 antibiotic consumption in humans in the UK increased by 6% despite several measures taken during and before this strategy period. Approximately 80% of all antibiotic prescribing was performed in General Practice, this sector saw a 4% increase in antibiotic prescribing during this period. The greatest increase (32%) in prescribing was seen in community prescriptions other than from general practice prescriptions (e.g. from dentists). Antibiotic sales in the veterinary sector has been stable between 2008 and 2013 (UK GOV, 2013d). Work to measure UK consumption of veterinary antibiotics more accurately is under development, in collaboration with the European Surveillance of Veterinary Antimicrobial Consumption project.

Antimicrobial stewardship

Positive results were recorded in the field of antimicrobial stewardship: implementation of proposed measures had been good; collaboration between the primary and secondary care sectors to develop antimicrobial guidelines had been improved and 90% of NHS trusts responding to the PHE's survey had established an antimicrobial stewardship committee. The latter had been advocated by the UK government through its Start Smart Then Focus campaign (PHE, 2014b).

1.9   Key success factors / Best practice examples

The UK was one of the first countries to respond to the growing AMR threat with introduction of its 2000 AMR Strategy and Action Plan. This was followed by a further Strategy in 2013, and the introduction of new structures such as the AMR High Level Steering Group and the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) that help drive the work, monitor the success of the strategy and refine national AMR policies as needed. At the local level AMR stewardship programmes and campaigns in hospitals such as Start Smart then Focus have proven to be successful, as have initiatives aimed at GP's such as TARGET and STAR. In addition to statutory surveillance requirements, the UK has conducted surveillance of resistance in veterinary pathogens since 1998, and was one of the EU member states which volunteered to work with ESVAC to develop a programme for monitoring of antibiotic consumption in the veterinary sector. More information on the UK's best practices can be found in the following chapters:

Key success factors / Best practice examples	Chapter
UK AMR High Level Steering Group	12.6.2
AMR stewardship programmes	12.2.4
Start Smart then Focus	12.2.4
TARGET, STAR	12.2.3

SWEDEN

2.1 Context

In comparison to most other countries Sweden has been using a relatively low amount of antibiotics (per capita) and also has fortunate antibiotic resistance conditions. This is especially due to the long-term commitment and strategic and well-coordinated work of many actors at the regional and national levels. Since its launch in 1995 as a voluntary network of agencies and organizations at the national level the *"Swedish strategic programme against antibiotic resistance"* (Strama), has played a central role. The Strama network and the Swedish government supported the National Board of Health and Welfare in developing a *"Swedish Plan for Action against Antibiotic Resistance"* (SPAR) in 2000 (SWE GOV, 2000). Realizing the urgent necessity of coordinated efforts to secure the availability of effective antibiotics for treating humans and animals the Swedish government approved the *"Bill Strategy for coordinated efforts to prevent antibiotic resistance and healthcare-associated infections"* in 2005 (SWE GOV, 2005). This has been part of the government's overall aim of controlling communicable diseases. In September 2009 the Swedish EU-Presidency held an expert conference under the theme of *"Innovative Incentives for Effective Antibacterials"* to explore ways of enhancing the development of new antibiotic substances in Stockholm (SWE GOV, 2009). The Public Health Agency of Sweden published a report on the *"Swedish work on the containment of antibiotic resistance, Tools, Methods, Experiences"*, focusing on the rational use of antibiotics and resistance monitoring in September 2014 (SWE GOV, 2014). In March 2015 the national action plan has been complemented with a new plan for the work of national authorities against antibiotic resistance and health care associated infections. At present this is only available in Swedish (SWE GOV, 2015).

2.2 Coordination

The Public Health Agency of Sweden is now the driving force behind the Swedish strategy. This is a government agency under the Ministry of Health and Social Affairs established in 2014 by the amalgamation of the Swedish National Institute of Public Health and the Swedish Institute for Communicable Diseases Control. Swedish AMR-related activities and policies have been characterized by a strong local and national cooperation involving many different actors. On the local level these include infectious-diseases specialists in many county hospitals, who have proved to be of key importance in controlling antibiotic usage, County Medical Officers for communicable disease control and local Strama groups, which are set up as multi-professional teams with representatives from general medicine, inpatient care and other AMR-related areas. The Ministry of Health and Social Affairs now works closely at the national level with the Public Health Agency of Sweden, the National Board of Health and Welfare and the Medical Products Agency. In particular the Strama network has been responsible for initiating several different forums for information exchange between the local and national levels. In addition to these the Swedish government, following the recommendations by the Council of the European Union, established a national *Intersectoral Coordinating Mechanism* in 2012 (SWE GOV, 2014). This is currently headed by the National Board of Health and Welfare and the Swedish Board of Agriculture and consists of 20 governmental agencies. From June 2015 onwards the Public Health Agency of Sweden will be leading the Intersectoral Coordinating Mechanism. At the international level Sweden has been working on AMR-related issues with the European Union and its member states, with WHO, OIE and FAO as well as with several countries

such as India, China and Ghana through bilateral agreements involving the Swedish International Development Cooperation Agency (SIDA) and ReAct, a Swedish-based international network working on the containment of antibiotic resistance (ReAct, 2014).

2.3 One Health integration

The Swedish 2006 *Strategy to prevent antibiotic resistance and healthcare-associated infections* included several measures to prevent infections in humans and animal husbandry as well as initiatives to prevent antibiotics being used as plant protection agents. The Swedish Board of Agriculture, the National Veterinarian Institute and the National Food Administration have been directly included in the development of the government's strategy, which aims at strengthening the intersectoral collaboration between human and veterinary medicine, agriculture, food production and the environmental sector (SWE GOV, 2006).

2.4   Focus

In its 2005 strategy paper the Swedish government focused on the following **strategic aims (2005):**

- Systematic monitoring of antibiotic resistance and use
- Measures to prevent infections in humans
- Measures to prevent infections in animal husbandry
- Initiatives to prevent antibiotics being used as plant protection agents
- Genes for antibiotic resistance are to be replaced by other safe technologies
- Establishment of a knowledge bank
- Cooperation in the EU and internationally

The *Swedish Work on the containment of antibiotic resistance*, published in 2014, emphasizing the Swedish governments long-term commitment and cross-sectoral work, focuses on the rational use of antibiotics and resistance monitoring and is divided into the following **areas of work (2014):**

1. National, local and cross-sectoral collaboration
2. Strama – the Swedish strategic programme against antibiotic resistance
3. Resistance monitoring with good geographic coverage
4. Monitoring the use of antibiotics including all sales
5. Evidence based treatment recommendations to support the prescriber
6. Communicating the rational use of antibiotics - Information for health care workers and the public.

2.5   Approach

Sweden is one of the first countries to implement a whole range of structured measures to contain antibiotic resistance. Despite the successes achieved, frequent adaptation of the measures to the given context has been necessary. Some of the current measures underpinning the key areas of work are listed below:

1. National, local and cross-sectoral collaboration

Sweden has initiated and is involved in many international (EU, WHO), national and local (esp. Strama) multi-sectoral collaborations working on issues in the field of antibiotic resistance.

2. Strama
– the Swedish strategic programme against antibiotic resistance

Strama is a multidisciplinary network with the aim of safeguarding the efficiency of antibiotic treatments. It is actively involved in many AMR-related fields like information and training of physicians, monitoring, analysis and feedback of antibiotic use and resistance, treatment recommendations, studies, international monitoring and advocacy. Local Strama groups can be found in inpatient (Hospital and / or ICU Strama) and outpatient settings as different efforts are necessary. These groups continuously communicate data and results to prescribers in order to inform them about developments and to guide them towards the best local interventions.

3. Resistance monitoring with good geographic coverage

Comprehensive national and local monitoring is used for the adaptation of treatment recommendations, to follow the resistance developments and to measure the effects of interventions. In addition Sweden has been establishing a quality-assured methodology for resistance surveillance and four complementary systems are currently used (ResNet, EARS-Net, SmiNet and Svebar).

4. Monitoring the use of antibiotics including all sales

According to Sweden's long-term experiences rational use of antibiotics can best be achieved if interventions are closely linked to the prescriber. The necessary data, e.g. pharmaceutical sales statistics, has been delivered by all pharmacies and maintained by the Swedish eHealth Agency. Furthermore registers and systems to automatically generate diagnosis-linked data have been set up in recent years (e.g. PRIS, Anti-Infection Tool).

5. Evidence based treatment recommendations to support the prescriber

The Public Health Agency and the Medical Product Agency of Sweden have published national treatment recommendations for common infections in the outpatient setting and the Swedish Society of Infectious Diseases has developed national care programmes for infections in hospitalized patients. Local Strama groups and pharmaceutical committees have been responsible for disseminating these national recommendations and using these as the basis of developing local guidelines and memoranda in relation to the local antibiotic resistance patterns.

6. Communicating the rational use of antibiotics

Various communication methods have been used to promote the rational use of antibiotics in Sweden and the local Strama groups have been the driving force behind these efforts. The main target groups are prescribers and patients. National and local campaigns and information tools (e.g. websites, newsletters etc.) have been used to address the general public and the demand for a coordinated approach between the many actors involved has been recognized (SWE GOV, 2014).

2.6   Campaigns

The Swedish authorities believe that communicating the need for rational use of antibiotics at the national and local level is of great importance in the fight against antibiotic resistances. The basis for this has been the establishment of networks, especially the Strama groups at the county and local level. The Swedish Infectious Diseases Institute Control presented a communication strategy in 2010, focusing on both physicians and patients, using statistics on antibiotic consumption and antibiotics resistance (SWE GOV, 2014). Pharmacists, nurses and other caretakers, working closely with physicians and patients, are also among the target groups of information services and campaigns using the various channels of communications (e.g. publications of treatment recommendations, leaflets, websites, newsletters and direct mailings, seminars, conferences etc.). It is critical that messages are being coordinated to provide similar information to different target groups. The Swedish authorities have been trying to inform the general public about antibiotic resistance and related issues through press releases, by participating in the European Antibiotic Awareness Day and by different activities of the local Strama groups. However there has been no major national campaign in Sweden until now. Local campaigns, initiated by County Councils and Strama groups, have been using general messages such as *"Healthy without antibiotics"*, *"Less antibiotics – more of your own defence"* or *"Do you get better more quick if you take antibiotics?"* (STRAMA, 2013).

2.7   Performance measurement

The Swedish National Board of Health and Welfare is responsible for coordinating the communicable disease control and for the follow-up of the national antibiotic resistance strategy. The Swedish Institute for Infectious Diseases Control, responsible for monitoring and analyzing the epidemiological situation, has been supporting the National Board particularly in its work on healthcare associated infections and antibiotic resistance. The Strama networks have also played a key role in monitoring and evaluating the strategic measures taken in the Swedish strategy, providing important data from the local and regional level. This data are an important basis for the annual SWEDRES-SWARM report on the antimicrobial resistance and antimicrobial usage in human and veterinary medicine (PHAS, 2013). This report, which is published annually by the Public Health Agency of Sweden and the Swedish Veterinary Institute, includes data from humans, animals and food products and comprises a detailed description of measures, indicators and evaluation procedures.

2.8   Results

In the 2013 SWEDRES-SWARM report Sweden's situation in regard to its antimicrobial resistance levels was described as *"favourable when seen in an international perspective"* (PHAS, 2013).

Antibiotic resistance

Between 2012 and 2013 a 13% increase of MRSA and of ESBL-producing Enterobacteriaceae cases were detected. The resistance levels to 3rd generation cephalosporins in Escherichia coli and Klebsiella pneumoniae had also increased to 4.9% and 3.1% respectively. The overall levels of resistance were still relatively low in comparison to many other countries and the majority of the observed infections had been acquired within the community or had been imported (e.g. 30% of MRSA cases).

Antibiotic consumption

Antibiotic consumption in Sweden had decreased steadily over the previous 20 years, especially in children under the age of five. Further reductions were observed since the launch of the Strama network in 1995 and the implementation of the Swedish antimicrobial resistance strategies in 2000 and 2005 (Fig. 3). The analysis of monitored data also shows that prescribers seemed to be increasingly following antibiotic treatment guidelines.

Figure 3: Antibiotic consumption in Sweden over time
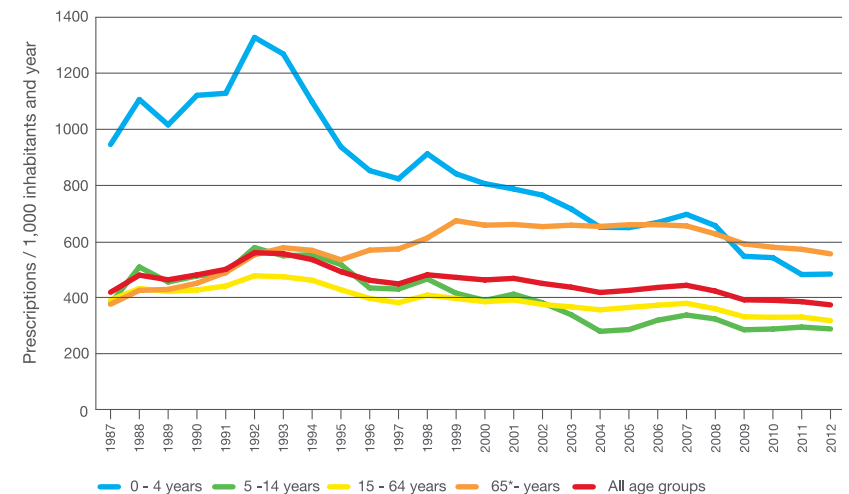
Source: SWEDRES - SWARM, 2012

In addition a 25% decrease in antibiotic sales for veterinary usage was observed between 2009 and 2012.

2.9   Key success factors / Best practice examples

Sweden's on-going success in securing its favorable AMR-situation is due to the initiation of Strama, the Swedish strategic programme against antibiotic resistance. This programme is responsible for various AMR-related measures, including surveillance and monitoring, infection prevention and control, prescriber support and public information. Strong political commitment and good collaboration at local, national and international levels have also been very important. More information on Swedish best practices can be found in the following chapters:

Key success factors / Best practice examples	Chapter
Strama	12.1.2
Evidence-based treatment guidelines	12.2
Infectious-Disease specialists and Community IPC experts	12.3
Awareness campaigns	12.4
Multi-level collaboration	12.6

DENMARK

3.1 Context

Denmark has often been described as being *"at the forefront in the fight against antimicrobial resistance"* and *"taking the lead in combating resistance"* (DTU, 2012b; GOV DK, 2011). During the 1990's a group of Danish researchers discovered a direct link between the routine use of antimicrobial substances as growth promoters in animal husbandry and an increasing resistance in bacteria, which, if transferred to humans could cause disease. Subsequently Denmark - as the first country worldwide - introduced a ban of these growth promoters, which later also led to a EU-wide ban in 2006 (WHO, 2002 and 2012).

In 1995 the Danish Ministry of Food, Agriculture and Fisheries and the Danish Ministry of Health established the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP, 2013a). This has proved to be a successful AMR surveillance program and the annual reports have been used as the basis of Danish AMR-related policies. The results of the EU-conference on *"The Microbial Threat"*, hosted by the Danish government in September 1998 (Rosdahl V, 1998), led to a resolution on a strategy against antibiotic resistance by the European Council in the following year (EC, 1999).

During the Danish EU-Presidency in 2012 a conference in Copenhagen was held under the theme „*Combating Antimicrobial Resistance – Time for Joint Action*", focusing on ways of improving EU-wide data collection and surveillance and on identifying measures to stop the overuse of antimicrobials in both humans and animals as well as on actions to reduce the use of critically important antimicrobials (GOV DK, 2012). In June 2012 the European Council adopted a resolution based on the outcome of this conference, stressing the urgent need for EU-wide and national action to tackle the ever-increasing global AMR threat and underlining the need for a holistic approach grounded on the *One Health* concept (EU Council, 2012).

3.2 Coordination

Despite all these AMR-related activities by the Danish government, it has not yet published an overarching national AMR-strategy. The Danish national antibiotics council is currently developing such a strategy, which is expected to be published until the end of 2015. As a contribution to the joint *"FAO/WHO/OIE Experts Meeting on Critically Important Antimicrobials"* in Rome in 2007, the Danish Veterinary and Food Administration, part of the Ministry of Family and Consumer Affairs, published a strategy-like paper called *"Risk management of antimicrobial use and resistance from food-producing animals in Denmark"* (GOV DK, 2007). This had been drawn up in close cooperation with the National Veterinary Institute, the National Food Institute and the Technical University of Denmark. These institutions together with the Statens Serum Institute (SSI) are the main participants of the DANMAP program, established in 1995 and funded by the Ministry of Health, the Ministry of Science, Innovation and Higher Education and the Ministry of Food, Agriculture and Fisheries.

3.3 One Health integration

The Danish AMR-related policies mostly covered the veterinary sector and the animal husbandry area. DANMAP has been described as using a *One Health* concept, *"comprising the entire chain from farm to fork to sickbed"* and establishing a strong collaboration between physicians, veterinarians, microbiologists, epidemiologists and specialists from other AMR-related disciplines (DTU, 2012a). However policies regarding AMR in the human health sector have actually been based on existing infection prevention and control measures and no direct environmental aspects are included in the Danish AMR policies.

3.4   Focus

The Danish risk management strategy has placed a strong focus on antibacterial resistance, emphasizing surveillance and control measures as well as taking legal actions against livestock owners and veterinarians for misusing antimicrobial medicines. In 2010 a "yellow card" card system was implemented to warn pig farmers whose livestock were shown to have relatively high levels of antibiotic consumption. Special campaigns have targeted these farmers aimed at increasing motivation for a reduced and more prudent use of antimicrobials and at involving them closely in the risk management process (Stärk, 2013).

3.5   Approach

The Danish AMR policies and actions have been based mainly on the strong scientific evidence presented in DANMAP's annual surveillance reports. An overarching AMR strategy hasn't been published but the Danish government has been deploying a continuing and evolving risk management strategy in 2007 (*"Risk management of antimicrobial use and resistance from food-producing animals in Denmark"*). The stated aim has been to: *"secure food safety and the future treatment possibilities for humans without jeopardizing animal health and welfare"* (GOV DK, 2007). The most important aspects of this risk management strategy are outlined here:

1995
Ban on usage of the livestock growth promoter *avoparcin* because of cross-resistance with the for humans critically important antimicrobial *vancomycin*
-> Stepwise EU-wide ban of avoparcin and other
   growth promoters
-> Danish animal producers voluntarily ceased growth
   promoter usage

1994 / 1995
Prophylactic use of antimicrobials prohibited and implementation of profit restrictions for veterinarians selling medicines

1995
Herd Health Contracts
Implementation of preventative veterinary strategies including a herd health contract between herd owners and veterinarians with monthly visits irrespective of the present health situation

1995
Establishment of the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP); (see above)

Since 1998
Source attribution of Salmonella
- Quantifying the contribution of animal-food sources to human halmonellosis
  -> Successful method and decision-support tool
      for risk managers

- Implementation of a zero-tolerance for multi-resistant types of Salmonella Typhimurium DT 104
  -> Increasing consumer protection

- Restrictions on veterinary prescriptions of Fluoroquinolones for food-producing animals (2002) to prevent the further growth of resistance and secure effectiveness in human medicine

2002

VeTStat

Enforcement of risk management on herd and veterinarian level to detect unacceptable trends in the use of antimicrobials

-> Effective control to detect violations of laws
concerning veterinary medicine

2003

Medicine Control Task Force

Establishment of a special unit in the Danish Veterinary and Food Administration to plan risk-based controls, to support regional veterinary officers, to assist the police and prosecution to carry out special actions concerning illegal treatments or illegal imports of veterinary antimicrobials

2005

Action Plan for reduction and prudent use of antimicrobials in pigs

- Treatment guidelines for veterinarians for the 10 most common swine diseases in Denmark
- Audit and supervision of veterinarians with a high usage of antimicrobials for pigs (usage in total and per pig).
   -> Successful approach, with an increasing focus on
   veterinarians usage and responsible consumption of antimicrobials

2006

Case-by-case investigation of meat for Salmonella

Testing of Danish and imported meat for Salmonella to improve food safety and aiming for the development of an international, standardized procedure

2007

Action Plan

- Bi-annual audit and supervisions of veterinarians working with food-producing animals
- Enforcement of treatment guidelines and diagnostic testing regulations
- Treatment guidelines: Antimicrobials for every disease and its pathogen(s) are listed and scored within four categories: efficacy, resistance, human importance and WHO criteria for Critically Important Antimicrobials (CIA)
- Establishment of a task force between the Danish Medicines Agency and the Danish Veterinary and Food Administration to prevent economical relationships between veterinarians and the medical industry

2010

Introduction of "Yellow Card"

Supplementation of guidelines to identify and warn farmers and veterinarians having a high consumption of antimicrobial agents

2010

Voluntary program by Danish Meat Association stopping the use of cephalosporins in pigs

3.6   Campaigns

Danish AMR-related policies have been focused on the reduction of antibacterial resistance and usage in animals and in the whole food chain. Most campaigns therefore have targeted veterinarians and farmers, e.g. the *Milk quality campaign*, organized by the Danish Cattle Association (Agriculture and Food Council). The awareness-raising campaign, *"Should my child have antibiotics?"* was launched on the European Antibiotic Awareness Day 2013 by the Danish Ministry of Health, the Statens Serum Institute and other partners, targeting prescribers and consumers and aiming at reducing unnecessary antibiotic usage (SSI, 2014).

