



## **MISSION** REPORT

# ECDC country visit to Italy to discuss antimicrobial resistance issues

9-13 January 2017

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This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Alessandro Cassini, Expert, Antimicrobial Resistance and Healthcare-associated Infections.

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This report was sent for comment to the Ministry of Health, Directorate General of Health Prevention, Italy.

#### *Acknowledgements*

The ECDC team would like to thank the Ministry of Health, Italy for the invitation to make a country visit. We would also like to thank Stefania Iannazzo, Infectious Diseases and International Prophylaxis Unit, Ministry of Health, for arranging and coordinating the visit; Fortunato D'Ancona (National Public Health Institute and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance) and Bruno Sarnelli (General Directorate for Health and Coordination of the Regional Health Service, Campania Region) for organising and coordinating the meetings in Campania Region; Annalisa Pantosti (National Public Health Institute, National Focal Point for Antimicrobial Resistance) and Maria Luisa Moro (Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-Associated Infections) for organising and coordinating the meetings in Emilia-Romagna Region.

Suggested citation: European Centre for Disease Prevention and Control. ECDC country visit to Italy to discuss antimicrobial resistance issues. Stockholm: ECDC; 2017.

Stockholm, December 2017

ISBN 978-92-9498-164-6

doi 10.2900/23589

TQ-05-17-227-EN-N

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# Abbreviations

AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
CRE	carbapenem-resistant <i>Enterobacteriaceae</i>
DDD	defined daily dose
EAAD	European Antibiotic Awareness Day
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EuSCAPE	European Survey on Carbapenamase-Producing <i>Enterobacteriaceae</i>
FTE	full time employee
GP	general practitioner
HAI	healthcare-associated infections
ICUs	Intensive care units
ICM	Intersectoral coordinating mechanism
ICN	infection control nurse
IPC	infection prevention and control
MDRO	multidrug-resistant microorganism
MIC	Minimum inhibitory concentration
MRSA	meticillin-resistant <i>Staphylococcus aureus</i>
OTC	Over the Counter
PPS	point prevalence survey
TB	tuberculosis
WHO	World Health Organization

# Executive summary

## Rationale and purpose of the country visit

A Council Recommendation dated 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat that AMR poses to human health and advocates a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) dated 10 June 2008 reiterate this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for country visits, which are carried out at the invitation of national authorities. **These visits are designed to specifically discuss and assess the situation in the country regarding prevention and control of AMR through prudent use of antibiotics and infection control.** The visits also help document how Member States have approached implementation of the Council Recommendation and deployed national resources in order to support the European Commission in evaluating implementation.

The main output of the visit is a report from ECDC provided to the national authority. To help ECDC ensure the consistency of the visits and follow up on progress, an assessment tool has been developed. The assessment tool includes ten topics which are regarded as the core areas for successful prevention and control of AMR, based on Council Recommendation 2002/77/EC and the Council Conclusions dated 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

## Conclusions

**Observations from this ECDC country visit confirm that the AMR situation in Italian hospitals and regions poses a major public health threat to the country.** The levels of carbapenem-resistant *Enterobacteriaceae* (CRE) and *Acinetobacter baumannii* have now reached hyper-endemic levels and, together with methicillin-resistant *Staphylococcus aureus* (MRSA), this situation causes Italy to be one of the Member States with the highest level of resistance in Europe.

During conversations in Italy, ECDC often gained the impression that these high levels of AMR appear to be accepted by stakeholders throughout the healthcare system, as if they were an unavoidable state of affairs.

The factors that contribute negatively to this situation seem to be:

- Little sense of urgency about the current AMR situation from most stakeholders and a tendency by many stakeholders to avoid taking charge of the problem;
- Lack of institutional support at national, regional and local level;
- Lack of professional leadership at each level;
- Lack of accountability at each level;
- Lack of coordination of the activities between and within levels.