3.7   Performance measurement

The annual DANMAP report on the Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark has been published by the Statens Serum Institute, the National Veterinary Institute and the National Food Institute in close cooperation with the Technical University of Denmark (DANMAP, 2013b). It includes detailed descriptions of the materials and methods used for the surveillance of antimicrobial consumption in animals and humans, of resistances in zoonotic bacteria (Salmonella, Campylobacter), indicator bacteria (Enterococci, Escherichia coli) and resistances in human clinical bacteria (Escherichia coli, Klebsiella pneumonia, Streptococci etc.). Over the past two decades Denmark has achieved good progress in reducing the prevalence of resistant bacteria especially in animals through this coordinated surveillance system and the resulting evidence-based AMR-related policies.

3.8 Results

In the past 20 years Denmark's policies against antimicrobial resistance have secured its favourable situation. The DANMAP 2013 report shows that antimicrobial resistance levels remain low and stable in comparison to many other European countries.

Antimicrobial resistance

Resistance to 3rd generation cephalosporins, for example, were only identified in 8% of Escherichia coli and in 9% of Klebsiella pneumoniae blood isolates. Despite the fact that the number of MRSA infections in patients with bacteraemia in Denmark was only 30 (1.7%), the number of new MRSA cases rose significantly in 2012-2013 (by about 25%). The reason for this was a rise in livestock associated MRSA. As a consequence contact with pigs was classified as a risk factor and therefore a MRSA screening is now mandatory for patients known to have contact with pigs before being admitted to a healthcare facility.

Antimicrobial use

The 1995 ban on antimicrobial usage as livestock growth promoters, the prohibition of prophylactic use of antimicrobials and the implementation of profit restrictions for veterinarians selling medicines led to a sharp decrease in antibiotic consumption in Denmark. This included an initial reduction of prescribed antimicrobials by about 40%. Nevertheless since 1997 there has been an observable consecutive increase in animal consumption of antimicrobials. (FIG 4). This was at least partially due to the growing production of pigs in Denmark. About 66% of the total antimicrobials prescribed in

Denmark were being used in the veterinary sector and 78% of these were used for the treatment of pigs.

Antimicrobials consumption in humans has increased by about 19% within the past decade. The Danish authorities believe that this has mainly been due to the prescription of significantly higher dosages of antibiotics for individual patients. Reasons for this development have not been identified so far. Since 2003 the antibiotic consumption in Danish hospitals had been constantly increasing (e.g. broad-spectrum antibiotics by +114%) and a close correlation between this and a decrease in the number of hospital bed-days was observed.

Figure 4: Consumption of antimicrobial agents in animals and humans
Source: DANMAP 2013
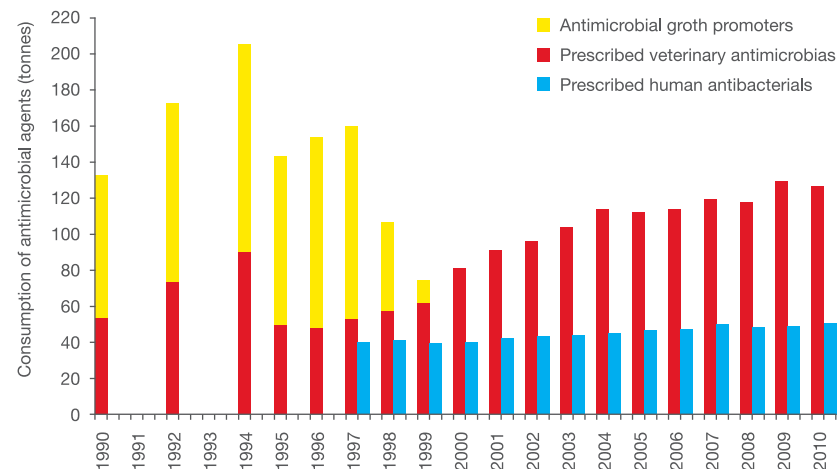
3.9   Key success factors / Best practice examples

Denmark has also been very active in combatting AMR for many years, focussing on the animal husbandry sector, which is vital for the Danish economy as a whole. Success has been achieved by banning antibiotics as growth promoters, by restricting veterinarians profiting through the sale of antibiotics and by several other policies and regulations targeted at veterinarians and farmers.

A key factor behind the current relatively low level of resistance in isolates from animals has been the collaboration with animal industries. This was behind the voluntary ban on cephalosporins in pigs in 2009, followed by a similar ban in cattle in 2014. In general there seems to be a very good appreciation in the animal industries of the issue of antibiotics that are critical in treatment of humans.

DANMAP, the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme, has been the essential basis for Denmark's evidence-based AMR-policies. In addition strong international political awareness and commitment have been achieved by hosting high-level conferences (e.g. during the EU-Presidency in 2012). More information on Danish best practices can be found in the following chapters:

Key success factors / Best practice examples	*Chapter*
DANMAP	12.1.1
Ban on Growth Promoters	12.2.5
Veterinary regulations	12.7
Regular farm visits / Yellow card system	12.7.1
Voluntary activities by farmers and Danish Meat Association	3.5
Political awareness and commitment by conferences, e.g.	12.4

- The Microbial Threat (1998)
- Combating Antimicrobial Resistance – Time for Joint Action (2012)

GERMANY

4.1 Context

The German Government published its *German Antimicrobial Resistance Strategy* (DART) in 2008 aiming at a targeted approach reducing the AMR risk and strengthening preventative measures at local, regional and national levels (GOV GER, 2008a). An intermediate DART strategy report in 2011 showed a high implementation level and has been used as the basis for the comprehensive update of the DART-Strategy currently under discussion (GOV GER, 2011).

4.2 Coordination

The Federal Ministry of Health (BMG) has developed the German AMR strategy together with the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV, now Federal Ministry of Food and Agriculture, BMEL) and the Federal Ministry of Education and Research (BMBF). In addition several governmental agencies (e.g. Federal Office for Consumer Protection and Food Safety, Robert Koch-Institute, Federal Institute for Risk Assessment, Federal Centre for Health Education etc.), professional organizations (e.g. German Medical Association, German Society for Infectious Diseases etc.) and other AMR-related stakeholders including the German Hospital Federation and the Association of Research-based Pharmaceutical Companies have all been involved in the strategy's developmental process. The Federal Ministry of Health (BMG) has headed the initiative since its launch and has been coordinating the subsequent strategy together with the BMEL and BMBF. The BMG has also requested public contributions to the strategy (GOV GER, 2013).

4.3 One Health integration

The strategy of the Federal Government has emphasized the need for a comprehensive cross-sector collaboration of stakeholders from the fields of human and veterinary health, animal husbandry, the food chain and the environment. While measures for the use of antimicrobials in the areas of human and veterinary medicines have been included in the strategy, there has been no measure directly related to the environmental aspects of AMR. Although no specific goals or measures related to environmental factors are included (GOV GER, 2013), environmental aspects on AMR are dealt with in the interministerial working group on AMR.

4.4 Focus

The Federal German Government's strategy has aimed at making "*a decisive contribution to reducing the number and spread of antimicrobial resistances in Germany*". It has been developed in close alignment with the *EU Council recommendations* (GOV GER, 2008a). The strategy is based on ten national goals grouped in four components:

1. Surveillance systems for AMR and antibiotic consumption

Goal 1: Strengthening of the surveillance systems for recording and assessing antimicrobial resistance

Goal 2: Systematic feedback of data on antimicrobial resistance and antibiotic consumption

2. Prevention and control measures for reducing AMR

Goal 3: Promotion of the application of guidelines

Goal 4: Safeguarding diagnosis

Goal 5: Promotion of the basic training, specialist training and continuing education of medical occupational groups, pharmacists and natural scientists

3. Cooperation and coordination

Goal 6: National cooperation

Goal 7: International cooperation

4. Research and Evaluation

Goal 8: Promotion of evaluation measures in human medicine

Goal 9: Promotion of knowledge transfer in the field of antimicrobial resistance

Goal 10: Networking and strengthening of science in the field of antimicrobial resistance

In addition to highlighting these human medicine related goals the German strategy has also described existing and planned measures for minimizing antimicrobial resistance in the field of animal husbandry, the food chain and veterinary activity as well as research activities.

4.5 Approach

A comprehensive plan of action for each human medicine related goal and sub-goal, including individual milestones for the achievement of these goals has been set up by the Federal German Government. In addition AMR-related projects and activities are described. A few examples are listed here:

1. Surveillance of antimicrobial resistance and antibiotic consumption
The Antibiotic Resistance Surveillance (ARS) was established at the Robert Koch-Institute in 2007. It integrates existing surveillance systems such as GENARS. ARS consists of an interactive database receiving routine AMR-data from laboratories. The collaboration with the National Reference Centres allow for an early-warning when new resistances emerge. On the local level monitoring the antibiotic consumption is mandatory according to the, revised in 2011. Voluntary antibiotic consumption monitoring in hospitals has been introduced at the national level by the Robert Koch-Institute.

2. Prevention and control measures for reducing antimicrobial resistances
A Commission for Antiinfectives, Resistance and Therapy (ART) has been established at the Robert Koch-Institute. ART aims to develop general principles for antibiotic therapy and reviews and initiates the development of specific guidelines by the responsible learned societies. According to the Infection Protection Act guidelines by ART and the Commission for hospital hygiene and infection prevention (KRINKO) became mandatory in 2011. Qualification programmes for Nosocomial Infection Prevention and Antibiotic Stewardship have also been initiated.

3. Cooperation and Coordination
Regional networks for prevention and control of antimicrobial resistances have been created, evaluated and adapted, covering whole Germany. They involve partners from all sectors (hospitals, practitioners, nursing homes etc.) in a region under the coordination of the public health service and aim to agree on consistent measures in the prevention and control of resistant pathogens. A national interministerial working group on AMR has been established. Internationally Germany has been strengthening its participation in international projects and networks (e.g. EARS-Net).

4. Research and Evaluation
Studies on the antibiotic prescribing practice of physicians and patient surveys have been carried out and research gaps in the AMR-field have been determined. A research program on AMR, hygiene and nosocomial infections has been conducted over a three-year period. Information packages on the use of antibiotics and the resistance problem for the general public and specific information packages for physicians and other target groups have been developed and distributed by different stakeholder (e.g. the Regional Networks).

The *German Antimicrobial Resistance Strategy* also defines measures for minimizing antimicrobial resistance in the field of animal husbandry, the food chain and veterinary activity. These include a comprehensive recording system and continuous monitoring of the AMR-situation, antibiotic sales data and a concept for minimizing antibiotic treatments in animal husbandry incorporated in the medicinal products act. It uses a benchmarking system to identify farms with a high antibiotic treatment level. These farms have – in cooperation with their veterinarians – to look for the reason of their high treatment levels and take measures to reduce them. In case those measures are considered insufficient, the competent authorities may order the animals holders to do more.

4.6 Campaigns

As the antibiotic consumption compared to other European countries is relatively low but with a high use of broad-spectrum and reserve antibiotics, the focus of information campaigns in Germany were on medical professionals and not on the general public.

The German government and its associated organizations (e.g. Robert Koch Institute etc.) have been using professional societies (e.g. German Doctors Association) and their publications to inform professionals working with antibiotics about treatment guidelines, the antibiotic resistance situation and related aspects. The general public has been addressed by information material provided e.g. by the Regional Networks and the Federal Centre for Health Education. In addition two Internet campaigns were initiated. In 2000 an Internet campaign, *Antimicrobial resistance – An explosive issue* was launched to educate and sensitize the general public. Another Internet campaign, *Targeted is Safe*, was initiated by a group of experts for infectious diseases, intensive therapy and pneumology in 2007 informing both professionals and the general public about the responsible usage of antibiotics and the growing AMR threat. According to the German government, the general public took little notice of these two campaigns (GOV GER, 2008a).

4.7 Performance measurement

To monitor and evaluate the antibiotic resistance and antibiotic usage situation Germany has been using a wide range of surveillance systems, institutions and networks. A good overview can be found in the annex of the DART strategy. The Robert Koch-Institute, Germany's public health institute under the Federal Ministry of Health, is responsible for the Antimicrobial Resistance Surveillance System (ARS) (RKI, 2014). GERMAP, a report on the antibiotic resistance and antibiotic usage situation in human and animal health in Germany published jointly by the German Federal Office of Consumer Protection and Food Safety, the Paul-Ehrlich Society for Chemotherapy and the Freiburg Centre for Infectious Diseases uses data from the different surveillance systems in human and veterinary medicine (GOV GER, 2012).

4.8 Results

In 2011 the Federal Ministries involved published an intermediate performance report on the DART strategy showing a high level of implementation of the proposed measures (GOV GER, 2011). The 2012 GERMAP report described various developments since the publication of the first report in 2008, and after the German antibiotic resistance strategy had come into force (GOV GER, 2008b; GOV GER, 2012).

Antibiotic resistance

While an increase in resistance to 3rd generation cephalosporins was observed in Escherichia coli and Klebsiella pneumoniae blood isolates, the rates of MRSA in Staphylococcus aureus isolates show a constant decrease since 2011. Overall Germany still had a relatively low number of resistances in comparison to many other European countries. Results presented by GERM-Vet, the national resistance monitoring system for animal bacteria, also show varied developments with regard to the antimicrobial resistance situation. More precise monitoring in addition to further studies was proposed to obtain a better overview of the AMR situation in the veterinary field (GOV GER, 2015).

Antibiotic consumption

Whereas only a slight increase in human antibiotic consumption had been observed since 2008, there had been a notable increase in the group of reserve antibiotics. In addition the surveillance data showed that surgery-related prophylactic antibiotic usage had often been prolonged and not been aligned with the respective guidelines. The overall consumption of antibiotics for veterinary use had only been monitored in Germany since 2011. From 2011 to 2013 a 15% decrease of usage was recorded. More data is needed for a structured analysis. In comparison to most other European countries Germany has a rather high consumption of antibiotics in the veterinary field, with only Cyprus, Spain and Italy reporting a higher PCU rate (sold mg of antibiotics / population correction unit).

4.9 Key success factors / Best practice examples

The first period of the DART strategy is currently being evaluated and a draft for the subsequent period is under preparation. The level of implementation of the set measures has been good, but it is still difficult to determine the specific outcomes of individual practices at this early stage. ARS has been successfully running since 2007. ARS and the Antibiotic Consumption Surveillance (AVS) will be expanded over the coming years. The establishment of an interministerial AMR working group and the Commission ART at the Robert Koch-Institute has also proved to be very helpful for the coordination, analysis and further development of the DART strategy. More information on German best practices can be found in the following chapters:

Key success factors / Best practice examples	Chapter
Antibiotic Resistance Surveillance (ARS)	12.1.4
Interministerial AMR working group	12.6
Commission Anti-infectives, Resistances and Therapy (ART)	12.6
Training program on Antibiotic Stewardship	4.5
Infection Protection Act	4.5

NORWAY

5.1 Context

Although Norway is one of the countries with the lowest levels of antibiotic resistance, the Norwegian government has approved several policies and strategies against the growing AMR threat, especially in the fields of hospital infections and food safety. The Norwegian government reacted to the AMR threat by approving the strategy policies laid out in the *Action plan to prevent antibiotic resistance 2000-2004* and the *Action plan to prevent hospital infections 2004-2006* (GOV NOR, 2000; 2004). The measures taken through these action plans have been important for Norway's relatively favorable AMR situation and have formed the basis for Norway's *National Strategy for prevention of infections in the health service and antibiotic resistance 2008-2012* (GOV NOR, 2008).

Internationally Norway has also been very active working together with many other countries including France, Indonesia, Senegal, South Africa, Thailand and Brazil and in close cooperation with WHO Norway hosted a Member State meeting on AMR in Oslo in November 2014 (NIPH, 2014a). This meeting, focusing on human usage of antimicrobials, was held to further prepare the proposed *WHO Global Action Plan on Antimicrobial Resistance* (WHO, 2014d).

5.2 Coordination

The national strategy development was coordinated by the Norwegian Institute of Public Health and headed by an interministerial steering committee including the Norwegian Ministries of Labor and Social Inclusion, Fisheries and Coastal Affairs, Agriculture and Food, Health and Care Services and the Ministry of Environment. The steering committee drafted a document taking both Norwegian and international research as well as results of national workshops and conferences into consideration (GOV NOR, 2008).

5.3 One Health integration

Although in the current Norwegian strategy the use of a *One Health* approach is not explicitly mentioned, the development of the strategy shows the government's conviction of the necessity of a multidisciplinary collaboration to tackle the AMR threat. The National Veterinary Institute, for instance, has been playing an important role as the responsible organization for the Norwegian surveillance programme for antimicrobial resistance in the veterinary sector (NORM-VET) and as the coordinating authority at both the national and the international level (NVI, 2014). In addition the reduction of the total environmental impact of antibiotics has been included as a sub-target of the Norwegian strategy.
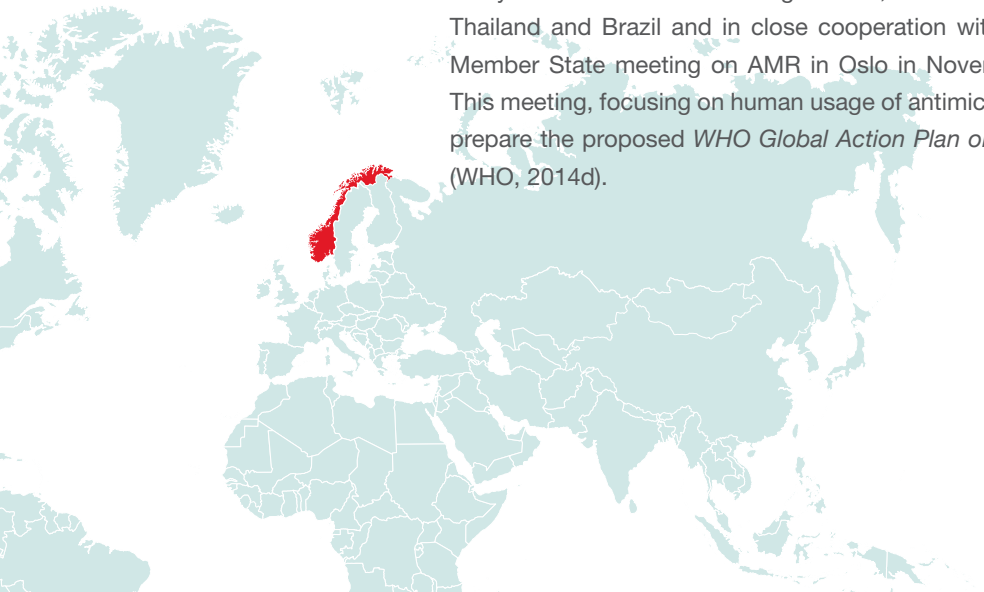
5.4 Focus

The comprehensive Norwegian *National Strategy for prevention of infections in the health service and antibiotic resistance* is build up around 3 primary goals, 31 sub-targets and almost 190 different measures (GOV NOR, 2008).

Primary Goal 1
The occurrence of antibiotic resistance in Norway shall not increase
The sub-targets linked with this goal focus on the improvement of AMR-related surveillance systems at national and international levels and on setting up databases and developing guidelines to improve use of antibiotics.

Primary Goal 2
The occurrence of infections acquired in the health service in Norway shall be reduced
The main activities for achieving this goal are development or improvement of surveillance systems within healthcare facilities (esp. in hospitals and municipal institutions for the elderly) and improvement of communicable disease prevention and control.