If the current trends of carbapenem resistance and colistin resistance in gram-negative bacteria such as *Klebsiella pneumoniae* and *A. baumannii* are not reversed, key medical interventions will be compromised in the near future. Untreatable infections following organ transplantation, intensive care or major surgical interventions are now a significant possibility in many Italian hospitals.

ECDC believes that the first step towards halting and reversing the current multidrug-resistant microorganism (MDRO) situation is to strengthen the current systems and introduce appropriate measures to reduce unnecessary antibiotic use (in communities and hospitals) while improving infection control.

Such corrective actions need to be taken at the following levels: national, regional and local (hospital).

There needs to be a greater sense of urgency regarding the current AMR situation at all levels and among all stakeholders in the country. This also includes the need to establish clear definitions of the responsibility of each stakeholder. During all the meetings held as part of the visit, ECDC were impressed by the enthusiasm and dedication of the many professionals who can contribute to this effort. These people represent an asset to the country and an opportunity to address or even reverse the current AMR situation.

**AMR is a national and cross-regional challenge, especially because the movement of patients (and resistant bacteria) is not restricted by regional borders. Therefore there is a significant risk that, with a regional framework such as that in Italy, it may not be possible to achieve cohesive and standardised action nationwide when dealing with a threat such as AMR.** For this reason, a comprehensive coordinated response is required that ensures central coordination, supervision and auditing of the progress being made in the regions, especially those with higher prevalence.

It is vital that the examples of good practice that we observed during our visit in some regions/hospitals across the country are extended to all the other areas, especially those with the highest levels of AMR. ECDC believes that this will not be possible without strong and coordinated activities at central level, which will result in concrete actions at regional and local level.

## Recommendations

Based on these observations, ECDC's team recommends the following actions:

**Designate AMR as a national public health threat.** The Ministry of Health should formally designate AMR as a national public health threat that affecting all regions. This state of affairs requires prioritisation of resource allocation and short/long term planning.

**National Action Plan.** The National Action Plan offers an opportunity to design an effective roadmap to achieve these goals. It should be finalised and strengthened as a matter of urgency by including actions, indicators and targets, with measurable outcomes and much shorter deadlines for its operational implementation.

**Learn lessons from the recent national vaccination initiative.** In the same manner, key performance indicators and targets for AMR should be identified and incorporated into the minimum levels of assistance.

**Estimate costs for activities at both national and regional level** to make available the appropriate budgets.

The regions with the greatest AMR challenges also tend to be those subjected to the repayment plan. Despite the financial situation, investment into antibiotic stewardship and infection prevention and control has been proven to be cost-effective and will (relatively quickly) result in savings that exceed the amount invested. Financial deficits should not therefore be a barrier to implementation of the National Action Plan and its activities.

**Intersectoral Coordinating Mechanism.** The Intersectoral Coordinating Mechanism under the Ministry of Health should have a clear mandate that goes beyond completion of the National Action Plan, and receive financial support for its activities.

**Appointment of regional AMR specialists.** Each region should formally appoint an expert with specialist knowledge of AMR control and clear terms of reference responsible for initiating and coordinating the necessary AMR prevention and control activities. These trained specialists should meet quarterly in an inter-regional assembly to share good practices and support one another.

**Central supervision.** The heterogeneity of the regional system requires a level of supervision coordinated at a central level. This could take the form of a team of auditors or peer-reviewers who would regularly visit the regions to assess and check that activities are implemented at regional level according to the National Action Plan.

**Milestones linked to financial incentives.** The achievement of agreed milestones should be linked to financial incentives in order to acknowledge progress and motivate further improvement. Achievement of milestones should be publicised to retain focus and initiative.

At central level, these initiatives are sufficiently significant to justify setting up an adequately resourced team within the Ministry of Health dedicated solely to tackling AMR. This will allow a consistent and uninterrupted level of activity as well as the development of an effective system that provides guidance and audits progress in the regions. The team would also coordinate national and regional public awareness campaigns.