Primary Goal 3
Knowledge about the occurrence, causal relations and effects of measures to prevent infections in the health service and antibiotic resistance shall be improved
A national plan for infectious diseases (incl. AMR) research and development and models for cost estimations have been planned to achieve this goal.

5.5 Approach

For the achievement of the first primary goal, the Norwegian government has selected 17 sub-targets with a number of specific measures for each of them. Major sub-targets include the improvement of existing surveillance systems and programs and the development of new ones, e.g. the Norwegian surveillance programme for antimicrobial resistance (NORM) or for antimicrobial resistance in bacteria from feed, food and animals (NORM-VET) (NIPH, 2014c). The further development of a Norwegian Prescription Database, a prescription database for use in the veterinary sector (VET-REG), and of special national guidelines for a more rational use of antibiotics in primary care and in hospitals as well as more restrictive practices for the approval of antibiotics have also been initiated. In addition measures have been agreed upon to improve communication of AMR-related information to the general public and for the reduction of the total environmental impact of antibiotics.

12 sub-targets and several measures have been selected for the second primary goal of the strategy. These include the improvement of existing and the development of new surveillance systems for infections and antibiotic use within hospitals and municipal health-care institutions for the elderly (NOIS). Effective infection prevention and control measures include the improvement of antimicrobial stewardship and of guidelines and control of their implementation, increased vaccination coverage and further revision of the existing IPC regulations.

A national plan for research and development in the fields of infectious diseases in the health services and antibiotic resistance has been drawn up to achieve the third primary goal. In addition models for estimating the costs of infections acquired in health care facilities are being developed.

5.6 Campaigns

An important sub-target of the Norwegian Strategy is to *"further develop the communication with and information to the general public"* (GOV NOR, 2008). The Norwegian Institute of Public Health has prepared information brochures on antibiotic usage and antibiotic resistance, especially targeting parents of small children. Brochures with titles such as *All children get ear infections* and *Antibiotic-free-prescriptions* have been distributed through public health centers and doctors' offices. In addition a special brochure has been prepared to support doctors during their consultations with parents of small children and a poster campaign under the theme of *Antibiotics – only when necessary* was launched in 2014 for use in waiting rooms of hospitals and doctors' offices nationwide. For better communication and easier use of the national antibiotic treatment guidelines, the Antibiotic Centre for Primary Care and the Norwegian Advisory Unit for Antibiotics in Hospitals have also been working on internet- and smartphone-based applications. During the late 1990s a campaign on prudent use of antimicrobials in the veterinary sector directed by the Norwegian husbandry organizations and the Norwegian Medicine Authority has led to improved prescribing patterns and reduced sales of antimicrobials (NIPH, 2014b).

5.7 Performance measurement

The Norwegian government has established monitoring systems for both the usage of antimicrobial agents and the occurrence of antimicrobial resistance (NORM / NORM-VET). The NORM surveillance programme for AMR in human pathogens was established in 1999 and has been coordinated by the Department of Microbiology and Infection Control at the University of Tromso. The NORM-VET AMR monitoring programme in the veterinary and food production sectors was set up in 2000 and is coordinated by the Norwegian Veterinary Institute. Since 2002 wholesalers have had to report data about the usage of antimicrobial agents on a mandatory basis and human prescription data must also be reported to the Norwegian Institute of Public Health. The data and the analysis of the AMR situation have been published annually in a joint NORM/NORM-VET report (NIPH, 2014b).

5.8 Results

The 14th joint NORM / NORM-VET report, published in 2013, showed that the AMR situation regarding clinical important bacteria in Norway had remained favourable in comparison to most other countries (NIPH, 2014b).

Antibiotic resistance

The Norwegian Surveillance System for Communicable Diseases (MSIS) registered an increase in mostly non-invasive infections with MRSA in primary health care settings over the preceding decade, but the number of invasive MRSA-infections continued to be low. Blood culture isolates for Escherichia coli and Klebsiella bacteria also showed a good susceptibility to broad-spectrum antimicrobials. As an exception to these positive results, several outbreaks of vancomycin-resistant bowel bacteria have been registered in Norwegian hospitals since 2010. The prevalence of antibiotic resistance in indicator bacteria in animals (e.g. Escherichia coli, Enterococcus faecalis etc.) has been stable on a low or moderate level, depending on animal species and other related factors.

Antibiotic usage

Norway's antibiotic consumption in both human and veterinary medicine is among the lowest in Europe. While the total consumption of antimicrobials for use in human medicine had been stable over time, a shift towards broad-spectrum antibiotics was observed. Although the consumption of antimicrobials for use in veterinary medicine has not decreased since 2000, an overall decrease by about 35% between 1995 and 2013 has been observed. This has mainly been due to a reduction in antibiotic usage in animal husbandry.

The authors of the NORM / NORM-VET report concluded that Norway was still in a favourable AMR-situation and that antimicrobial-related policies seemed to have been successful, but that a continuous coordinated effort (nationally and internationally) was still vital. At the end of the strategy period (2008-2012) specific needs were identified including the need for an improvement in IPC programmes, especially in the health services on the local level, for a standardization of the computers systems used for monitoring AMR and infections in general and for an increase in vaccination coverage among healthcare personal and vulnerable groups.

5.9 Key success factors / Best practice examples

Norway's strategy has been based on a clear set of goals and sub-targets as well as a comprehensive list of measures to be taken. An extensive regulatory framework has been build since the implementation of the strategy in 2008. The success of the Norwegian AMR-related policies has been mainly due to the vigorous surveillance and reporting systems in both the human (NORM) and veterinary sectors (NORM-VET) and to its strong focus on the prevention and control of hospital-acquired infections. Newer initiatives such as the National Plan for research and development in the fields of infectious diseases in the health services and antibiotic resistance (GOV_NOR, 2008) and the development of easy-to-use web- and mobile phone based treatment guidelines seem to be very promising. In addition the Norwegian approach towards a greater involvement of the environmental (One Health) and the economic sectors (e.g. AMR cost analysis study) could lead to some interesting results and innovative solutions. More information on Norwegian best practices can be found in the following chapters:

Key success factors / Best practice examples	Chapter
NORM / NORM-Vet	12.1
Focus on hospital-acquired infections	12.3
Treatment Guidelines – Web- and Mobile Phone-applications	12.2.3
Campaigns focusing on General Practioners and families	12.4.1

FRANCE

6.1 Context

Despite the dramatic decrease in antibiotic prescriptions of 15-20% in communities and 10-15% in hospitals between 2000 and 2008, France is still the third largest antibiotic consumer in Europe. The primary objective of the *Plan national d'alerte sur les antibiotiques 2011-2016* has been to establish correct practices regarding the prescription of antibiotics with the goal of reducing antibiotic consumption in France by 25%, bringing the country closer to the average European usage (GOV FRA, 2011b).

6.2 Coordination

Numerous groups within the French and other European governments have worked on this problem since the early 2000s and European-wide surveillance systems have been created under the administration of the ECDC (e.g. ESAC-Net) (ECDC, 2011). Since 2002 the French Directorate General of Health (DGS) has been responsible for motivating and coordinating the implementation and development of the plans for European-wide surveillance systems (e.g. ESAC-Net) in France. Within this framework, the National Health Insurance Fund for Employees (CNAMTS) has headed a campaign to educate the media and the public and has been assisting in professional exchange between health care professionals and insurance groups (AMELI, 2015).

The national health insurance group has also signed agreements with health care establishments regarding good practices in antibiotic prescription. The *French Mutual*, the national health insurance fund, has also issued publications, in particular *Médicamento*, regarding the issue, designed to help mutual insurance companies share drug information with their patients.

Additionally since the 1990s health care facilities have been monitoring cross transmission multi-drug resistant strains, strengthened by the 2010 Hospitals, Patients, Health and Territory (HPST) law, which established an operational team and hygiene management coordinator within each facility. This law created Regional Health Agencies (ARS) to mobilize and monitor local health agencies and facilities and to relay actions to the national level. They have been supported by the Ministry of Health's national warning plan, which has been monitoring and promoting the appropriate use of antibiotics (GOV FRA, 2011a). In 2009 France also launched a program to combat hospital-acquired infections to reduce the selective pressure forming antibiotic resistant strains.

6.3 One Health integration

France has recognized the importance of the many and diverse stakeholders in combatting antibiotic resistance, seeking to promote health of animals and the environment as well as human health. The French government believes that it is of critical importance to work with actors and professionals involved with the over-utilization of antibiotics in the domain of veterinary medicine. Therefore several aspects of the new national plan specifically call for an increased cooperation among medical, veterinary, agricultural, and environmental groups (GOV FRA, 2011b).

6.4 Focus

The French National Antibiotic Plan has a strong focus on the reduction of antibiotic use and on the improvement of infection prevention and control, especially in in hospitals and other health-care settings. The three **strategic objectives** of the plan include 21 actions:

1. To improve effectiveness and efficiency in the treatment of patients
2. To preserve the efficacy of antibiotics
3. To promote research

The first two goals focus on current practices and perceptions, while the third seeks to create new means of combatting antibiotic resistance in the future. Multiple measures and supporting actions have been outlined to achieve these three primary goals (GOV FRA, 2011b).

6.5 Approach

Three measures have been laid down to reach the first strategic objective of improving patient treatment efficiency. Firstly, the plan has called for improvement in the antibiotic prescription guidelines, including standardization, improved references and protocols, the development of rapid diagnostic tests and the expansion of the use of these tests to improve targeted treatment with antibiotics. Health professionals have to be informed and trained in the new practices, mobilizing them to be the frontline in the fight against antibiotic resistance and requiring them to develop forms of self-evaluation to maintain good practices instated during initial and continuing training. Finally, it is important to raise public awareness about the issue targeting patients, children's caregivers, school-aged children and elderly people as particularly important groups.

The first measure for the second strategic objective, preserving the antibiotic efficacy in combatting disease, is increased surveillance of the antibiotic use and the appearance of resistant strains. This helps to monitor the degree of selective pressure being exerted under current practices. The next step is reduction of these pressures by decreasing antibiotic usage globally, including in veterinary medicine. The plan has called for a focus on those antibiotic classes, generating the most virulent resistance and on controlling the spread of emerging resistant strains. Finally, increased oversight of antibiotic delivery coordinated with the development of specific standards is necessary to achieve this goal.

Defining priorities is regarded to be a prerequisite for achieving the third strategic objective, promoting research. These priorities include a better understanding of the mechanisms by which bacteria gain resistance, the development of novel antibiotic molecules and the development of rapid diagnostic tests for bacterial infections. Research should be encouraged across all levels, from fundamental scientific studies and applied research to socio-medical-economic investigations.

6.6 Campaigns

The French government has been seeking to improve patient treatment effectivity using a number of campaigns and communication channels. Since 2002 the National Health Insurance has successfully implemented the national campaign *Antibiotics are not automatic*. Using various channels of communication (e.g. pamphlets and posters, print media, television, radio, websites etc.) the general public and especially physicians have been targeted (MG, 2007). This first period of this campaign (2002-2007) has been scientifically evaluated and the use of antibiotics in outpatients has been analyzed. The researchers concluded that the campaign has led to a visible reduction of unnecessary antibiotic prescriptions, especially for children (Sabuncu et al., 2009). In 2014 the French government extended this campaign to include animal health aspects as well (*Antibiotics are not automatic- for neither of us*) (GOV FRA, 2014).

6.7 Performance measurement

Specific indicators have been developed to measure progress in all areas outlined in the national plan. In terms of the first objective numerous measures have been focusing on the practices of health care providers. These have included the percentage of medical specialists with scientifically validated reference materials for antibiotic prescription procedures, the number of special diagnostic tests ordered, the number of physicians who have received continual professional development training on the subject of antibiotic resistance, and the number of physicians who have sought or given advice regarding antibiotic prescription with health insurance agencies or other practitioners (GOV FRA, 2011b). Further targets have included the publication of an updated guideline on *Antibiotic therapy and prevention of*

bacterial resistance in healthcare organisations, the number of physicians using this guide, and the number of facilities sharing information via this indicator framework (HAS, 2008). Public reception of the campaign should be monitored through surveys serving as *knowledge barometers* among targeted groups and via the E-Bug project for school-aged children, the number of schools, teachers, and students who have had contact with the campaign can be measured (GOV FRA, 2011a).

Indicators have also been specified for the second strategic goal of preserving the efficacy of antibiotics. These include the number of health facilities tracking their antibiotic consumption the number of infectious agents for which resistance is being monitored and the annual volume of antibiotic sales for veterinary medicine. Further measures have been focusing on more detailed methods of combatting increased antibiotic resistance in healthcare settings such as the number of health facilities implementing the guidelines for limiting prescriptions, the number of health facilities practicing routine re-evaluation after antibiotic prescription and the number of health facilities implementing and updating lists of "last resort" antibiotics.

With regard to the third objective, promoting research, the plan has called for the monitoring of the number of research projects being pursued in the various related domains – bacterial resistance and antibiotic efficacy, new antibiotics and rapid orientation tests, the number of new molecules being developed, and the number of studies targeting socio-medico-economic factors in antibiotic resistance.

6.8 Results

Progress has been made in several domains since France first began to combat the problem of antibiotic resistance in the early 2000s. An organizational system promoting the correct use of antibiotic treatment had been set up in 93% of hospitals. Lists of controlled antibiotics with limits on duration of prescription had been created by 55% and surveillance systems to monitor antibiotic consumption had been implemented in 94% of the evaluated health facilities (GOV FRA, 2011a; HAS, 2008).

Antibiotic resistance

Despite these positive results the implementation of the new national action plan in 2011 has been critical, as the levels of antibiotic resistance and consumption still remain alarmingly high in comparison to most other European countries. From 2008 to 2013 an increase in resistance to 3rd generation cephalosporins was observed in blood isolates of Escherichia coli (from 3.8% to 9.5%) and Klebsiella pneumoniae (from 15.2% to 28.0%). The resistance of Staphylococcus aureus isolates to *Methicillin* (MRSA) decreased slightly (from 24.5% to 17.1%) during the same period (ECDC, 2015a).

Antibiotic consumption

By 2008 the French AMR policies and campaigns led to a decline in the prescription of antibiotics by 15-20% in communities' practices and 10-15% in hospitals (GOV FRA, 2011a). Although the government set a new goal of reducing the nationwide consumption of antibiotics by a further 25%, the consumption of antimicrobials in human medicine has remained relatively constant at a high level compared to other European countries (e.g. Germany

and Sweden; Fig 5) (ECDC, 2015b). However between 2010 and 2012 sales of veterinary antimicrobials for food-producing species decreased by 22% and are now at the average European consumption level (ESVAC, 2012).

Figure 5: Trend of the consumption of antibacterials for systemic use primary care sector in France, Sweden and Germany from 1997 to 2013
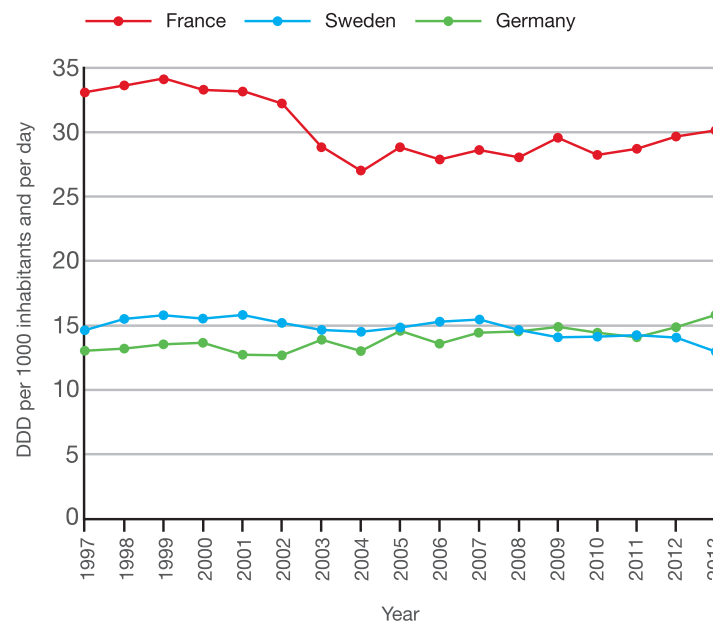
Source: ECDC, ESAC-Net-database (online)

6.9 Key success factors / Best practice examples

The experience gained from preceding national plans has enabled France to detect and respond rapidly to new forms of resistance and to communicate their research through the European epidemic control surveillance networks. An important step has been identifying antibiotics as "special drugs" requiring special legislative and regulatory practices. The French authorities have focused on regional or socio-economic differences through the implementation of the *Hospitals, Patients, Health and Territory Law* and the creation of Regional Health Agencies. One of the main limiting factors of these measures has been the difficulty in inducing long-term behavioral change among health care professionals. Other difficulties include changing public expectations, raising awareness, and increasing understanding. However the guideline on antibiotic therapy and prevention of bacterial resistance in healthcare organisations has proved to be an effective support for physicians. The national educational campaign, *Antibiotics are not automatic* and an E-Bug project targeting both the general public and schoolchildren have both been successful.

The French strategy has two very interesting aspects: firstly the financial aspect of antibiotic therapies and AMR-related issues (prevention, treatment, consequences of resistance) is very important as the National Health Insurance is involved as a key player. Secondly the French government has set a clear goal of reducing antibiotic prescriptions by 25% by the end of the strategy period, emphasizing the political will and safeguarding accountability and public awareness. More information on French best practices can be found in the following chapters: 12.7.1

Key success factors / Best practice examples	Chapter
Hospitals, Patients, Health and Territory Law	12.7.1
Regional Health Agencies	12.6.2
Guideline on Antibiotic therapy and prevention of bacterial resistance in healthcare organisations	12.2.3
National campaign: *Antibiotics are not automatic*	12.4.1
E-Bug project	12.4.2

USA

7.1 Context

The Center for Disease Control and Prevention (CDC) has estimated that more than two million illnesses and 23,000 deaths in the United States are caused annually by antibiotic-resistant bacteria (HHS, 2013a). In December 2013 the President of the United States directed the National Security Council and the Office of Science and Technology Policy to review past and current federal efforts to address antibiotic resistance and develop a multi-sectoral plan. This has formed the basis of the 2014 *National Strategy For Combating Antibiotic-Resistant Bacteria* (GOV USA, 2014). The development and implementation of this National Strategy has been further triggered by the recent endorsement of the World Health Assembly resolution on antimicrobial resistance (WHO, 2014a).

7.2 Coordination

The National Security Council, in collaboration with the Office of Science and Technology Policy, the Domestic Policy Council and the Office of Management and Budget, has been coordinating the development and implementation of this strategy. An interagency Task Force for Combating Antibiotic-Resistant Bacteria co-chaired by the secretaries of Health and Human Services, Defense, and Agriculture is responsible for the development of a 5-Year National Action Plan. The President's Council of Advisors on Science and Technology has provided recommendations as published in the Report to the President on Combating Antibiotic Resistance in September 2014 (PCAST, 2014).

7.3 One Health integration

The US Strategy aims to detect and control antibiotic resistance in a *One Health* approach through appropriate surveillance and antibiotic stewardship in human and animal health sectors as well as agriculture. The government believes that a close collaboration with industry, academia and the human and animal health sectors at local, regional, national and global level is required for combating antibiotic resistance. Furthermore, the strategy aims to promote research and development in diagnostics and therapeutics, including new antibiotics or alternatives, for humans as well as animals (GOV USA, 2014).

7.4   Focus

In order to detect, prevent, and control illness and death related to antibiotic-resistant infections, the strategy has identified and outlined the following interrelated goals:

Goal 1
Slow the development of resistant bacteria and prevent the spread of resistant infections

Goal 2
Strengthen national *One Health* surveillance efforts to combat resistance

Goal 3
Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria

Goal 4
Accelerate basic and applied research and development for new antibiotics, other therapeutics and vaccines

Goal 5
Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control and antibiotic research and development

7.5   Approach

Specific objectives have been provided for each of the five goals helping to reduce the incidence of priority pathogens identified by the CDC as urgent or serious threats, including carbapenem-resistant Enterobacteriaceae (CRE), methicillin-resistant Staphylococcus aureus (MRSA), ceftriaxone-resistant Neisseria gonorrhoea and Clostridium difficile.