**Improve central collection of surveillance data.** The surveillance data on AMR and antimicrobial use that is collected centrally needs to be improved. This can be done by improving the geographical representativeness and timeliness of the MICRONET system. In addition, notification of new cases of CRE and MRSA bacteraemia should become mandatory and be undertaken through a simple online reporting system that automatically transmits the information in real time both to the regional and central coordinating entities.

**Tackle unaccredited microbiology laboratories.** The substantial number of unaccredited microbiology laboratories should be tackled by introducing a programme of minimal accreditation criteria for laboratories that perform analysis of microbiological samples. This intervention would ensure quality results and maximise the effectiveness of the subsequent antibiotic treatments.

**Agree minimal structural indicators** for effective infection prevention and control and antimicrobial stewardship at hospital level, linked to bed occupancy and type of care provided. This will ensure that the necessary staff are involved at local level. Clear job descriptions and responsibilities should be included.

**Increase the number of hospital professionals specialising in infection prevention and control and antimicrobial stewardship and the resources for training them.**

**Publish national guidelines on the use of antibiotics.** Italy would benefit greatly from developing and publishing national guidelines with general principles on the use of antimicrobial agents in human medicine.

**Check the appropriateness of antibiotics dispensed at pharmacies.** In all regions of the country the appropriateness of the antibiotics dispensed at community pharmacies should be checked to establish whether and to what extent antibiotics are being sold over-the-counter without medical prescriptions.

**Organise a national antibiotics awareness campaign.** Given the Italian population's low level of awareness concerning antibiotics and AMR, Italy would also benefit greatly from the organisation of a national antibiotic awareness campaign on the prudent use of antibiotics. In addition, national communication strategies on the prudent use of antibiotics would benefit from a higher level of cooperation in the regions.

# 1. Background

## 1.1 Rationale for country visits to discuss antimicrobial resistance (AMR) issues

After the introduction of antibiotics in the 1940s, it soon became clear that antibiotic usage promoted the rise of antibiotic-resistant bacterial strains in common bacteria such as *Staphylococcus aureus* and *Mycobacterium tuberculosis* (TB). In the decades which followed, the increasing number of antibiotic-resistant strains could be managed thanks to the continuous availability of new antibiotics providing new means of treating patients infected with resistant bacteria. However, from the 1990s onwards, development of new antibiotics decreased and at the same time, the emergence of bacteria resistant to multiple antibiotics became an ever-increasing problem in clinical medicine. Treatment guidelines had to be rewritten and the need to take bacteriological samples for antibiotic susceptibility testing became essential.

Once a resistant bacterium has developed, it will spread from a colonised person to another person if appropriate hygienic precautions (e.g. hand hygiene, isolation) are not taken. The risk of resistant bacteria spreading is higher in crowded environments and even greater when people in the surrounding area are receiving antibiotics - a common situation in hospitals and other healthcare facilities.

Today, bacteria that are totally (or almost totally) resistant to antibiotics (i.e. untreatable with antibiotics) are spreading in Europe. This represents a patient safety issue.

In 1998, the Chief Medical Officers of the EU Member States recognised this evolving problem and took the initiative to arrange the first major conference on AMR, which resulted in the Copenhagen Recommendations (Report from the Invitational EU Conference on the Microbial Threat, Copenhagen, Denmark, 9–10 September 1998).

In November 2001, the EU Health Ministers adopted a [Council Recommendation on the prudent use of antimicrobial agents in human medicine \(2002/77/EC\)](#), which covers most topics of importance for the prevention and control of AMR. The Commission has to report back to the Council on progress in implementing the Council Recommendation.

In 2005, the European Commission reported to the Council on progress in Member States in the Report from the Commission to the Council on the basis of Member States reports on the implementation of the Council recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine (COM (2005) 0684). This states that 'ECDC should be able to assist the Commission in the future preparation of implementation reports and of recommendation proposals.'