1. Slow the development of resistant bacteria and prevent the spread of resistant infections

Antibiotic stewardship programs need to become routine in healthcare delivery as well as in agricultural settings to help slow the emergence of resistance. The *Guidance for Industry # 213* issued in December 2013 by the US Food and Drug Administration (FDA) has outlined voluntary measures to eliminate the use of medically important antibiotics for growth promotion and control other therapeutic uses of antibiotics in veterinary medicine (HHS, 2013b). The transmission of infections with antibiotic-resistant bacteria across community and healthcare settings is to be prevented through rapid infection detection and control as well as better communication regarding the management and transfer of infected patients.

2. Strengthen National One-Health Surveillance Efforts to Combat Resistance

Improved data collection systems to detect and monitor antibiotic resistance, antibiotic sales and use in healthcare and agricultural settings have to be developed. Existing surveillance systems such as the National Healthcare Safety Network, the National Antimicrobial Resistance Monitoring System and the Emerging Infections Program should be enhanced and expanded. Laboratories would also be linked into a regional network to allow standardized, accurate and complete data sets and help establish a national specimen repository for resistant bacteria and a national database of their DNA sequences.

3. Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Point-of-need diagnostic tests to rapidly distinguish between viral and bacterial infections should be developed as well as rapid molecular tests to identify the infecting pathogen and its antibiotic-resistance profile. These measures, combined with the on-going use of culture-based tests, should greatly advance the detection, control and prevention of multidrug-resistant organisms. The US Government would provide representative clinical isolates to advance development of diagnostics and help to address issues related to test development and validation, FDA review and reimbursement.

4. Accelerate Basic and Applied Research and Development for New Antibiotics, other Therapeutics and Vaccines

The Strategy Plan recognises the urgent need for new antibiotics and therapeutic approaches as alternatives to antibiotics to address antibiotic-resistant pathogens, particularly multidrug-resistant Gram-negative bacteria in both human and animal populations. Further research would be vital to understand the environmental factors facilitating the development and spread of antibiotic resistance as well as the nature of microbial communities and how antibiotics affect them. The Biomedical Advanced Research and Development Authority (BARDA) aims to advance innovative research on antibiotic resistance by encouraging the formation of public-private partnerships through research forums and biopharmaceutical incubator.

5. Improve International Collaboration and Capacities for Antibiotic Resistance Prevention, Surveillance, Control and Antibiotic Research and Development

Domestic action alone is seen to be insufficient to protect the nation's public and agriculture health and security. The United States and international partners, such as ministries of health, agriculture, and food safety, WHO, FAO, OIE and the EU, have been working together to promote all the goals listed above by increasing political awareness and mobilizing broader international support. The **Trans-Atlantic Taskforce on Antimicrobial Resistance (TAFTAR)** established in 2009 has furthered collaboration with the European Union enabling intensive technical exchanges, facilitating transparency and identifying Best Practices. In addition prevention and detection of antimicrobial resistance is a key component of the **Global Health Security Agenda (GHSA)**, launched by the US and nearly 30 partner countries in February 2014 (TATFAR, 2011; HHS, 2014).

The National Strategy intends to promote greater investment and coordination of US Government resources to reduce antibiotic-resistant bacteria, while strengthening ongoing partnerships between the Federal government, industry and other non-governmental organizations as well as international partners. All activities in the National Strategy remain subject to budgetary constraints and other approvals (GOV USA, 2014). In January 2015 the US President proposed to almost double the governmental budget for combating antibiotic resistance to more than US$ 1.2 billion (GOV USA, 2015).

7.6 Campaigns

A broad array of initiatives to educate key partners and the public have been carried out, amongst others (CDC, 2012):

Get Smart: Know When Antibiotics Work
Launched in 1995, this campaign had promoted appropriate antibiotic prescribing and use, through health education and behavioural change materials for patient and providers as well as establishing guidelines for appropriate antibiotic use, particularly in upper respiratory infections, which account for more than three quarters of all office-based prescribing. Since 2008, the campaign has also coordinated the *Get Smart About Antibiotics Week*, an annual one-week observance generating media interest and engaging partners.

Get Smart for Healthcare
Focuses on improving prescribing practices in inpatient healthcare facilities through the implementation of antibiotic stewardship programs, which has shown to reduce rates of Clostridium difficile infection and antibiotic resistance, improve individual patient outcomes, and reducing healthcare costs.

Get Smart: Know When Antibiotics Work on the Farm
Has been promoting appropriate use of antibiotics in veterinary medicine and animal agriculture since 2004 and is now further supported by the new web based educational tool **Antimicrobial Resistance Learning Site.**

7.7 Performance measurement

The Task Force's 5-Year National Action Plan was released on March 27, 2015, detailing the specific measures for achieving the national strategy's objectives with associated timelines for implementation and metrics for measuring progress. Within 180 days of the release of the Action Plan and each year thereafter, the Task Force is to evaluate the strategy's success and provide a report to the President on the progress made as well as plans for addressing any barriers and recommendations for new or modified actions. The strategy has set national targets for combating antibiotic-resistant bacteria to be met by 2020 (GOV USA, 2014).

7.8 Results

For this comparative study of national strategies and policies the 2014 *National Strategy for Combating Antibiotic-Resistant Bacteria* has been selected. A 5-year-National Action Plan has been released on March 27, 2015; first results will be published 6 months after the implementation of the plan.

7.9 Key success factors / Best practice examples

Over the past years the US Get Smart Programme, including various AMR-related campaigns, initiatives and educational tools has been very successful. The establishment of the national Interagency Task Force against AMR has effectively supported the coordination of the great number of actors involved and the planning for the 2015 National AMR strategy. Internationally the US has shown its responsibility by creating the Transatlantic Task Force against AMR (TATFAR) together with the European Union in 2009 and by initiating the Global Health Security Agenda in 2014, an initiative, which will also include international cooperation in the AMR-sector. An interesting approach is also a program led by the Biomedical Advanced Research and Development Authority (BARDA) aiming to improve AMR-related research through the formation of public-private partnerships.

Key success factors / Best practice examples	Chapter
Interagency Task Force on Antimicrobial Resistance	12.6.2
Get Smart campaigns / stewardship program	12.4.1
Transatlantic Task Force against AMR (TATFAR)	12.6.1
Global Health Security Agenda	12.6.1
BARDA – Advance innovative research on antibiotic resistance / PPP	12.5.1

SWITZERLAND

8.1 Context

The Swiss government believes that the AMR threat is one of the greatest challenges in the 21st century. Switzerland initiated a national research program from 2001-2006 to explore the level of antibiotic resistances, including research projects within the fields of human medicine, veterinary medicine and the environment (FNSNF, 2006). In addition national surveillance systems have been built and solutions to secure the efficacy of antibiotics have been investigated. As these activities seemed to be inadequate a national Antibiotic Resistance Strategy (StAR) has now been developed and is currently under discussion. The Swiss government anticipates publishing the final document at the end of 2015 (GOV CH, 2014b).

8.2 Coordination

The Swiss Antibiotic Resistance Strategy is the result of a close cooperation between a great number of governmental institutions including – among others - the Federal Office of Home Affairs, the Federal Office of Public Health, the Federal Food Safety and Veterinary Office, the Federal Office for Agriculture and the Federal Office for the Environment. In addition the Swiss Conference of regional health directors, professional associations, expert groups, representatives from the private sector and other AMR-related fields have been regularly consulted throughout the drafting process, which has been headed by the Federal Office of Public Health (GOV CH, 2014b)

8.3 One Health integration

The Swiss parliament has approved a resolution on a *"One-Health-Approach for a coherent Antibiotic Strategy in human and veterinary medicine"*, which the government is ordered to follow (SWP, 2012). The proposed Swiss Antibiotic Resistance Strategy (StAR) takes a *One Health* approach, including AMR-related measures in the fields of human and animal health, agriculture, food safety and the environment. From the beginning, the whole strategy has been elaborated with representatives of all four offices. In addition, close collaboration and coordination between all stakeholders (policy, science, economy) is being emphasized to reinforce the *One Health* approach.

8.4   Focus

The main aim of the proposed Swiss Antibiotic Resistance Strategy is to secure the long-term efficacy of antibiotics in human and veterinary health. The strategy is goal-oriented and is based on four **key principles** (GOV CH, 2014b):

Key principles
1.   Interdisciplinary collaboration following a *One Health* approach
2.   International cooperation
3.   Need for urgent action
4.   Joint action and improved coordination between all AMR-related stakeholders

Together with the main stakeholders the Swiss government has set up eight **strategic goals**, with each relating to all of the affected fields (human health, veterinary health, agriculture and environment).

1. Surveillance
Establishment of a standardized, interdisciplinary and multisectoral surveillance system

2. Prevention
Implementation of preventive measures and use of alternative treatment options to reduce the need for usage of antibiotics

3. Reasonable use of antibiotics
Updating obligatory guidelines and supervision of their implementation

4. Combating resistance
Reducing the transmission and dissemination of resistant pathogens

5. Research and Development
Gaining more knowledge about the development and transmission of antibiotic resistance and finding solutions for better diagnostic tools and to combat AMR

6. Cooperation
Improving interdisciplinary cooperation and coordination (policy, academia, economy) at the national and international levels following the *One Health* approach

7. Information and Education
Increasing awareness and knowledge on antibiotic resistance within specialist groups and the general public

8. Framework requirements
Creating necessary requirements (political, legal and financial) to secure the availability and reasonable use of effective antibiotics

8.5   Approach

The proposed strategy will be approved by the government at the end of 2015 and probably be implemented in 2016 aligned with the introduction of the revised Epidemics Act. The Swiss government will have a legal framework with the implementation of the Epidemic Law in January 2016. This will include the adaptation of key acts like the Epidemics Act, the Health Insurance Act, the Ordinances on Human and Veterinary Medicines as well as on Epizootic Diseases, the Agriculture Act and Environmental Act among others (GOV CH, 2014b).

For the achievement of its eight strategic goals the Swiss Government has set up a comprehensive plan of strategic measures. The development and implementation of a wide-ranging multidisciplinary surveillance system has been planned to achieve the first strategic goal of *Surveillance*. This also includes the establishment of a network of reference laboratories specialized in antibiotic resistance diagnostics and national standardization guidelines. Several measures will be used to achieve the second strategic goal of *Prevention* such as increased vaccination coverage, increased use of on-the-spot diagnostics or the optimization of handling methodologies within the field of animal husbandry. Another important measure will be the enhancement of the surveillance, prevention and fight against health-care associated infections. This measure refers to a national Swiss strategy on health-care associated infections, which is currently being elaborated. The development of obligatory guidelines for prescription, provision and handling of antibiotics and the supervision of their implementation is seen as a necessary prerequisite to reach the third strategic goal *(Reasonable use of antibiotics)*. Achieving strategic goal 4 *(Combating antibiotic resistance)* will involve the reduction of the transmission and dissemination of resistant pathogens within healthcare facilities, in animal husbandry and throughout the entire food chain, the preparation of outbreak guidelines and actions to reduce the development of resistant pathogens during wastewater treatment.

The establishment of an interdisciplinary research platform to gain more knowledge and evidence about the development and transmission of antibiotic resistance will be essential for the attainment of the fifth strategic goal, research and development. Furthermore support for the innovation of diagnostic tools in this area is being planned. The strategy also includes the recommended establishment of a central coordination unit and an expert commission for antibiotic resistance and antibiotic usage for improving interdisciplinary cooperation (6th strategic goal). In addition the exchange of information with professional associations and with other countries (especially the support of developing countries) has been envisaged. Concerning the 7th goal (*Information and Education*) the proposed measures include raising awareness in the general public of the threat of antibiotic resistance and possibly, preventive solutions involving training and further education of health-care workers, veterinarians and livestock farmers. Several measures have also been foreseen for the provision of the framework requirements (political, legal and financial) to secure the availability and the reasonable use of effective antibiotics. These include, among others, the creation of market incentives (e.g. for the development of new antibiotics) and the evaluation of special programs for the correct use of antibiotics.

8.6 Campaigns

Until now, no nationwide AMR-related campaign for the general public had been launched in Switzerland. In its proposed strategy the Swiss government plans to improve the level of information about antibiotics and antibiotic resistance in the general population and within specific target groups (physicians, veterinarians, farmers etc.). This will especially include preventative aspects (incl. vaccinations) in the field of animal health and issues concerning food safety and quality (GOV CH, 2014b).

8.7 Performance measurement

The proposed Swiss strategy not only describes the methods used to monitor the results of implemented measures (e.g. surveillance systems and AMR situation reports etc.) but it also articulates clearly the evaluation procedure for the strategy itself. According to Art. 81 of the revised Epidemic Act, the Swiss Federal Council is responsible for the supervision of the effectiveness, the appropriateness and the economic viability of the measures taken (GOV CH, 2014a). There will be an intermediate report on the outcome of the strategy 5 years after its enactment; followed by a final evaluation report to be published after 10 years. Both reports are to include detailed analyses considering the changed national and international circumstances and will be used as a basis for necessary adaptations of a subsequent strategy (GOV CH, 2014b).

8.8 Results

For this comparative study of national strategies and policies, the proposed National Antibiotic Resistance Strategy (StAR) has been selected. The Swiss government is planning to release the final strategy by the end of 2015, its implementation will start early in 2016 (GOV CH, 2015).

8.9 Key success factors / Best practice examples

The most promising factor of this new strategy is the formulation of almost all strategic measures across human, veterinary, agriculture and environmental sectors and a common coordination organ, which will oversee the implementation and the evaluation of this *One Health* strategy. Also, the strategy was elaborated with a large participatory and consultative approach among all involved actors and stakeholders with the aim of assuring the commitment during implementation of the strategy.

Switzerland's proposed national AMR strategy continued efforts and discussions resulting from the national research program *NFP 49*, initiated to determine the AMR situation in Switzerland in the human, animal and environmental sectors in 2001-2006. An important outcome of the *NFP 49* programme was the establishment of the Swiss Centre for Antibiotic Resistances (ANRESIS) and a national surveillance system (ARCH-Vet) (UoB, 2015; GOV CH, 2013).

Key success factors / Best practice examples	Chapter
Strategic aims across all four involved sectors	12.6.4
Large participatory and consultative approach with all involved actors	12.6
National research program NFP 49	12.5
Swiss Centre for Antibiotic Resistances (ANRESIS)	8.9
Report on sales of antibiotics in veterinary medicine and antibiotic resistance monitoring of livestock (ARCH-Vet)	8.9

SOUTH AFRICA

9.1 Context

In the final draft of its *Antimicrobial Resistance National Strategy Framework* the government of South Africa states that "*AMR is a major threat to the long-term security of public health and has the potential to negatively impact our society*" (GOV SA, 2014b). The development of this strategy framework has been triggered by two main factors: South Africa has very high levels of antibiotic resistance, particularly in connection with tuberculosis treatment, where there is great concern caused by multi-drug- and extensively-drug-resistant bacteria (MDR-TB and XDR-TB). In addition South Africa has responded to the call by WHO to complement the development of the Global Action Plan by setting up a national AMR strategy as agreed upon by the member states during the World Health Assembly in May 2014 (WHO, 2014a). The *AMR Background Report,* a comprehensive guidance document, is also to be published to facilitate the implementation of the national strategy on all levels of the health system (GOV SA, 2014a).

9.2 Coordination

The South African Department of Health is the driving force behind the *AMR National Strategy Framework*, which has been developed in close cooperation with the Department of Agriculture, Forestry and Fisheries and the Department of Science and Technology, and members of the South African Antibiotic Stewardship Programme (SAASP). Multiple other stakeholders from various AMR-related sectors have been included in the strategy's development, including the National Health Laboratory Services, clinician societies, civil society organizations and regulatory societies (e.g. Pharmacy Council, Veterinary Council, Medicines Control Council etc.) (GOV SA, 2014c).

9.3 One Health integration

The South African government believes that the development and implementation of its AMR strategy is a crucial step towards containment of the AMR threat in human and animal health as well as in the agriculture sector. A multidisciplinary Ministerial Advisory Committee including representatives from academia (human and veterinary health), other governmental departments and agencies (incl. Agriculture, Forestry and Fisheries, Education etc.) will be established to further strengthen and institutionalize the interdisciplinary efforts (GOV SA, 2014b).

9.4　Focus

The aim of the proposed AMR National Strategy framework is "to provide a structure for managing AMR, to limit further increases in resistant microbial infections, and improve patient outcomes". With this strategy the government is also trying to achieve four **main goals** (GOV SA, 2014b):

Goal 1
To define the principles and short- to medium-term interventions needed to preserve the effectiveness of antimicrobials for future generations

Goal 2
To improve the appropriate use of antibiotics in human and animal health

Goal 3
To improve the effective management of antibiotic resistant organisms and to prevent their transmission

Goal 4
To create an enabling environment for the successful and sustainable implementation of the strategic objectives

The strategic framework is built around four **strategic objectives:**

1. Strengthen, coordinate and institutionalize interdisciplinary efforts through national and health establishment level governance structures

2. Optimise surveillance and early detection of antimicrobial resistance to enable reporting of local, regional, and national resistance patterns to optimise empiric and targeted antibiotic choice.

3. Enhance infection prevention and control of the spread of resistant microbes to patients in healthcare settings, focusing on improvement in hand hygiene and the identification and isolation of patients with resistant organisms. Community measures include preventing infection through wide-reaching vaccination programmes and improvements in water and sanitation.

4. Promote appropriate use of antimicrobials in human and animal health through antimicrobial stewardship

9.5   Approach

For the achievement of the first strategic objective (*Strengthen, coordinate and institutionalize interdisciplinary efforts*) the establishment of an interdisciplinary national advisory committee and additional governance structures at the operational level are planned. To optimize surveillance and early detection of antimicrobial resistance (2nd strategic objective) measures to strengthen surveillance of local and national resistance patterns and of the usage of antimicrobials as well as the development of an early warning system are going to be implemented. To reach the third strategic objective (*Enhance IPC*) the proposed measures are especially focused on the prevention of new infections and the control of the spread of resistant microorganisms. In order to promote the appropriate use of antimicrobials in human and animal health (4th strategic goal) the government aims to ensure access to safe, effective and affordable antimicrobials, to institutionalise antimicrobial stewardship and to raise awareness of the use of antimicrobials in animal health and crop production.

Key enablers underpin the four strategic objectives:

1. **Legislative and policy reform for strengthening health systems** to support the quality of antimicrobials in the country and to enable control over prescribing of antimicrobials in the animal health sector

2. **Education** of all levels of health providers in human health and agriculture in the critical concepts of antimicrobial stewardship, infection control, infectious diseases, microbiology and pharmacology.

3. **Communication** to educate the public, create awareness and enhance patient advocacy of the dangers of inappropriate antimicrobial use.

4. **Research** into novel diagnostics such as point-of-care testing and clinical trials of treatment duration, antimicrobial consumption, and new antimicrobials.

9.6 Campaigns

The South African government is planning to develop campaigns targeted at the general public in order to raise awareness on infectious diseases and their prevention and control measures. In addition AMR-specific information campaigns are being considered using target-group orientated communication channels. The use of community health workers and close cooperation with the media are of high priority for the effectiveness of the planned AMR-related campaigns.

9.7 Performance measurement

The proposed South African AMR National Strategic Framework includes a table describing the indicators and targets (short-, medium- and long-term) for the monitoring and evaluation of strategy implementation. For every strategic objective and sub-objective indicators have been defined. In the field of infection control and prevention, for instance, indicators include the percentage of districts having at least one IPC practioner or the ration of IPC practioners per 250 acute beds per hospital. Another example for an indicator is the percentage of institutions reporting against the standards for institutional surveillance (GOV SA, 2014b).

9.8 Results

For this comparative study of national strategies and policies the proposed *Antimicrobial Resistance National Strategy Framework* has been selected. The South African government is planning to release the final document and to start implementing the chosen measures in 2015.

9.9 Key success factors / Best practice examples

In 2011, the *Global Antibiotic Resistance Partnership* South Africa (GARP-SA) network undertook a situational analysis of antimicrobial resistance in South Africa, published in the national medical journal (Duse, 2011). In 2012, SAASP was formed to introduce antibiotic stewardship nationally and support the Department of Health in developing the South African Strategy Framework. Concurrently, a multidisciplinary partnership between the Department of Health, GARP-SA, and SAASP has planned and is implementing the South African national norms and standards for antimicrobial stewardship (and infection control). Since 2006 the National Health Laboratory Service at the National Institute for Communicable Diseases has published comprehensive annual reports on communicable diseases and the AMR situation in South Africa. The data for these reports has been provided by a nationwide network of about 200 laboratories participating in the national surveillance program, GERMS-SA (NIFCD, 2013).

Key success factors / Best practice examples	Chapter
Global Antibiotic Resistance Partnership (GARP)	12.6.1
GERMS-SA	9.9
South African Antibiotic Stewardship Program (SAASP)	12.2.4

AMR RELATED POLICIES / ACTIVITIES IN LOW- AND MIDDLE-INCOME COUNTRIES

Apart from South Africa a rising number of low- and middle-income countries are committing themselves to the fight against antimicrobial resistance, setting up national policies and strategies and becoming increasingly involved in international efforts. In addition to the great burden of infectious diseases (e.g. malaria, tuberculosis and HIV / AIDS) these countries often have additional AMR-related challenges to tackle, e.g. substandard and counterfeit drugs, inefficient health systems, high level of over-the-counter sales of antibiotics and a lack of laboratory, monitoring and surveillance capacities. In the following sections some AMR-related policies, activities and best practice examples from Ghana, Thailand and India will be discussed briefly.

10.1 Ghana

Morbidity and mortality rates due to infectious diseases are extremely high in Ghana and antibiotic resistance is worsening the situation. There are the widespread problems connected with availability, affordability and accessibility of antibiotic drugs. In addition overusage especially in the informal health sector and the very low quality of the drugs available is causing great concern. In 2010 the *Antibiotic Drug use, Monitoring and Evaluation of Resistance* (ADMER) project was initiated with support from the Danish Ministry of Foreign Affairs (ADMER, 2010). This project has only been partially successful due to the complexity of the AMR problem, the weak regulatory systems and the rising threat caused by counterfeit drugs. Therefore the government of Ghana has set up a national multi-stakeholder AMR platform and together with a group of partner organizations (e.g. ReAct, Swedish Development Agency) is currently working on a *Comprehensive policy on antimicrobial resistance in Ghana*. The subgroup, the *Technical Task Team on AMR policy development for Ghana* (TTT) is leading this initiative (GHNDP, 2013). This subgroup is comparable to GARP working groups (e.g. in South Africa), and is focusing on the use of antibiotics solutions protecting their effectiveness in both humans and animals. In contrast to the GARP working groups it is very closely linked to the national government.

10.2 India

Indian public health authorities are becoming increasingly aware of the problems caused by antimicrobial resistance. As health governance and infrastructure, especially at regional and local levels are weak, the magnitude of the AMR threat is difficult to determine. Surveillance and monitoring measures are extremely difficult to establish in an overpopulated country with great regional variations.

In 2011, the Indian government published a *National Policy for containment of antimicrobial resistance* to develop and strengthen national policies and activities related to antimicrobial resistance (GOV IND, 2011). The aim has been to establish a nationwide well-coordinated AMR program including the promotion of research activities to improve knowledge about AMR and the influencing factors. Additionally control measures and regulations for the rationalization and responsible use of available antimicrobials were to be implemented and the development of new antimicrobials and diagnostic tests should be supported. In addition to the national policy the appropriate use of antimicrobials has been regulated through various existing national health programmes, e.g. the Revised National Tuberculosis Programme, the National AIDS control programme or the National Vector Borne Disease Control Programme. The Ministry of Health and Family Welfare, which is also the Indian drug regulatory authority, has been working on restrictions to the entry and availability of antibiotics by limiting the number of defined antibiotics for use in special levels of health facilities. This governmental activitiy has also been a result of a joint conference held in August 2012, in which the medical societies of India published their *Chennai Declaration*

calling for national recommendations and a national action plan in response to the growing AMR threat. Recognizing that over-the-counter-sales of all antibiotics would be difficult to regulate in India, where many people do not have access to or can afford a doctor's consultation, a list of second- and third-line antibiotics and tuberculosis drugs was prepared. The listed drugs can now be purchased by prescription only. This policy initiated by the medical societies and taking economic aspects of populations into account, is now being seen as a best practice example for developing countries (Holmes and Sharland, 2013).

The Indian Government also hosted a meeting of Ministers of Health from the WHO Southeast-Asian region on AMR in Jaipur in 2011, which resulted in the *Jaipur Declaration* showing political commitment at both national and international levels, proposing actions to be taken and raising awareness about the AMR threat (SEARO, 2011). Since 2009 the Indian National Center for Disease Control (NCDC) has been working in close collaboration with the Public Health Agency of Sweden on solutions to achieve a more rational use of antibiotics and an improved surveillance of antibiotic resistance (NCDC, 2010).

10.3 Thailand

The government and health authorities of Thailand have reacted to the high rate of inappropriate use of antimicrobials in teaching hospitals (30-90%) and the AMR problem in general.

In 2011 the Policy for Rational Drug Use was introduced, followed by the 2012 National Strategy for Emerging Infectious Diseases (GOV THA, 2011). Both policies included a specific focus on AMR. In addition a Committee on AMR containment was selected in 2012 to discuss goals, approaches and the design of a national strategy roadmap. The Thailand AMR Containment Package 2013-2016 incorporates five interconnected systems: Surveillance of AMR and the usage of antibiotics, rational use of antibiotics, infection prevention and control, public awareness and research and development (Thamlikitkul, 2014). The National Alliance for AMR Prevention and Control and the National Antimicrobial Resistance Surveillance Center (NARST) have also been supporting the implementation of the national strategy (Kiatying-Angsulee, 2011).

A best practice example for promoting the rational use of antibiotics is the Antibiotic Smart Use Programme (ASU) set up in 2007 in close collaboration with the Sweden-based NGO ReAct. This programme has involved multiple interventions aiming at changing prescription practices and maintaining behavior change at the individual level (physicians, patients) as well as efforts at organizational, network and political levels. The creation of local ownership and mutual recognition has been key success factors for the ASU program (Sumpradit, 2012).

SUMMARY
OF NATIONAL STRATEGIES AND POLICIES

The previous chapters have demonstrated the complexity of challenges, stakeholders, measures and initiatives in the field of antimicrobial resistances. Comparing national strategies and policies and identifying key success factors and best practice examples are difficult tasks. The countries included in this study started their fight against AMR in a variety of circumstances at different points in time. When analyzing AMR-related strategies and policies the respective contexts have to be considered. The numerous national differences in public health systems, epidemiology, culture, laws and the economic status should be taken into account in addition to the baseline data of antimicrobial usage and antimicrobial resistance levels. Therefore to get an even more comprehensive picture further research in the various fields is essential.

The national health ministries head AMR-related strategies and policies in most of the countries included in this study. Several other national ministries and authorities (e.g. Public Health institutes, Medicine Licensing agencies) are also involved in the development and implementation of these strategies and policies. To improve national coordination most countries have established a steering group (e.g. UK: High-Level Steering Group), an interministerial working group on AMR (e.g. Germany, Norway) or an intersectoral coordination mechanism (e.g. Sweden). International coordination activities are mainly linked together at the European Union level (in EU countries, Norway, Switzerland, US) and to WHO and its Regional Offices.

A *One Health* approach is specifically mentioned by some of the countries (UK, Denmark, Norway, USA, Switzerland) and other countries (Sweden, Germany, France, South Africa) include some aspects of this approach in their strategies and policies. However environmental topics are rarely included within the goals, focus areas or measures. Only Norway has set a sub-target aiming at the reduction of the total environmental impact of antibiotics. The policies of all the other countries mainly focus on human health (France), veterinary health (Denmark) or both (UK, Sweden, Germany). The three proposed strategies (USA, Switzerland, South Africa) have a stronger emphasis on the *One Health* approach.

The national AMR-related strategies and policies studied have many focal areas and approaches in common, but there are also some differences, which can be explained in various ways. Historical context, changing national and international circumstances, geographical and political aspects, levels of health-care systems and other issues all need to be taken into account. A categorization of the measures used has been prepared as the basis of a more structured analysis of these approaches. The main areas of work presented in the AMR-related strategies and policies included in this study are listed in the following table:

Category	Related aspects
Surveillance and Monitoring	National monitoring of AB use and AMR levels
Prescription practices and use	Treatment guidelines, stewardship programs, point-of-care and rapid diagnostics
Infection Prevention and Control	Specialists training, community officers, hygiene programs
Awareness and Education	Public information, campaigns, education programs
Innovation, Research and Development	Academic research, evidence-based approaches, industry involvement, investments, new antibiotics, vaccines, diagnostics
Coordination and Cooperation	International, national, local, cross-sectoral
Framework requirements	Regulations and financial resources

Individual national governments have chosen similar performance measurements for their national AMR strategies and policies. Most countries have set a strong focus on the strengthening or development and implementation of national surveillance systems and a close collaboration with international networks especially within the European Union (e.g. EARS-NET, ESAC-Net), allowing a certain degree of comparability between the countries. The results have been presented either annually (e.g. in Denmark, Sweden) or a few years after the implementation of the strategy (e.g. in Germany). In addition to this some countries have defined certain indicators to measure progress in the areas outlined in the national plan (e.g. France).

A comparison of the results achieved by different countries is difficult due to the complexity of the field and to data comparability limitations. In addition some countries (e.g. Germany and Norway) are currently evaluating their progress and independent, academic research in this area is still lacking. A direct relationship between implemented measures and achieved outcomes is not measurable in many cases. The effectiveness of individual AMR-related policies are difficult to identify and it is also difficult to determine at what point in time the collective effects of a set of policies or a national strategy will be recognizable.

Despite these limiting factors some key success factors and best practice examples have been identified in the comparison between the selected countries.

OVERVIEW OF FOCUS AREAS AND BEST PRACTICE EXAMPLES

The following table displays the AMR-related activities of each of the countries included in this study. A categorization of the focus areas has been developed, closely linked to the results of a previous study by the Swiss Federal Office of Public Health and to the strategic objectives of the WHO Global Action Plan, currently under discussion. For this overview the content of the main AMR-strategies and policy documents used in this study has been studied. Additional policy documents, e.g. infection control strategies not explicitly mentioned in the respective AMR-strategy, haven't been included in the table below or in the following chapters. As the proposed strategies of the USA, Switzerland and South Africa are still being finalized the current status (February 2015) has been used for this overview. In addition these countries' best practice examples are taken from experiences with previous AMR-related policies. The selection of best practice examples from all of the studied countries was based on the following criteria:

Relevant	Must be relevant in this context
Effective	Must work and achieve results that have been measured or acknowledged
Efficient	Must produce results with a reasonable level of resources and time
Ethical	Must respect the current rules of ethics
Sustainable	Able to be maintained over a long period of time without causing excessive costs
Usable	Can be adapted for use in other countries
Partnership	Satisfactory collaboration between the involved stakeholders

The table displays only those activities, which are explicitly mentioned in the respective main AMR-strategy and related policy documents.

		UK	Sweden	Denmark	Germany	Norway	France	USA	Switzerland	South Africa
	Publication year	2000 / 2013	2005 / 2014	2007	2008	2000 / 2008	2000 / 2011	2015	2015 (planned)	2015 (planned)
12.1	**Surveillance and Monitoring**	ESPAUR	Strama	DANMAP	GERMAP	NORM	ESAC	NARMS		
	Lab Capacity							Standards	Network	
	Monitor use Monitor AMR		SWEDRES SWARM	Copenhagen 2012	GERM-Vet ARS					
12.2	**Prescription practices and use**		Strama	DANMAP	AB Therapy Commission		Main Goal - 25%			
12.2.1	Regulation			VeTStat						
12.2.2	Improved diagnosis						Rapid tests	Rapid tests		Point-of care diagnostics
12.2.3	Treatment Guidelines	TARGET STAR	Evidence-based			Internet Mobile Phones	CIGPA			
12.2.4	Patient Care / GPs	Stewardship Start smart	Strama Awareness				HPST	Stewardship		Stewardship Access
12.2.5	Animal Husbandry	Farm HP						Stewardship		Stewardship
12.3	**Infection Prevention and Control**					AMR + HAI				
12.3.1	Human Health		Strama County MO							
12.3.2	Animal Health	Farm HP		Herd Health Contracts				Get Smart		

Main goals / Focus areas

Fields of activity mentioned in the strategy

Other related activities, e.g. conferences, etc.

No activity mentioned in the main document

The table displays only those activities, which are explicitly mentioned in the respective main AMR-strategy and related policy documents.

			UK	Sweden	Denmark	Germany	Norway	France	USA	Switzerland	South Africa
12.4	**Awareness and Education**				Copenhagen 1998						
12.4.1	Awareness				Families		GP level Families	National campaign	Get Smart		
12.4.2	Education		TARGET STAR	Strama	E-Bug project			E-Bug project	Learning Site		
12.5	**Research and Development**										
12.5.1	Evidence-based approach			Knowledge Bank	DANMAP		NPID		NIH BARDA	Research Platform	
12.5.2	Private sector			Stockholm 2009					PPP	Market incentives	
12.6	**Collaboration and Coordination**			EU / WHO			Oslo 2014				
12.6.1	International			SIDA					TATFAR GHSA		GARP
12.6.2	National		HLSG	ICM Strama	DANMAP	ImWG AB Th Com	ImSC	Regional Health Agencies	Task Force	CCU Exp Com	Min Adv. Com
12.6.3	Cross-Sectoral			ICM ReAct							
12.6.4	One Health Approach		H = V	H > V / (E)	V > H	H = V	H > V / E	H > V	H = V / (E)	H = V / E	H = V / E
12.7	**Framework requirements**				VET regulations					Legal Framework	
12.7.1	Regulatory framework				Yellow card			HPST			
12.7.3	Financial Resources						Cost study	Economic analysis		Private sector	

� dark gray▪	▪medium gray▪	▪light gray▪	▪white▪
Main goals / Focus areas	Fields of activity mentioned in the strategy	Other related activities, e.g. conferences, etc.	No activity mentioned in the main document

12.1 Surveillance and Monitoring

All of the countries in this study have included the establishment and strengthening of national and international surveillance systems into their strategies or national policies. Various studies have presented strong evidence for a close correlation between the level of consumption of antibiotics and the level of resistance to antibiotics. Most countries emphasize the need for monitoring the use of antibiotics and antibiotic resistance levels in all sectors to identify key areas for action and to measure the effectiveness of the implemented measures over time. Well functioning surveillance systems are also important for the preparation of treatment guidelines and for providing evidence to policy makers and developers of new antibiotics. During the Danish EU-Presidency in 2012 a conference in Copenhagen was held under the theme *Combating Antimicrobial Resistance – Time for Joint Action*, focusing on ways of improving EU-wide data collection and surveillance.

12.1.1 Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP)

Denmark was one of the first countries worldwide to establish a national cross-sector AMR surveillance system. The 1995 DANMAP, the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme has had 4 main objectives:

- To monitor the consumption of antimicrobial agents for food animals and humans
- To monitor the occurrence of antimicrobial resistance in bacteria isolated from food animals, food of animal origin and humans
- To study associations between antimicrobial consumption and antimicrobial resistance
- To identify routes of transmission and areas for further research studies

The annual DANMAP report on the *Use of antimicrobial agents and occurrence of antimicrobial resistance* in bacteria from food animals, food and humans in Denmark is published by the Statens Serum Institute, the National Veterinary Institute and the National Food Institute in close cooperation with the Technical University of Denmark and is used as the basis of Danish AMR-related policies. DANMAP has been described as using a *One Health* concept, *"comprising the entire chain from farm to fork to sickbed"* and establishing a strong collaboration between physicians, veterinarians, microbiologists, epidemiologists and specialists from other AMR-related disciplines. The main actors and the reporting systems of DANMAP are shown in Figure 6.
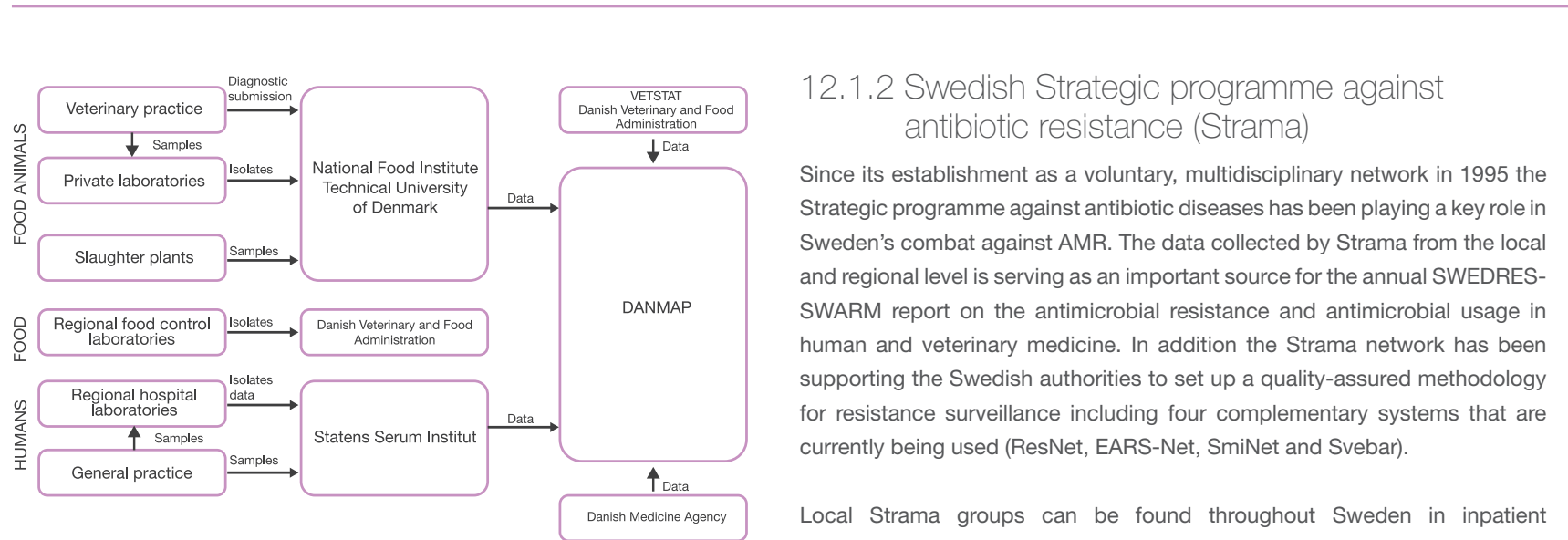
Figure 6: Organization of DANMAP

Source: National Food Institute: Data for action, 2012

The DANMAP concept has widely been acknowledged as a best practice example for of a well-structured national AMR surveillance program, as it is building the basis for Denmark's successful evidence-based policy making in the field of AMR.

12.1.2 Swedish Strategic programme against antibiotic resistance (Strama)

Since its establishment as a voluntary, multidisciplinary network in 1995 the Strategic programme against antibiotic diseases has been playing a key role in Sweden's combat against AMR. The data collected by Strama from the local and regional level is serving as an important source for the annual SWEDRES-SWARM report on the antimicrobial resistance and antimicrobial usage in human and veterinary medicine. In addition the Strama network has been supporting the Swedish authorities to set up a quality-assured methodology for resistance surveillance including four complementary systems that are currently being used (ResNet, EARS-Net, SmiNet and Svebar).

Local Strama groups can be found throughout Sweden in inpatient (Hospital and / or ICU Strama) and outpatient settings as different efforts are necessary. In addition to its surveillance and monitoring activities the Strama groups are actively involved in many AMR-related fields like information and training of physicians, analysis and feedback of antibiotic use and resistance, treatment recommendations, studies and advocacy. This integrated approach has significantly improved the coordination between the stakeholders involved. Linking surveillance activities and evidence-based treatment recommendations to support the prescriber has also proved to be very successful in Sweden.

12.1.3 Other best practice examples in the field of surveillance and monitoring

The English surveillance programme for antimicrobial utilization and resistance (ESPAUR), led by Public Health England, has been implemented to monitor the successfulness of the national strategy and to refine national AMR policies as needed. The first comprehensive report was published in 2014. The authors conclude, amongst other aspects, that the improvement of laboratory surveillance systems and an expansion of drug-bug combinations included in the AMR surveillance are essential to guide antibiotic policies and improve antibiotic stewardship.

The success of the Norwegian AMR-related policies has been mainly due to the presence of vigorous surveillance and reporting systems for the usage of antimicrobial agents and the occurrence of antimicrobial resistance in both the human (NORM) and veterinary sectors (NORM-VET). The NORM surveillance programme for AMR in human pathogens was established in 1999 and has been coordinated by the Department of Microbiology and Infection Control at the University of Tromso and the NORM-VET AMR monitoring programme in the veterinary and food production sectors was set up in 2000 and has been coordinated by the Norwegian Veterinary Institute. The institutions and programmes have been working in close collaboration and the joint, annual NORM/NORM-VET report includes the data and the analysis of the Norwegian AMR situation.