In June 2008, EU Health Ministers adopted Council Conclusions on antimicrobial resistance (AMR) that reiterated the call for action to contain antimicrobial resistance and called upon Member States 'to ensure that structures and resources for the implementation of the Council recommendation on the prudent use of antimicrobial agents in human medicine are in place and to continue with the implementation of specific strategies targeted towards the containment of the antimicrobial resistance'.

In June 2009, EU Health Ministers adopted a [Council Recommendation on patient safety, including the prevention and control of healthcare-associated infections \(2009/C 151/01\)](#), which further stresses the importance of combating AMR as a patient safety issue.

In April 2010, the European Commission published its second report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine. While acknowledging that Member States have made significant progress since 2003, this report highlights many areas where implementation is not optimal and identifies directions for future work.

In November 2011, the European Commission published a new five-year [action plan against the rising threats from antimicrobial resistance](#) with the aim of addressing AMR by implementing a coordinated approach in all those sectors concerned (public health, animal health, food safety, environment, etc.) and strengthening and further developing EU initiatives against AMR and HAI at EU and international levels.

Finally, the new cross-sectorial approach has been further strengthened with the adoption of the [Council Conclusions on antimicrobial resistance of 22 June 2012](#) and the [Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance of 17 June 2016](#).

ECDC's mission, as part of its [Founding Regulation No 851/2004](#), is (i) to identify, assess and communicate current and emerging threats to human health from communicable diseases; (ii) in the case of other outbreaks of illness of unknown origin which may spread within or to the Community, the Centre shall act on its own initiative



until the source of the outbreak is known; and (iii) in the case of an outbreak which clearly is not caused by a communicable disease, the Centre shall act only in cooperation with the competent authority upon request from that authority. As part of this mission, ECDC may be requested, by the European Commission, a Member State, or another country to provide scientific or technical assistance in any field within its mission.

Following the official invitation by Dr. Ranieri Guerra, Director General of Health Prevention, Ministry of Health (24 May 2016), ECDC conducted an assessment mission on 9–13 January 2017 to discuss antimicrobial resistance (AMR) issues in Italy, with the objective of providing an evidence-based assessment of the situation in Italy in relation to prevention and control of AMR through prudent use of antibiotics and infection control.

## 1.2 Purpose

Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat posed by AMR to human health and advocates for a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for country visits. At the invitation of the national authorities, these visits are undertaken to specifically discuss and assess the national situation regarding prevention and control of AMR through prudent use of antibiotics and infection control. The country visits also help document how Member States have approached implementation and deployed national activities and they support the European Commission in evaluating implementation.

The main output of the visit is a report from ECDC provided to the national authority. To help ECDC ensure the consistency of the visits and monitor progress, an assessment tool has been developed (see Annex 5.2 of this report). The assessment tool includes ten topics regarded as core areas for successful prevention and control of AMR based on Council Recommendation 2002/77/EC and the Council Conclusions of 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

The country visit to Italy to discuss AMR-related issues was the 25th country assessment visit conducted by ECDC using the same methodology, process and tool. This was also the 21st country assessed in the area of AMR.

The ECDC country visit team consisted of Dominique L. Monnet, who led the mission, Alessandro Cassini (ECDC) and three experts from EU/EEA Member States: Dr Michael A. Borg (Malta), Dr José Miguel Cisneros (Spain) and Dr Ute Wolff Sönksen (Denmark), as well as Giovanni Mancarella (ECDC, only 9 January 2017). Graeme Jones (European Commission, DG SANTE F) participated as an observer with the aim of sharing experiences for future EC country visits on animal health. At national level, the visit was organised by Dr. Raniero Guerra (Director General for Health Prevention, Ministry of Health) and coordinated by Dr Stefania Iannazzo (Infectious Diseases and International Prophylaxis Unit). The visit and meetings to the Campania Region (Naples) were coordinated by Fortunato D'Ancona (National Public Health Institute (ISS) and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance) and Bruno Sarnelli (General Directorate for Health and Coordination of the Regional Health Service, Campania Region). The visit and meetings to the Emilia-Romagna Region (Bologna and Modena) were coordinated by Annalisa Pantosti (National Public Health Institute (ISS), National Focal Point for Antimicrobial Resistance) and Maria Luisa Moro (Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-Associated Infections). For the full list of national experts met during the ECDC country visit, please refer to Annex 5.1 of this report.

## 2 Overview of the situation in Italy

### 2.1 Antimicrobial resistance (AMR)

Data on AMR in invasive bacterial isolates - mainly from bloodstream infections - are available from the European Antimicrobial Resistance Surveillance Network (EARS-Net) which Italy has been a member of since 2000. Seen from a European perspective, the present AMR situation in Italy is worse than in many other Member States. This is exemplified by data from the latest EARS-Net 2015 report (published in January 2017) that confirm a high percentage of invasive bacterial isolates with disturbing AMR characteristics, significantly above the EU/EEA average. This was confirmed by local data presented during the visit.

For example, the proportion of *Klebsiella pneumoniae* blood isolates that are resistant to carbapenems increased from 1.3% in 2006 to 33.5% in 2015, whereas combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycosides) increased from 2.8% in 2005 to 29.7% in 2015.

For *Escherichia coli*, the proportion of blood isolates that are resistant to carbapenems remained low: 0.1% in 2007 to 0.2% in 2015 (0.6% in 2013), but combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycosides) increased from 0.8% in 2002 to 14.6% in 2015.

The proportion of *Acinetobacter* spp. blood isolates that are resistant to carbapenems is very high - 83% (2012) and 78.3% (2015), similar to combined resistance (fluoroquinolones, aminoglycosides and carbapenems) - 77.4% (2012) and 72.6% (2015).

The proportion of *Staphylococcus aureus* blood isolates that are resistant to meticillin (MRSA) remains high, but has decreased from 44.3% in 2000 to 34.1% in 2015. The proportion of *Enterococcus faecium* that are resistant to vancomycin is rather high, but has decreased from 15.0% in 2001 to 11.2% in 2015.

One particular observation is that Italy reports the second highest percentage of *K. pneumoniae* blood isolates resistant to the last-line group of antibiotics, the carbapenems (33.5%, 2015 data from EARS-Net), and Italian experts have reported an endemic situation in the country regarding carbapenemase-producing, carbapenem-resistant *Enterobacteriaceae* (expert self-assessment from the European Survey on Carbapenemase-Producing Enterobacteriaceae - EuSCAPE project). Since this publication in 2015, the situation has not changed. Moreover, the healthcare system in the country remains at risk of other types of carbapenem-resistant *K. pneumoniae* or *E. coli* being introduced that could rapidly spread and exacerbate the already endemic situation in the country.

A recent development highlighted by the EuSCAPE project is the rapid and country-wide dissemination of colistin-resistant, carbapenem-resistant *K. pneumoniae* and the detection of pandrug-resistant isolates - i.e. isolates resistant to all antibiotics.

For other bacteria, the percentages of resistance reported by Italy to EARS-Net are generally above the EU/EEA average and often among the highest for all EU/EEA Member States.

### 2.2 Healthcare-associated infections

In September–November 2011, a total of 1 023 Italian acute care hospitals participated in the first ECDC point prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use in acute care hospitals. Italy was the third largest participant of all EU Member States. The percentage of patients with at least one HAI (6.3%) on a given day in Italian hospitals was similar to the EU/EEA average (5.7%).