At the European level, the ECDC has implemented the European AMR Surveillance Network (EARS-NET) and the European Surveillance of Antimicrobial Consumption Network (ESAC-NET). In addition the European Medicines Agency has been coordinating a program on the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC). These surveillance networks have been building a good basis for comparisons between the EU countries, which national governments have been able to use to improve their national AMR policies and which could be seen as best practice examples for other world regions. In the future, global surveillance systems could be an option for immediate AMR detection and response solutions. These systems could include e.g. the development of a global database for the collection of the genetic codes of all identified microorganisms.

12.2 Prescription practices and reasonable use

One of the main reasons for the development of antimicrobial resistance is the imprudent use of antimicrobials including unreasonable prescriptions in both human and the veterinary sectors.

Even the discoverer of penicillin, the world's first antibiotic, Sir Alexander Fleming himself was aware of the potential danger of AMR predicting in his Noble prize acceptance speech: *"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant"*.

Studies have shown that his predictions have proved to be right. However several countries have developed various ways of responding to this danger. A reduction of antibiotic consumption by 25% is one of the main goals the French government has set for its national strategy plan. To improve the reasonable use of antimicrobials the German government has established an Antibiotic Therapy Commission at the Robert Koch Institute, which among other functions is focusing on an increased use of diagnostic procedures, improving treatment guidelines and implementing antibiotic stewardship programs.

In principle, there are various ways of achieving rational prescribing and a more reasonable use of antimicrobials can be achieved in different ways: by stricter regulations, the development of better diagnostics, the improvement and increased use of treatment guidelines and by measures enhancing patient care and cooperation. Most of these solutions are also applicable in the field of animal husbandry.

12.2.1 Regulation

Although restrictive antibiotic prescription policies aiming at a reduction of antibiotic consumption have shown to be successful in a number of European countries (e.g. Spain, Czech Republic), (Jover 2007), regulatory interventions in this area haven't been specifically included in the majority of the national strategies included in this study. This can be partially explained by the existence of rules and regulations for the use of medical products at the national, but also at the European level, where the approval and use of antibiotics is primarily regulated.

A high percentage of prescription free over-the-counter sales of antibiotics can often be observed in low- and middle-income countries. The national governments of these countries not only need to tackle this problem but also additional aspects such as the limited access to medical services and essential good quality medicines as well as the growing problem of counterfeit medicines containing sub-therapeutic dosages. The Indian government has been working on availability restrictions by limiting the number of defined antibiotics for use in special levels of health facilities. The Indian medical societies' Chennai Declaration has encouraged this process. A similar physician's initiative of such a high visibility has not been observed in the countries included in the present study.
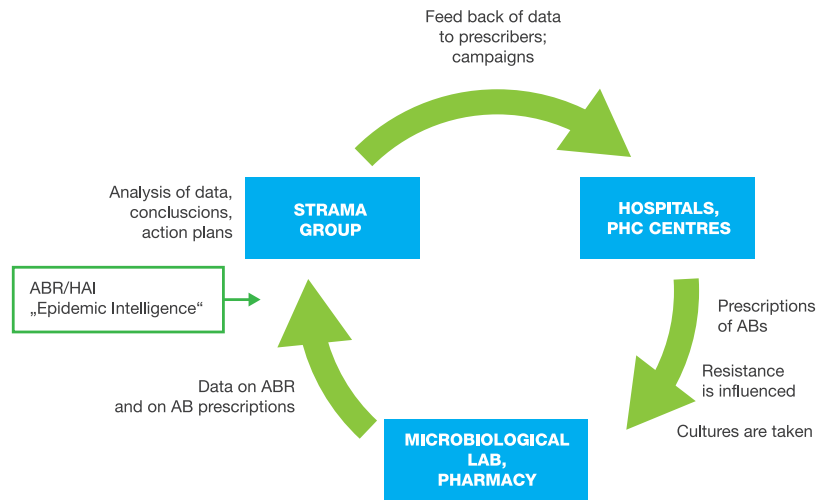
12.2.2 Improving diagnosis

Improving existing and developing new diagnostic tests for both the identification of the bacteria and their susceptibility to specific antimicrobial drugs can also lead to more rational prescribing and reasonable use of antibiotics. Prescription tailored diagnosis is playing an important role in the fight against AMR. The French government has therefore been supporting the development of rapid diagnostic tests and the expansion of the use of these tests to improve targeted antibiotic treatment. The German government has been trying to enhance an increased use of diagnostic procedures (incl. rapid-tests) at ambulatory and hospital levels. However this measure has only been implemented for MRSA-diagnostics in the ambulatory sector so far due to complex legal and financial issues regarding the reimbursement process.

Advancing the development and use of rapid and innovative diagnostic tests has also been one of the US government's national AMR strategy goals. New point-of-need diagnostic tests and rapid molecular tests to identify the infecting pathogen and its antibiotic-resistance profile should be developed to improve the detection, control and prevention of multidrug-resistant organisms. In addition existing culture-based tests should be used more frequently to distinguish between viral and bacterial infections more rapidly. The US Government is planning to provide representative clinical isolates to advance development of diagnostics and help to address issues related to test development and validation, FDA review and reimbursement. Progress of all these initiatives still needs to be monitored. A close link between prescribing regulations and the reimbursement process, e.g. allowing the use of a certain reserve antibiotic only if adequate testing has been completed, could also be an option to be discussed in this context.

12.2.3 Treatment guidelines

To achieve a more reasonable use of antimicrobials prescribing behavior needs to be influenced not only by the implementation of additional regulations and by increasing measures for surveillance and monitoring. Updating national guidelines, adapting these to local circumstances and supporting the prescriber through various ways are also very important factors in the fight against AMR.

Strama, the Swedish strategic programme against antibiotic resistance, has been widely acknowledged for integrating a number of measures to support the prescriber establishing a nationwide system for evidence-based treatment recommendations. The Swedish government has defined this system as one of the key areas of its AMR-related work. The Public Health Agency and the Medical Product Agency of Sweden have published national treatment recommendations for common infections in the outpatient setting and the Swedish Society of Infectious Diseases has developed national care programmes for infections in hospitalized patients. Local Strama groups and pharmaceutical committees have been responsible for disseminating these national recommendations and using these as the basis of developing local guidelines and memoranda in relation to the local antibiotic resistance patterns. The local Strama groups continuously communicate data and results to prescribers in order to inform them about developments and to guide them towards the best local interventions.

Feed back of data
to prescribers;
campaigns

Analysis of data,
concluscions,
action plans

STRAMA
GROUP

HOSPITALS,
PHC CENTRES

ABR/HAI
„Epidemic Intelligence"

Prescriptions
of ABs

Resistance
is influenced

Data on ABR
and on AB prescriptions

Cultures are taken

MICROBIOLOGICAL
LAB,
PHARMACY

Improved antbiotic prescription requires continous work.

Figure 7: The cyclical process of the Strama work
Source: Swedish work on containment of antibiotic resistance 2014

The UK has been implementing two successful programs to support general practioners prescribing. *Treat Antibiotics Responsibly, Guidance, Education, Tools* (TARGET) is a web-based toolkit, designed as a resource centre for clinicians, primary care staff and patients, which can be used also for a one-hour workshop within the GP's practice. *Stemming the Tide of Antibiotic Resistance* (STAR) is a theory-based blended education program including the presentation of research evidence and guidelines, a practice-based seminar, online clinician's reflection and videos to improve communication skills. First results show that TARGET and STAR have helped to deliver changes in local prescription practice reducing unnecessary antibiotic use.

Other promising approaches and activities to improve the use of treatment guidelines include the French update of its *Composite Indicator of Good Practices in Antibiotics guide* and the development of easy-to-use web- and mobile phone based treatment guidelines in Norway.

12.2.4 Patient care

While most of the national policies for a more rational use of antibiotics focus on GP's and primary health care workers, some countries are using additional measures aiming at an increase in appropriate prescribing of antimicrobials in hospitals and other healthcare facilities. In particular the use of antimicrobial stewardship programmes, awareness campaigns targeting doctors and nurses and strict admission and isolation policies (e.g. in Denmark or in the Netherlands) should be mentioned in this context.

The United Kingdom has been successfully implementing antimicrobial stewardship programmes to promote rational prescribing, a better use of existing diagnostics as well as an increased use of new rapid diagnostics as one of the key areas of work within the national AMR strategy. Since 2011 the *Start Smart then Focus* initiative has been providing guidance on antibiotic stewardship in the secondary healthcare setting. A reduction in inappropriate prescribing has been observed in more than 75% of hospitals, which have responded to this initiative conducting formal reviews of their antimicrobial stewardship programme (ESCMID-ISC survey). Tentative evidence from the UK CPA survey also suggests that nearly a quarter of hospitals have already demonstrated a reduction in antimicrobial resistance in their settings.

The US government has stated in its strategy that antibiotic stewardship programs need to become routine in healthcare delivery as well as in agricultural settings to help slow the emergence of resistance. Over the past years the US has been implementing the *Get Smart for Healthcare* campaign focussing on improving prescription practices in inpatient healthcare facilities

through the implementation of antibiotic stewardship programs. This has proved to be effective leading to a reduction of *Clostridium difficile* infections and antibiotic resistance, improving individual patient outcomes, and reducing healthcare costs.

Effective antimicrobial stewardship programmes require multiple measures and a close collaboration between the different specialties within a health-care institution. These measures include education of doctors and nurses, formulary restrictions, approval processes, strategic switching of antibiotics and computer-assisted treatment models. Many of these measures have already been used in Sweden by local Strama groups in inpatient settings (Hospital and / or ICU Strama). In addition infectious-diseases specialists and County Medical Officers for communicable disease control have proved to be of key importance in controlling antibiotic usage in many county hospitals.

In the Netherlands a s*earch and destroy* policy has led to relatively low antibiotic resistance prevalence rates in hospitals. This policy includes prescreening of patients before admission, isolating patients suspected to have an infection with resistant bacteria and, if these are detected, keeping these patients quarantined. In addition hospital staff members are being screened for resistant bacteria on a regular basis. In China all hospitals have had to set up antibiotic administrative groups, formulary restrictions have been enforced, doctors have been given prescription rights for different antibiotic classes depending on their positional titles and antibiotic procurement has been restricted to a certain number of antimicrobials (50% in secondary and

35% in tertiary hospitals). These measures have led to reduction in antimicrobial prescriptions in hospitalized patients.

In contrast to these positive developments, antimicrobial consumption had been constantly increasing in Danish hospitals since 2003 (e.g. broad-spectrum antibiotics by +114%). However a close correlation between this and a decrease in the number of hospital bed-days has been observed. As this appears to be a common trend in many countries now, this specific aspect obviously needs to be taken into close consideration while developing hospital-focused AMR-strategies.

12.2.5 Animal husbandry

Policies aimed at more rational prescribing and reasonable use of antimicrobials in the field of animal husbandry are also very important in combatting AMR. Despite the various approaches used in different countries the level of consumption of antimicrobials in healthy animals (for infection control and growth promotion) is often higher than the level of consumption in unhealthy humans.

Denmark's AMR-related policies have been focused mainly on the reduction of antimicrobial use in the animal husbandry sector. Success has been achieved by banning antibiotics as growth promoters, by restricting veterinarians profiting through the sale of antibiotics and by several other policies and regulations targeted at veterinarians and farmers. Among these are the *Herd Health Contracts* between herd owners and veterinarians including monthly visits irrespective of the current health situation, a risk management program (VeTStat) and the introduction of a *Yellow Card* system to publicly "warn" farmers and veterinarians who have been found to have a high consumption of antimicrobial agents.

While the antibiotic resistance situation has remained stable, the overall antibiotic consumption in Denmark's animal husbandry sector has been gradually increasing again partially due to the increased pig production. Apart from this development an interesting initiative in Denmark has been the voluntary program by the Danish Meat Association to stop the use of cephalosporins in pigs.

As part of the UK strategy a number of initiatives and campaigns have been promoting responsible veterinary use of antibiotics. These have included antimicrobial stewardship programmes and the introduction of Farm Health Plans and biosecurity measures. The inclusion of professional associations such as the British Veterinary Association in the development and distribution of national treatment guidelines as well as the formation of the *Responsible Use of Medicines in Agriculture Alliance* have also been key components of the UK's approach.

The responsible use of medicines (especially antimicrobials) in the prevention and control of animal diseases has been promoted by the European Platform for the Responsible Use of Medicines in Animals (EPRUMA), a multi-stakeholder platform established in 2005. EPRUMA has been using a coordinated and integrated approach communicating and engaged with all stakeholders involved in veterinary medicines (including farmers, veterinarians, pharmacists, manufacturers, retailers etc.). Besides promoting the responsible use of medicines EPRUMA has been developing best-practice frameworks, which can be adapted nationally. The *Best practice framework for the use of antimicrobials in food-producing animals*, published in 2008, has been made available in various European languages.

12.3 Infection prevention and control

Most of the national AMR-strategies and policies included in this study have included infection prevention and control measures such as improving hospital hygiene, increasing immunization coverage and public campaigns focusing on aspects such as hand washing to reduce the need for antibiotics and to improve public health in general.

12.3.1 Infection prevention and control for human health

Norway's *National Strategy for prevention of infections in the health service and antibiotic resistance* has particularly emphasized the close link between infection prevention and control in healthcare facilities and the antibiotic resistance threat. Two of the three primary goals of the Norwegian strategy have focused on this issue: the reduction of the occurrence of infections acquired in the health service (Goal 2) and the improvement of knowledge about the occurrence, causal relations and effects of measures to prevent infections in the health service and antibiotic resistance (Goal 3). Measures taken have included the improvement of surveillance systems for infections and antibiotic resistance within hospitals and municipal health-care institutions for the elderly, the improvement of guidelines and control of their implementation, increased vaccination coverage and further revision of the existing IPC regulations. A national plan for research and development in the fields of infectious diseases in the health services and antibiotic resistance has been drawn up and models for estimating the costs of infections acquired in health care facilities have been developed.

Several measures included in the Swedish strategic programme against antibiotic resistance focus on infection prevention and control in healthcare facilities. Multiple specialties are organized in hospital and ICU Strama groups to exchange information and discuss necessary changes. Infectious-diseases specialists and County Medical officers for communicable disease control support them. In addition the Swedish Society of Infectious Diseases has developed special national care programmes for infections in hospitalized patients.

Following an MRSA outbreak in pigs Denmark has now implemented a mandatory MRSA screening before hospital admission for all patients known to have contact with pigs, especially those who are working in the meat production sector. In the Netherlands a significant decrease in the number of MRSA infections in hospitals has been realized by prescreening all patients before they enter the hospital. While most of the AMR-related policies and research activities are concentrating on infection prevention and control in hospitals, more data is needed about the IPC and AMR situation in other healthcare settings like nursing homes.

12.3.2 Infection prevention and control for animal health

The Danish AMR policies have been mainly focused on antimicrobial use and resistance from food-producing animals and Denmark has also been very active in the field of infection prevention and control in the animal health sector for the past 20 years. This is due to their early recognition of the AMR threat and to the importance of the meat-producing industry for Denmark's economy. There has been successful implementation of measures such as Herd Health Contracts with regularly visits by veterinarians, the modernization of animal production facilities and DANMAP, the strong surveillance and monitoring system.

Following an analysis of its previous AMR-related activities the UK government has now decided to emphasize infection and control measures in the *UK Five Year Antimicrobial Resistance Strategy 2013 – 2018*. Several areas of work have been identified to prevent infections in all sectors of human and animal health. Among the objectives are the minimization of disease and a reduction of susceptibility to bacterial disease leading to a decrease of antibiotic consumption in animals. The UK has started working on an improvement in farm management and animal husbandry systems to strengthen health and welfare of food-producing animals. These activities also include the establishment of Farm Health Plans and the implementation of bio-security measures.

12.4 Awareness and Education

Raising awareness and educating both professionals and the general public are essential to achieve progress in the fight against AMR. International health agencies and national governments have started several activities and campaigns in this field. National AMR policies are also increasingly including educational programs for healthcare professionals, farmers and especially families and school-aged children.

12.4.1 Awareness

The Danish government has hosted two high-level EU conferences (in 1998 and during its EU-presidency in 2012) to raise awareness among other member states of the rising AMR threat. These have led to a resolution on a strategy against antibiotic resistance by the European Council and other activities within the member states of the European Union. The European Centre for Disease Control is leading several activities and campaigns especially on its annual European Antibiotic Awareness Day, on November 18, to increase public awareness and to promote sensible use of antimicrobial agents.

Since 2002 the French government and the French National Health Insurance have successfully implemented the national campaign *Antibiotics are not automatic*. The general public and physicians in particular have been targeted using various channels of communication (e.g. pamphlets and posters, print media, television, radio, websites etc.). A scientific evaluation has shown that the campaign has led to a visible reduction of unnecessary antibiotic prescriptions, especially for children. In 2014 the French government extended this campaign to include animal health aspects as well.

Norway has focused its nationwide AMR-campaign on families with small children and has been supporting doctor's and healthcare workers by preparing brochures, posters and other information material for distribution in healthcare facilities. In the US the *Get Smart: Know When Antibiotics Work* campaigns have proved to be successful and an annual, nationwide Get Smart About Antibiotics Week has been held since 2008.

In Thailand the government has been promoting the rational use of antibiotics is the *Antibiotic Smart Use Programme* (ASU) since 2007. This programme has involved multiple interventions aiming at changing prescription practices and maintaining behavior change at the individual level (physicians, patients). The creation of local ownership and mutual recognition has proved to be essential for the success of this program.

In a 2010 systematic review on the characteristics and outcomes of public AMR-related campaigns Huttner et al. came to the conclusion that national awareness campaigns seem to lead to a reduction in antibiotic use, but a direct effect on resistance to antimicrobials couldn't be assessed accurately due to the field's complexity.

12.4.2 Education

Some countries have also included educational programs for healthcare professionals, farmers, families and school-aged children into their AMR strategies and policies in addition to campaigning for national awareness.

In 2010 the Swedish Infectious Diseases Institute presented a communication strategy focusing on physicians, nurses, pharmacists and patients. Educational services and information campaigns have been making use of various channels of communications (e.g. publications of treatment recommendations, leaflets, websites, newsletters and direct mailings, seminars, conferences etc.).

Local Strama groups have also been actively involved in AMR-related training of healthcare professionals continuously communicating data and results to prescribers in order to inform them about developments and to guide them towards the best local interventions.

The UK has been running two educational programs for general practitioners leading to both an improvement in prescribing practices and a reduction of antimicrobial use among the participating physicians. *TARGET* is a web-based toolkit, designed as a resource centre for clinicians, primary care staff and patients, which can be used for one-hour GP practice workshops. *STAR* is a theory-based blended educational program including the presentation of research evidence and guidelines in addition to a practice-based seminar.

Some countries have also developed special AMR-related education programmes focusing on families and school-aged children. An educational program based on the e-Bug project developed by the European Commission has been adapted nationally and successfully implemented by France, the UK, Denmark and several other European countries. This program includes the dissemination of a resource pack, worksheets, a website with games and quizzes designed to educate school-aged children and the general public about hygiene measures and the prudent use of antibiotics.

The US government has developed the web-based educational *Antimicrobial Resistance Learning Site* as part of its *Get Smart: Know When Antibiotics Work on the Farm* campaign, which has been running since 2004.

12.5 Research, Innovation and Development

All the countries included in this study have recognized the need for more research activities. In addition to identifying reasons for AMR, the causal relations between antibiotic usage and AMR, and studying the associated costs and the overall impact on health systems, new diagnostics, antimicrobial drugs and other preventative and treatment options (e.g. vaccines, antivirals) have been undergoing research. Several national and international research projects have been initiated, especially at the European level. WHO has been promoting AMR-related research to strengthen the knowledge and evidence base suggesting new collaborative and financial models and further incentives for the development of rapid diagnostic tests and new medicines.

12.5.1 Academic research and evidence-based approach

The Danish government has been one of the first to base its AMR-related policies on evidence gained from the comprehensive surveillance and monitoring programme, DANMAP, and by working closely with academic research institutions. Collected data has been analyzed and action plans reviewed and revised accordingly. Sweden has been using a similar model, using its nationwide network of local Strama groups to build up a knowledge bank linking community-based data with national research activities and providing prescribers with research results and locally adapted treatment guidelines.