Italy contributes to the ECDC-coordinated surveillance of surgical site infections (HAI-Net SSI) via three networks: Sorveglianza Nazionale Infezioni in Chirurgia (SNICH), Infezioni Sito Chirurgico in Interventi di Artroprotesi (ISChIA) and Infezioni del Sito Chirurgico-Gruppo Italiano di Studio di Igiene Ospedaliera (ISC-GISIO). Italy also contributes to the ECDC-coordinated surveillance of HAIs in intensive care units (HAI-Net ICU) via the Italian Nosocomial Infection Surveillance in ICUs (SPIN-UTI). Italy's participation in HAI-Net SSI and HAI-Net ICU is coordinated by the Regional Health Authority of Emilia-Romagna and funded by the Ministry of Health. The geographical coverage of the country by these networks is uneven, with a larger number of participants from the northern regions of Italy.

Italian intensive-care units (ICUs) tend to report a high incidence of intubation-associated pneumonia and central venous catheter-associated bloodstream infections. Italian ICUs also tend to have a longer average length of stay, as well as longer durations for intubations and catheters. Gram-negative bacteria, including *Klebsiella* spp. and *Acinetobacter baumannii* are among the most common bacteria responsible for HAIs in Italian ICUs, and these are usually resistant to multiple antibiotics.

## 2.3 Antimicrobial consumption

In Italy, on the basis of the data approved in ESAC-Net 2015, antimicrobial consumption in humans is among the highest of all EU/EEA Member States. With 28 defined daily doses (DDD) per 1 000 inhabitants and per day of antibiotics for systemic use in the community, Italy consumes many more antibiotics than the EU/EEA average of 21 DDD per 1 000 inhabitants and per day. Data from ESAC-Net also indicate that the trend in antibiotic consumption in the community in recent years has neither increased nor decreased. Italy also has a high percentage of broad-spectrum antibiotic consumption (compared to other Member States) and the highest consumption of penicillin–beta-lactamase inhibitor combinations (ATC group J01CR). Extensive use of broad-spectrum agents has been linked to a high level of resistance.

Data from the latest Eurobarometer survey on AMR show that the proportion of the general population that had taken antibiotics during the past year increased from 36% in 2013 to 43% in 2016, the fourth highest of all EU Member States. This is much higher than the EU average of 34% for 2016 (decrease from 35% in 2013). As indicated in the Eurobarometer survey, in Italy a large proportion of antibiotics are taken in the community for viral infections such as common colds, influenza and sore throat. This survey also indicated that the level of knowledge about antibiotics and their absence of effectiveness against viruses, including colds and influenza, was below the EU average. In particular, the percentage of respondents who knew that unnecessary use of antibiotics makes them become ineffective was lower in Italy than in any other EU Member State, and the percentage of Italian respondents who knew that antibiotics are not active against viruses ('do not kill viruses') decreased by five percentage points between 2013 and 2016.

In the hospital sector, the consumption of antibiotics for systemic use (2.4 DDD per 1 000 inhabitants and per day) is among the highest of all EU/EEA Member States and more than double the EU/EEA average consumption in the hospital sector (1.0 DDD per 1 000 inhabitants and per day). This was confirmed in the ECDC point prevalence survey (PPS) during which, on any given day, 44% of patients in Italian acute care hospitals received at least one antimicrobial agent - a significantly higher percentage than the EU/EEA average (33%). Data from ESAC-Net also show that Italy reports the third highest consumption of polymyxins (ATC group J01XB, mainly colistin), a group of antibiotics used to treat patients infected with carbapenem-resistant *Enterobacteriaceae* (see Section 2.1).

Finally, as stated in the ESVAC report 2014, antimicrobial consumption in food animals in Italy was the third highest of all EU Member States.

In conclusion, the data on AMR and antimicrobial consumption in Italy indicate that in Italy the situation is much worse than in most EU Member States.