The Norwegian government has developed a national plan for research and development in the fields of infectious diseases in the health services and antibiotic resistance. In addition models to estimate AMR-related costs have been planned improving knowledge about the occurrence, causal relations and effects of measures. The UK has included several research aspects into its 2013 national AMR strategy to improve the understanding of AMR and to be able to better prioritize its AMR-related policies. The Swiss government is also planning the establishment of an interdisciplinary research platform to gain further knowledge and evidence about antibiotic resistance development and transmission. The US government has included several research and development components into its new AMR strategy and announced an investment of more than US$ 650 million into research programs at the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA). In addition the development of rapid diagnostic tests will be given considerable funding.

The *Joint Programming Initiative on Antimicrobial Resistance* is an international group of public and academic institutions aiming at coordinating AMR-related research in Europe to improve outcome and avoid duplication. The European Union has also launched the *Innovative Medicine Initiative* (IMI) together with the European Federation of Pharmaceutical Industries and Associations (EFPIA). IMI, presently Europe's largest public-private initiative, has been established to support collaborative research projects and cooperation between academia and industry. Several IMI projects are targeting AMR-related issues (e.g. development of new antimicrobials or rapid-point-of-care platforms).

12.5.2 Private sector

To improve research, innovation and development in the field of antimicrobial resistance close collaboration between policy makers, research councils, academia and industry is necessary. More and more governments are including these aspects into their national AMR strategies and policies. In 2009 the Swedish EU-Presidency held an expert conference under the theme of *Innovative Incentives for Effective Antibacterials* to explore ways of enhancing the development of new antibiotic substances. The UK has also been emphasizing this aspect by enhancing collaboration between the various stakeholders and by encouraging greater public-private investment in the discovery and development of effective new antimicrobials, rapid point-of-care diagnostics, alternative treatments and complementary instruments for use in health, social care, and veterinary systems.

The US government has decided to invest in the development of new point-of-need diagnostic tests and rapid molecular tests to identify the infecting pathogen and its antibiotic-resistance profile. Further discussions are to be held to advance the developmental process issues related to test development and validation, the review process by the Federal Drug Administration and the reimbursement processes. The US Strategy Plan also recognises the urgent need for new antibiotics and therapeutic approaches as alternatives to antibiotics. Within this context the Biomedical Advanced Research and Development Authority (BARDA) aims to advance innovative research on antibiotic resistance by encouraging the formation of public-private partnerships through research forums and a *biopharmaceutical incubator*. Similarly the Swiss government has been discussing the creation of market

incentives (e.g. for the development of new antibiotics) and the increasing involvement of the private sector in various AMR-related areas of work.

The 2014 World Health Assembly AMR resolution has called for the strengthening of overall pharmaceutical management systems and laboratory infrastructures essentially requiring a closer cooperation with the private sector. Other aspects highlighting this need include drug enhancement (e.g. for shorter treatment durations), the design of new drug combinations (to reduce resistance) and the improvement of packaging and information to increase patient compliance and the correct usage of antimicrobial therapies.

12.6 Collaboration and Coordination

AMR remains a constantly evolving global threat through globalization, travel, trade and other processes, as pathogens don't respect borders. The fight against AMR needs both national and international collaboration and coordination between the great number of stakeholders from various sectors. Therefore national governments are increasingly integrating collaboration and coordination as key aspects of their AMR strategies.

At the global level, WHO has been leading various coordination efforts by setting up action plans, raising awareness and calling governments to develop national AMR strategies. WHO also co-hosted a two-day Ministerial Conference on Antibiotic Resistance in The Hague, Netherlands in 2014, under the theme of *Joining Forces for Future Health*. Ministers and senior officials from more than 20 countries and delegates from key partners (e.g. FAO, OIC, EC, World Bank) called for intensified international political action, strongly supporting the development of the WHO AMR Global Action Plan and many other specific actions, in particular a cross-governmental approach to AMR at the national level. In addition the proposed WHO Global Action Plan on AMR has emphasized the need for a whole-of-society engagement as AMR also impacts sectors beyond human health, such as agriculture, food security and economic development.

12.6.1 International collaboration and coordination

In its *European strategic action plan on antibiotic resistance 2011–2016* the WHO Regional Office for Europe is urging its Member States – among other aspects - to establish means for multisectoral coordination and cooperation. WHO/EURO and the European Commission have been cooperating closely with many regional partners and multilateral organizations, such as FAO, OIE to strengthen international cooperation against the AMR threat. The European Commission and its agencies working on AMR (ECDC, EFSA, EMA) have been supporting the cooperation and coordination between the member states of the European Union in various AMR-related areas of work.

Since 2009 the European Commission has also been working closely with the US, setting up a bilateral cooperation, the Transatlantic Task Force against AMR. The *Global Health Security Agenda*, launched by the US and nearly 30 partner countries in February 2014, is another example of a global coordination mechanism. One of the key objectives is to improve prevention and detection of antimicrobial resistance worldwide.

The *Global Antibiotic Resistance Partnership* (GARP) was started in 2009 as a platform for development of AMR policies in low- and middle-income countries. National, multidisciplinary working groups have been established in India, South Africa, Kenya, Vietnam, Mozambique, Tanzania, Uganda and Nepal. The GARP secretariat is based in Washington, DC and New Delhi and funded by the Bill and Melinda Gates Foundation.

Further best-practice examples of international collaboration in the AMR field are bilateral cooperations e.g. between Sweden and China. Between 2011 and 2013 the *Sino-Swedish Bilateral Cooperation on Management of Antibiotic Resistance* project carried out research and educational programs in various AMR areas (e.g. surveillance, prescribing, education). The Swedish International Development Organization (SIDA) has been supporting Ghana to develop national AMR policies through the NGO ReAct, an independent, multidisciplinary, global network of AMR experts based in Uppsala, Sweden. ReAct has developed into a comprehensive knowledge base, providing strategic policy guidance, raising awareness and promoting best practices.

12.6.2 National collaboration and coordination

Close collaboration and improved coordination at the national level between the many stakeholders involved is essential in the fight against AMR.

Several best practice examples can be observed in Sweden. Although the Public Health Agency of Sweden is now the driving force behind the Swedish strategy, the Strama network has been the basis for Sweden's success in securing its favorable AMR-situation. Swedish AMR-related activities and policies have been characterized by a strong local and national cooperation involving many different actors. These include local infectious-diseases specialists in many county hospitals, who have proved to be of key importance in controlling antibiotic usage and local Strama groups. These groups have been set up as multi-professional teams with representatives from general medicine, inpatient care and other AMR-related areas. In particular the Strama network has been responsible for initiating several different forums for

information exchange between the local and national levels. In addition to the Strama groups the Swedish government established a national *Intersectoral Coordinating Mechanism* in 2012. This is currently headed by the National Board of Health and Welfare and the Swedish Board of Agriculture and consists of 20 governmental agencies.

Figure 8: Strama's relationship with several other actors
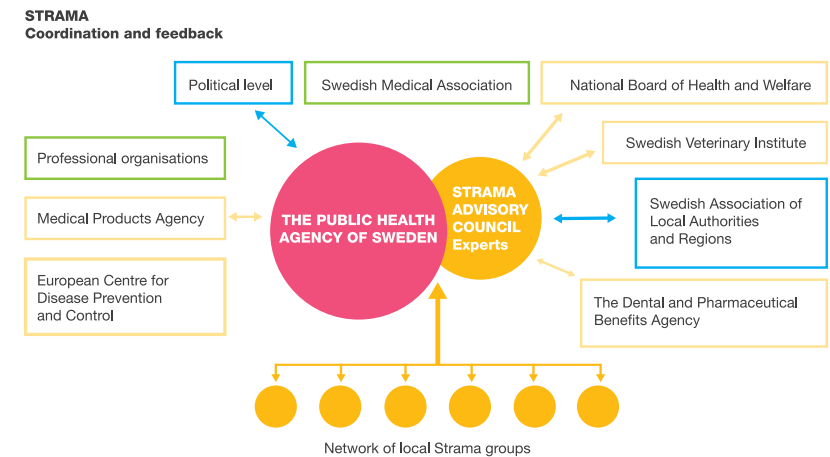
Source: Swedish work on containment of antibiotic resistance 2014

12.6.3 One Health approach

The national AMR strategies and policies included in this study noticeably highlight the need for intersectoral collaboration and coordination, some even claim to be actually using a *One Health* approach. A commonly used definition for this *One Health* approach is *"the collaborative effort of multiple health science professions, together with their related disciplines and institutions – working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants and our environment."*

The analysis of the national AMR strategies and policies has shown that most countries have a strong focus on human health, and that veterinary health is often also integrated in different ways. If just the currently implemented strategies are taken into consideration, only Sweden and Norway clearly include AMR-related environmental aspects into their programs. In Norway the Ministry for Environment has been closely involved in the development of the strategy and efforts to reduce the total environmental impact of antibiotics have been included. These measures include monitoring the biocide regulations, reducing the use of triclosan, an antibacterial that is extremely toxic for aquatic organisms and a strict policy regarding approval of genetically modified organisms containing antibiotic resistance coded genes.

The majority of governments have still not effectively based their national strategies on a *One Health* approach. The proposed strategy of Switzerland would follow this approach more consistently.

12.7 Framework requirements

Combatting antimicrobial resistance is a highly complex issue requiring a great number of different measures. These will only be successful if they are implemented consequently and if there is good coordination with the multiple actors from all sectors. In addition the adaptation of regulatory frameworks and an increase in available financial resources are essential.

12.7.1 Regulatory framework

Many AMR-related measures included in national strategy papers require adaptations of national regulations taking international treaties and regulations into account. This especially applies for member states of the European Union. Some countries, such as the UK, have attempted to organize their national AMR-strategy without creating new regulatory requirements avoiding complicated decision-making processes and ensuring speedy implementation. In contrast other countries have based their national AMR-strategies on new comprehensive regulatory systems: Denmark has several new laws in the field of veterinary medicine and animal husbandry, France has strengthened its fight against AMR through several measures included in the 2010 *Hospitals, Patients, Health and Territory law* (HPST) and the Swiss government has also been preparing a legal framework for its proposed national AMR strategy.

At the international level, the European Commission has adopted several AMR resolutions and has been working actively with its member states and other international bodies, e.g. WHO, OIE or FAO to identify additional solutions against AMR, which could be included within the European Union's regulatory framework. Hoffmann et al. believe that the global fight against AMR can only be successful if WHO's member states agree on a binding international legal framework. Alternatively the UN General Assembly could negotiate an international treaty.

12.7.2 Financial resources

National governments need to mobilize additional financial resources to implement measures to combat AMR at local, national and international levels. The economic burden of AMR and the height of necessary investments still need to be determined.

The London School of Hygiene and Tropical Medicine and the University of Birmingham have carried out an investigation commissioned by the UK Department of Health. In 2012 they came to the conclusion that a definite calculation of the potential economic burden caused by AMR was not possible because there were too many uncertain factors. However the authors did emphasize that AMR would probably have a major economic impact. Further studies (*e.g.in* Norway, the UK and France) are now under way. A 2014 study by a professional services company (KPMG) concludes that rising AMR levels causing increasing morbidity and mortality worldwide will have a great economic impact, especially in low-income countries. In addition the social loss associated with the AMR threat needs to be taken into consideration when discussing further investments in combatting AMR (e.g. investments for the development of antibiotics).

The US government is proposing doubling its current AMR-related funding and is planning to invest US$ 1.2 billion in the fight against AMR. If approved by the US congress this investment would be used for a wide range of AMR-related activities including e.g. surveillance and antibiotic stewardship programs, the development of new antimicrobials and diagnostics and measures to reduce farmyard antibiotic use. Switzerland has been working closely with multiple stakeholders in the development of its AMR strategy. The private sector is being encouraged to increase investment in AMR-related measures, especially in the development of new antimicrobials. The development of a business case for sustainable investment is also one of the strategic objectives proposed by the WHO Global Action Plan.

An alternative and less cost-intensive approach of involving the private sector in the fight against AMR could be the closer involvement of the food industry. US researchers have been urging food companies and fast-food chains such as McDonalds to update their policies on the use of antibiotics in food-producing animals. This could have an immediate and great impact without creating high costs for the taxpayer. Increased involvement of health insurance companies in national AMR strategies and policies and the co-funding of measures chosen would also be beneficial in many ways.

CONCLUSION

Since the late 1990's WHO has warned its member states of the rising global AMR threat, but the majority of countries don't seem to have been taken these warnings seriously enough. Over the last 20 years international health activities have been mainly focused on the globalization process including the development and work on the Millennium Development Goals. In addition, national and international health authorities and organizations have been paying a lot of attention to other fields such as Non-Communicable Diseases, Mental Health or Climate Change and Health.

Meanwhile the situation with regard to AMR has changed and more and more countries have been developing AMR-policies or strategies, partly based on the intervention framework proposed by WHO. The country strategies reviewed in this study all have a strong focus on building surveillance systems, improving infection prevention and control, reducing the usage and promoting a more reasonable use of antimicrobials. A great number of measures have been implemented or are being planned by governments and their institutions at national and local levels. These vary considerably among the countries in this study. This is due to many differing factors involved in the complex field of AMR, e.g. baseline AMR situations, national rules and regulations, health systems, pre-existing AMR policies or the importance of the food producing industry. In addition relations between a single measure and a direct outcome are very difficult to determine due to the complexity of the AMR field.

Despite all these challenges best practice examples could be identified in all of the studied strategies and policies. These could be used as the basis for the development of new or the revision of existing national strategies.

In response to WHO's repeated call for action against the global AMR threat countries should implement national AMR strategies or action plans, accurately based on a One Health approach using evidence-based solutions appropriate for national and local contexts.

ADMER. 2010. ADMER - Antibiotic Drug use, Monitoring and Evaluation of Resistance [Online]. Accra: ADMER c/o University of Ghana Medical School.
Available: *http://www.admerproject.org*].

AMELI. 2015. Présentation de la Cnamts [Online]. Paris: Securite Sociale l'Assurance Maladie.
Available: *http://www.ameli.fr/l-assurance-maladie/connaitre-l-assurance-maladie/missions-et-organisation/l-assurance-maladie/presentation-de-la-cnamts. php* [Accessed 10 January 2015].

BRONZWAER, S., LÖNNROTH, A. & HAIGH, R. 2004. The European Community strategy against antimicrobial resistance.
Euro surveillance: bulletin Europeen sur les maladies transmissibles= European communicable disease bulletin, 9, 30-34.

CDC. 2012. Get Smart - Know when antibiotics work [Online]. Atlanta: US Centers for Disease Control and Prevention.
Available: *http://www.cdc.gov/getsmart/* [Accessed 15 January 2015].

CHAN, M. 2011. Combat drug resistance: no action today means no cure tomorrow. World Health Organization.

DANMAP. 2013a. Danish Programme for surveillance of antimicrobial consumption and resistance in bacteria from animals, food and humans. [Online].
Copenhagen: Statens Serum Institute. Available: *http://www.danmap.org* [Accessed 15 December 2014].

DANMAP 2013b. Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark
Copenhagen: Statens Serum Institute, National Food Institute.

DAVIES, S. 2011. Annual Report of the Chief Medical Officer - Infections and the rise of antimicrobial resistance. London: Chief Medical Officer.

DTU 2012a. Data for Action. 2 ed. Copenhagen: Technical University of Denmark.

DTU. 2012b. Denmark is at the forefront in the fight against resistance [Online]. Copenhagen: National Food Institute.
Available: *http://www.food.dtu.dk/english/News/2012/03/Denmark_at_the_forefront_in_the_fight_against_resistance* [Accessed 15 December 2014].

DUSE, A. G. 2011. The Global Antibiotic Resistance Partnership (GARP). SAMJ: South African Medical Journal, 101, 551-551.

EC 1999. Council Resolution on antibiotic resistance: a strategy against the microbial threat Official Journal C 195 of 13.07.1999 ed. Brussels: European Council.

EC 2011. Action plan against the rising threats from Antimicrobial Resistance. Brussels: European Commission, DG Health and Consumers.

EC. 2014. Action Plan Against the rising threats from Antimicrobial Resistance:Road Map [Online]. Brussels: European Commission.
Available: *http://ec.europa.eu/health/antimicrobial_resistance/docs/roadmap_amr_en.pdf*%5D.

EC 2015. Progress report on the Action plan against the rising threats from Antimicrobial Resistance. Brussels: European Commission.

ECDC. 2008. European Antibiotic Awareness Day [Online]. Stockholm: European Center for Disease Control.
Available: *http://www.ecdc.europa.eu/en/eaad/Pages/Home.aspx* [Accessed December 21 2014].

ECDC. 2011. European Surveillance of Antimicrobial Consumption Network [Online]. Stockholm: European Centre for Disease Prevention and Control.
Available: *http://ecdc.europa.eu/en/activities/surveillance/ESAC-Net/Pages/index.aspx* [Accessed 29 December 2014].

ECDC 2012. Antimicrobial resistance surveillance in Europe In: EARS-NET (ed.). Stockholm: European Center for Disease Control.

ECDC. 2015a. Antimicrobial resistance interactive database EARS-NET [Online]. Stockholm: European Centre for Disease Prevention and Control.
Available: *http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/table_reports.aspx* [Accessed 10 January 2015].

ECDC. 2015b. Trend of antimicrobial consumption by country [Online]. Stockholm: European Centre for Disease Prevention and Control.
Available: *http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/trend-consumption-by-country.aspx*
[Accessed 10 January 2015].

EFSA. 2014. About EFSA [Online]. European Food Safety Authority. Available: *http://www.efsa.europa.eu* [Accessed 10 December 2014].

EMA. 2014. European Surveillance of Veterinary Antimicrobial Consumption [Online]. Brussels: European Medicines Agency.
Available: *http://www.ema.europa.eu/ema/index.jsp?curl=pages*/regulation/document_listing/*document_listing_000302.jsp* [Accessed 10 December 2014].

ESVAC 2012. Sales of veterinary antimicrobial agents in 26 EU/EEA countries in 2012. Brussels: European Medicines Agency.

EU_COUNCIL 2012. Council conclusions on the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective. Luxembourg: Council of the European Union.

FAO, O. 2010. The FAO--OIE--WHO Collaboration: Sharing responsibilities and coordinating global activities to address health risks at the anima--human--ecosystems interfaces: A Tripartite Concept Note. O. FAO, WHO, Rome, Paris, Geneva.

FAO/OIE/WHO 2010. The FAO-OIE-WHO Collaboration - A Tripartite Concept Note. Rome.

FNSNF 2006. National Research Programme NRP 49 Antibiotic Resistance. Bern: Swiss National Science Foundation.

GHNDP. 2013. Ghana AMR Project [Online]. Accra: GNDP / ReACT.
Available: *http://ghndp.org/antimicrobialresistance/index.php?start=4* [Accessed 10 January 2015].

GIBBS, E. P. J. 2014. The evolution of One Health: a decade of progress and challenges for the future. Veterinary Record, 174, 85-91.

GOV CH 2013. ARCH-Vet - Report on sales of antibiotics in veterinary medicine and antibiotic resistance monitoring of livestock Bern: Federal Food Safety and Veterinary Office.

GOV CH 2014a. Revision of the Epidemics Act (EpG). Bern: Federal Office of Public Health.

GOV CH 2014b. Swiss Antibiotic Resistance Strategy - DRAFT. Bern: Swiss Ministries.

GOV CH. 2015. STAR Swiss Antibiotic Resistance Strategy [Online]. Bern: Federal Office of Public Health.
Available: *http://www.bag.admin.ch/themen/medizin/14226/index.html?lang=de* [Accessed 18 January 2015].

GOV DK 2007. Risk management of antimicrobial use and resistance from food-producing animals in Denmark. Copenhagen: National Veterinary Institute, National Food Institute.

GOV DK. 2011. Denmark takes the lead in combaring antimicrobial resistance [Online]. Copenhagen.
Available: *http://www.sum.dk/Aktuelt/Nyheder%20English/Health/2011/Maj/Denmark-takes-the-lead-in-combating-antimicrobial-resistance.aspx*
[Accessed 15 December 2014].

GOV DK 2012. Combating Antimicrobial Resistance – Time for Joint Action. Copenhagen: Ministry of Health.

GOV FRA 2011a. 2011-2016 National Antibiotic Plan. Paris: Ministry of Health and Social Affairs.

GOV FRA 2011b. Plan national d'alerte sur les antibiotiques 2011-2016 Paris: Ministry of Health and Social Affairs.

GOV FRA. 2014. Les antibiotiques pour nous non plus c'est pas automatique! [Online]. Paris: Ministry of Agriculture.
Available: *http://agriculture.gouv.fr/ecoantibio-les-antibiotiques-pour-nous-non-plus-cest-pas-automatique* [Accessed 2 Janurary 2015].

GOV GER 2008a. DART - German antimicrobial resistance strategy. Berlin: Federal Ministry of Health.

GOV GER 2008b. GERMAP 2008. Berlin: Federal Office of Consumer Protection and Food Safety.

GOV GER 2011. DART Deutsche Antibiotika-Resistenzstrategie - Zwischenbericht. Berlin: Federal Ministry of Health.

GOV GER 2012. GERMAP 2012. Berlin: Federal Office of Consumer Protection and Food Safety.

GOV GER 2013. DART Deutsche Antibiotika-Resistenzstrategie - ENTWURF. Berlin: Federal Ministry of Health.

GOV GER 2015. GERM-VET Resistenzmonitoringstudie 2011/2012. Berlin: Federal Office of Consumer Protection and Food Safety.

GOV IND 2011. National Policy for containment of antimicrobial resistance
In: Ministry of Health and Family Welfare (ed.). New Delhi: Directorate General of Health Services.

GOV NOR 2000. Tiltaksplan for a motvirke antibiotikaresistens 2000-2004. Oslo: Ministry of Health.

GOV NOR 2004. Handlingsplan for a forebygge sykehusinfeksjoner 2004-2006. Oslo: Ministry of Health.

GOV NOR 2008. National Strategy for prevention of infections in the health service and antibiotic resistance 2008-2012 Oslo: Norwegian Ministries.

GOV SA 2014a. Antimicrobial Resistance Background Report. Pretoria: Department of Health.

GOV SA 2014b. Antimicrobial Resistance National Strategy Framework. Pretoria: Department of Health.

GOV SA 2014c. Antimicrobial Resistance National Strategy Framework Commitments. Pretoria: Department of Health.

GOV THA 2011. Antimicrobial resistance control in Thailand. In: Suriya Wongkongkathep (ed.). Oslo: Thailand Ministry of Public Health

GOV USA 2014. National Strategy For Combating Antibiotic-Resistant Bacteria. Washington DC: The White House.

GOV USA. 2015. FACT SHEET: President's 2016 Budget Proposes Historic Investment to Combat Antibiotic-Resistant Bacteria to Protect Public Health [Online]. Washington DC: The White House.
Available: *https://www.whitehouse.gov/the-press-office/2015/01/27/fact-sheet-president-s-2016-budget-proposes-historic-investment-combat-a* [Accessed 10 February 2015].

HAS 2008. Antibiotic therapy and prevention of bacterial resistance in healthcare organisations - Guidelines. Paris: Haute Autorité de Santé.

HHS 2013a. Antibiotic resistance threats in the United States, 2013. Atlanta: CDC. US Department of Health Human Services.

HHS 2013b. Guidance for Industry #213. Washington DC: Food and Drug Administration.

HHS. 2014. The Global Health Security Agenda [Online]. Washington DC: US Departmen of Health and Human Services.
Available: *http://www.globalhealth.gov/global-health-topics/global-health-security/ghsagenda.html* [Accessed 10 January 2015].

HOLMES, A. & SHARLAND, M. 2013. The Chennai Declaration: India's landmark national commitment to antibiotic stewardship demonstrates that 'truth alone triumphs'. Journal of Antimicrobial Chemotherapy, 68, 1453-1454.

KIATYING-ANGSULEE, N. 2011. Experiences from Thailand [Online]. Bangkok: ReAct.
Available: *http://www.reactgroup.org/uploads/publications/presentations/Thai-process-2011.pdf* [Accessed 10 January 2015].

LEUNG, E., WEIL, D. E., RAVIGLIONE, M. & NAKATANI, H. 2011. The WHO policy package to combat antimicrobial resistance.
Bulletin of the World Health Organization, 89, 390-392.

MG. 2007. Antibiotiques: nouvelle campagne [Online]. Paris: La Mutuelle Generale.
Available: *http://www.lamutuellegenerale.fr/qui-sommes-nous/actualites/antibiotiques-nouvelle-campagne.html* [Accessed 2 January 2015].

NCDC. 2010. Role of NCDC in containment of Antimicrobial resistance (AMR) [Online]. New Delhi: National Centre for Disease Control. Available: *http://www.ncdc.gov.in/index3.asp?sslid=526&subsublinkid=309* [Accessed 10 January 2015].

NETHERLANDS 2014. Outcome Statement, The Hague ministerial meeting "Joining Forces for Future Health". The Hague: Government of the Netherlands.

NIFCD. 2013. GERMS South Africa [Online]. Johannesburg: National Institute for Communicable Diseases. Available: *http://www.nicd.ac.za/?page=germs-sa&id=97* [Accessed 31 December 2014].

NIPH. 2014a. Commitments to the responsible use of antimicrobials [Online]. Oslo: Norwegian Institute of Public Health. Available: *http://www.fhi.no/artikler/?id=112149* [Accessed December 20 2014].

NIPH. 2014b. NORM NORM-VET 2013 Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway. Tromso/Oslo: University Hospital Northern Norway, Norwegian Veterinary Institute, Norwegian Institute for Public Health.

NIPH. 2014c. Norwegian surveillance programme for antimicrobial resistance [Online]. Oslo: Norwegian Institute for Public Health. Available: *http://www.fhi.no/eway/default.aspx?pid=240&trg=MainContent_6894&Main_6664=6894:0:25,7555:1:0:0:::0:0&MainContent_6894=6706:0:25,9003:1:0:0:::0:0* [Accessed 29 December 2014].

NORRBY, R., POWELL, M., ARONSSON, B., MONNET, D., LUTSAR, I., BOCSAN, I., CARS, O., GIAMARELLOU, H. & GYSSENS, I. 2009. The bacterial challenge: time to react. ECDC. EMEA Joint Technical Report, Stockholm: European Centre for Disease Prevention and Control, 2009. Available: *http://www.ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf*.

NVI. 2014. Antimicrobial Resistance (NORM-VET) [Online]. Oslo: Norwegian Veterinary Institute. Available: *http://www.vetinst.no/eng/Surveillance-programmes/Antimicrobial-*resistance-NORM-VET [Accessed 29 December 2014].

O'NEILL 2014. The Review on Antimicrobial Resistance. London: Chatham House.

PCAST 2014. Report to the president on combating antibiotic resistance In: President's Council of Advisors on Science and Technology (ed.). Washington DC: The White House.

PHAS 2013. SVEDRES/SVARM - Use of antimicorbials and occurence of antimicrobial resistance in Sweden.
In: Public Health Agency of Sweden / National Veterinary Institute (ed.). Stockholm.

PHAS. 2014. Surveillance of Antimicrobial Resistance for Local and Global Action [Online]. Stockholm: Public Health Agency of Sweden.
Available: *http://www.folkhalsomyndigheten.se/documents/projektwebbar/sar/surveillance-antimicrobial-programme.pdf* [Accessed December 20 2014].

PHE. 2014a. Antibiotic Guardian - UK support for European Antibiotic Awareness Day [Online]. Public Health England.
Available: *http://antibioticguardian.com* [Accessed 5 January 2015].

PHE 2014b. English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) - Report 2014. London: Public Health England.
RCGP. 2009. TARGET [Online]. London: Royal College of General Practioners.
Available: *http://www.rcgp.org.uk/TARGETantibiotics/* [Accessed 10 December 2014].

REACT. 2014. ReAct - Action of Antibiotic Resistance [Online]. Uppsala.
Available: *http://www.reactgroup.org/who-we-are.html* [Accessed 12 December 2014].

RKI. 2014. ARS - Antibiotika Resistenz Surveillance [Online]. Berlin.
Available: *https://ars.rki.de/History.aspx* [Accessed 20 December 2014].

ROSDAHL V, P. K. 1998. The Microbial Threat - the Copenhagen Recommendations. Copenhagen: Statens Serum Institute.

SABUNCU, E., DAVID, J., BERNÈDE-BAUDUIN, C., PÉPIN, S., LEROY, M., BOËLLE, P.-Y., WATIER, L. & GUILLEMOT, D. 2009.
Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002–2007. PLoS medicine, 6, e1000084.

SEARO 2010. Regional Strategy on Prevention and Containment of Antimicrobial Resistance 2010-2015. WHO Regional Office for South-East-Asia.

SEARO 2011. Jaipur Declaration on Antimicrobial Resistance. WHO, Regional Office for South-East-Asia.

SSI. 2014. Skal mit barn ha' antibiotika? [Online]. Copenhagen: Statens Serum Insitute.
Available: *http://www.antibiotikaellerej.dk/Kampagner/Skal%20mit%20barn%20have%20antibiotika.aspx* [Accessed 15 December 2014].

STÄRK, K. 2013. Brief overview of strategies to reduce antimicrobial usage in pig production. Brussels: EIP-AGRI

STRAMA. 2010. Strama - Collaboration against antibiotic resistance [Online]. Stockholm.
Available: *http://en.strama.se/dyn//,85,3,1.html* [Accessed 10 December 2014].

STRAMA. 2013. Do you get better more quickly if you take antibiotics? [Online]. Stockholm:
Strama Stockholm and Swedisch Association of Local Authorities and Regions.
Available: *http://www.antibiotikaellerinte.se/eng/index.html* [Accessed 12 December 2014].

SUMPRADIT, N. 2012. Antibiotics Smart Use: a workable model for promoting the rational use of medicines in Thailand.
Bulletin of the World Health Organization, 90, 905-913.

SWE GOV 2000. Swedish Plan for Action against Antibiotic Resistance. In: National Board of Health and Welfare (ed.). Stockholm.

SWE GOV. 2005. Bill Strategy for coordinated efforts to prevent antibiotic resistance and healthcare-associated infections [Online]. Stockholm.
Available: *http://www.government.se/sb/d/15473/nocache/true/a/183498/dictionary/true* [Accessed 12 December 2014].

SWE GOV 2006. Strategy to prevent antibiotic resistance and healthcare-associated infections. In: Ministry of Health and Social Affairs (ed.). Stockholm.

SWE GOV 2009. Innovative Incentives for Effective Antibacterials. In: Ministry for Health and Social Affairs (ed.). Stockholm.

SWE GOV 2014. Swedish work on the containment of antibiotic resistance. In: Public Health Agency of Sweden (ed.). Stockholm: Government of Sweden.

SWP 2012. One-Health-Ansatz für eine kohärente Antibiotika-Strategie in der Human- und Veterinärmedizin. Bern: Swiss Parliament.

TATFAR 2011. Recommendations for future collaboration between the US and EU. Brussels / Washington DC: Transatlantic Taskforce on Antimicrobial Resistance.

THAMLIKITKUL, V. 2014. AMR Containment & Prevention in Thailand [Online]. Geneva: Graduate Institute
Available: *http://graduateinstitute.ch/files/live/sites/iheid/files/sites/globalhealth/ghp-new/Events%202014/21%20March/Chatham%20House%20March%20 2014%20FINAL_Visanu%20Thamlikitkul_V2.pdf* [Accessed 10 January 2015].

UK GOV 2000. UK Antimicrobial Resistance Strategy and Action Plan. London: Department of Health.

UK GOV 2011. Antimicrobial stewardship: Start smart - then focus. London: Department of Health.

UK GOV 2013a. Antimicrobial Resistance Strategy - Impact Assessment. London: Department of Health.

UK GOV 2013b. UK 5 Year Antimicrobial Resistance Strategy 2013-2018 - Measuring Success. London: UK Government.

UK GOV 2013c. UK Five Year Antimicrobial Resistance Strategy 2013 to 2018. London:
Department of Health, Department for Environment, Food and Rural Affairs.

UK GOV 2013d. UK Veterinary Antibiotic Resistance and Sales Surveillance. In: Veterinary Medicines Directorate (ed.) UK_VARSS. London.

UK GOV 2014a. Antimicrobial Resistance - Empirical and Statistical Evidence-Base. London: Department of Health AMR Strategy Analytical Working Group.

UK GOV 2014b. Progress Report on the UK 5 year AMR strategy - 2014. In: Department of Health (ed.). London: UK Government.

UK GOV 2015. Start Smart - Then Focus, Antimicrobial Stewardship Toolkit for English Hospitals. London: Public Health England.

UK MRC. 2005. STAR Educational Program [Online]. UK Medical Research Council.
Available: *http://www.stemmingthetide.org* [Accessed 10 December 2014].

UOB. 2015. ANRESIS - Swiss Centre for Antibiotic resistance [Online]. Bern: University of Bern.
Available: *http://anresis.ch/index.php/indexen.html* [Accessed 18 January 2015].

WHO 1998. Emerging and other communicable diseases: antimicrobial resistance. World Health Assembly

WHO 2001. WHO global strategy for containment of antimicrobial resistance.

WHO 2002. Impacts of antimicrobial growth promoter termination in Denmark. Foulum: World Health Organization.

WHO 2008. International Health Regulations (2005), World Health Organization.

WHO 2012. The evolving threat of antimicrobial resistance: options for action. 2012.
Available at: http://www.who.int/patientsafety/implementation/amr/publication/en/ (date last accessed: 1st October 2012).

WHO 2013a. Antimicrobial drug resistance. In: Executive Board (ed.). Geneva: Secretariat.

WHO. 2013b. Strategic and Technical Advisory Group (STAG) on antimicrobial resistance [Online]. Geneva: WHO.
Available: *http://www.who.int/drugresistance/stag/en/* [Accessed December 12 2014].

WHO 2014a. Antimicrobial Resistance - Resolution. In: WHA (ed.). Geneva: WHO.

WHO 2014b. Antimicrobial resistance: global report on surveillance, World Health Organization.

WHO 2014c. Combating antimicrobial resistance, including antibiotic resistance. Geneva: Executive Board.

WHO 2014d. Draft global action plan on antimicrobial resistance. Geneva: WHO.

WHO. 2014e. Ministerial Conference on Antibiotic Resistance - Joining Forces for Future Health [Online]. The Hague / Geneva: World Health Organization. Available: *http://www.who.int/drugresistance/netherlands_meeting_june_2014/en/* [Accessed 10 December 2014].

WHO/EURO 2010. European Strategic Action Plan on Antibiotic Resistance 2011-2016. In: Health Security and Environment (ed.). Copenhagen: WHO, Regional Office for Europe.

WHO

- Drug resistance: *http://www.who.int/drugresistance/en/*
- Global report on surveillance: *http://www.who.int/drugresistance/documents/surveillancereport/en*
- Draft global action plan on AMR: *http://www.who.int/drugresistance/global_action_plan/en/*
- World Health Day 2011 – Policy Package: *http://www.who.int/world-health-day/2011/presskit/WHDIntrototobriefs.pdf?ua=1*
- Commitments to Responsible Use of Antimicrobials in Humans (Oslo 2014): *http://www.who.int/drugresistance/activities/Oslomeeting/en/*
- Surveillance of antimicrobial resistance for local and global action (Stockholm 2014): *http://www.who.int/drugresistance/activities/SwedenMeeting/en/*

European Union

- Communication from the Commission on a Community Strategy against antimicrobial resistance:
  http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1418244911859&uri=CELEX:52001DC0333
- Action plan against the rising threats from Antimicrobial Resistance:
  http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf
- European Antibiotic Awareness Day: *http://ecdc.europa.eu/en/EAAD/Pages/Home.aspx*

One Health

- One Health Commission: *https://www.onehealthcommission.org/en/why_one_health/*
- The Evolution of One Health: *http://veterinaryrecord.bmj.com/content/174/4/85.full*
- FAO and Tripartite AMR activities: *http://ec.europa.eu/health/antimicrobial_resistance/docs/ev_20131211_co19_en.pdf*
- The FAO-OIE-WHO Collaboration: *http://www.who.int/influenza/resources/documents/tripartite_concept_note_hanoi_042011_en.pdf*

Denmark

- Risk management of antimicrobial use and resistance from food-producing animals in Denmark:
  http://www.foedevarestyrelsen.dk/english/SiteCollectionDocuments/25_PDF_word_filer%20til%20download/05kontor/Risk_management_ antimicrobia_%20use_and%20resistance_Denmark_E.pdf
- DANMAP: *http://www.danmap.org*
- Combating Antimicrobial Resistance (Copenhagen 2012): *http://en.fvm.dk/fileadmin/user_upload/ENGLISH_FVM.DK/Themes/Antimicrobial_Resistance/ Godkendt_konferencerapport__med_sidetal_ekstra_fodnote_.pdf*

France

- Plan national d'alerte sur les antibiotiques 2011-2016:
  http://www.sante.gouv.fr/des-politiques-publiques-pour-preserver-l-efficacite-des-antibiotiques.html#plan
- "Antibiotics Are Not Automatic Anymore"—The French National Campaign To Cut Antibiotic Overuse:
  http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000080
- Guidelines - Antibiotic therapy and prevention of bacterial resistance in healthcare organisations:
  http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-03/antibiotic_therapy_and_prevention_of_bacterial_resistance_-_guidelines.pdf

Germany

- DART 2008: German Antimicrobial Resistance Strategy:
  http://www.bmg.bund.de/fileadmin/dateien/Publikationen/Gesundheit/Sonstiges/DART_-_German_Antimicrobial_Resistance_Strategy.pdf
- DART - Deutsche Antibiotika-Resistenzstrategie - Zwischenbericht
- *http://www.bmg.bund.de/fileadmin/dateien/Downloads/A/Antibiotikaresistenzstrategie/DART_Zwischenbericht_110407.pdf*
- Draft DART 2013: German Antimicrobial Resistance Strategy:
  http://www.bmg.bund.de/fileadmin/dateien/Downloads/A/Antibiotikaresistenzstrategie/111113_DART_Entwurf_Druck.pdf

Norway

- National Strategy for prevention of infections in the health service and antibiotic resistance 2008-2012: *https://www.regjeringen.no/globalassets/upload/hod/dokumenter-fha/nasjonal-strategi-infeksjoner-antibiotikaresistens-engelskversjon.pdf*
- NORM / NORM-VET Report: *http://www.vetinst.no/eng/Publications/NORM-NORM-VET-Report*
- Antibiotic resistance in Norway - Public Health Report 2014: *http://www.fhi.no/eway/default.aspx?pid=240&trg=MainContent_6898&Main_6664=6898:0: 25,9069:1:0:0:::0:0&MainContent_6898=6706:0:25,9070:1:0:0:::0:0*

Sweden

- Strategy to prevent antibiotic resistance and healthcare-associated infections: *http://soapimg.icecube.snowfall.se/strama/Prop%20Engelsk.pdf*
- STRAMA: *http://en.strama.se/dyn/,84,,.html*
- Swedish work on containment of antibiotic resistance: *http://www.folkhalsomyndigheten.se/pagefiles/17351/Swedish-work-on-containment-of-antibiotic-resistance.pdf*
- ReAct - Action on Antibiotic Resistance: *http://www.reactgroup.org*

Switzerland

- StAR: Strategie gegen Antibiotikaresistenzen – Entwurf: *http://www.bag.admin.ch/themen/medizin/14226/index.html?lang=de*
- Anresis - Schweizerisches Zentrum für Antibiotikaresistenzen: *http://www.anresis.ch*
- National Research Programme NRP 49 Antibiotic Resistance: *http://www.snf.ch/SiteCollectionDocuments/NFP49_finalreport.pdf*

United Kingdom

- UK AMR Strategy and Action Plan 2000:

  http://antibiotic-action.com/wp-content/uploads/2011/07/DH-UK-antimicrobial-resistance-strategy-and-action-plan.pdf

- UK Five Year Antimicrobial Resistance Strategy 2013 to 2018:

  https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

- UK Five Year Antimicrobial Resistance Strategy 2013 to 2018: - Progress report:

  https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/322358/Outcome_measures.pdf

USA

- National Strategy for combating antibiotic resistant bacteria: *https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf*

- Transatlantic Taskforce on Antimicrobial Resistance (TATFAR): *http://www.cdc.gov/drugresistance/tatfar/index.html*

- Global Health Security Agenda: GHSA Antimicrobial Resistance Action Package:

  http://www.cdc.gov/globalhealth/security/actionpackages/antimicrobial_resistance.htm

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