## 3 Observations

### 3.1 Development of an Inter-sectoral Coordinating Mechanism (ICM)

Currently, there is a group that functions as an Intersectoral Coordinating Mechanism (ICM), as defined in Council Recommendation 2002/77/EC. This group was formed by the Director General for Prevention at the Ministry of Health by Decree no. 158508461 (24 April 2015) and has the mandate to write a 'national plan to address AMR'. This multi-stakeholder group consists of representatives from the Ministry of Health (human and animal health), the National Reference Laboratories, the regional authorities, the National Public Health Authority (Istituto Superiore di Sanità, ISS), the National Association of Hospital Doctors, the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA), the Italian Association of Clinical Microbiologists, the Italian Federation of Pharmacists, the Italian Society for Prevention of Healthcare-associated Infections, the Italian Society of Hygiene, Preventive Medicine and Public Health, the Italian Association of General Medical Doctors (General Practitioners —GPs) and Primary Care, the Italian Association of Microbiology, the Italian Society of Infectious and Tropical Diseases, and the Italian Society of Paediatrics, and has met on an ad hoc basis to write the national plan.

It is unclear whether this working group will continue as an ICM once the national plan is finalised. It is also unclear whether the ICM and actions in the national plan will be financially supported by the Ministry of Health once the national plan is finalised and starts being implemented.

The national plan was only available as a first draft. We acknowledge that changes will be made to the current version which contains several gaps. In particular, the national plan contains neither a prioritisation of actions nor clear deliverables, milestones and quantitative targets for both processes and outcomes. In addition, the draft plan lacks an indication of the funds required for its implementation at both national and regional level.

### 3.2 Organised multidisciplinary and multi-sectoral collaboration at local level

There is evidence that, in some regions, multidisciplinary and multisectoral collaboration is taking place. Where this was present, a similar pattern was observed:

- A highly motivated and influential expert leader with in-depth knowledge and experience of AMR prevention and control.
- A clear sense of urgency.
- A core group supported by regional decision makers with necessary financial and human resources support.
- Focused data collection and analyses of both AMR and consumption together with feed-back to local stakeholders.
- Infection control support to hospitals and other healthcare institutions in the region.
- Specific interventions and campaigns aimed at healthcare professionals as well as the general public.

We do not believe it is a coincidence that these regions are among those with the lowest levels of AMR in Italy. By way of contrast, other regions that we visited, where levels of carbapenem-resistant Enterobacteriaceae (CRE) and/or MRSA are high, had less comprehensive multidisciplinary and multisectoral collaboration at regional level.

### 3.3 Laboratory capacity

Not all hospitals have an on-site microbiology laboratory supported by a microbiologist.

The accreditation of laboratories varies among regions, using different accreditation systems.

All public hospitals are served by public laboratories, and all public laboratories are accredited. However, not all private laboratories are accredited; in particular this is the case for a substantial number of small, private laboratories (approximately one-third of all laboratories in the country), that analyse microbiology samples for outpatients.

In primary care, the results from microbiological analyses are referred to the general practitioner (GP)/paediatrician through the patient. There is little or no communication between the laboratory and the GP/paediatrician. As a result, GPs/paediatricians do not receive summaries of epidemiological data on antimicrobial resistance in the area and for the patients that they serve. Around 70% of hospital laboratories provide rapid preliminary feedback to clinicians, following a defined priority scale, and all of them within the 24-hour limit. Neither hospitals, nor primary care receive guidance on how to take microbiological samples and interpret the results of microbiological analyses. Both GPs and paediatricians mentioned the use of rapid diagnostic tests in their practice, but it seemed that none of them received guidance on how these were to be applied and interpreted.

Laboratories (microbiology units) are not necessarily run by a medical doctor.

In one laboratory that we visited, the number of bacteriological samples seemed very low compared to the number of beds in the hospital. In general, it seemed that samples for microbiology culture were not taken systematically before initiating each empirical antimicrobial treatment, but only where there were suspected complications or rare conditions. This practice makes decision-making on the choice of the most appropriate empirical antimicrobial treatment more complicated, and it contributes to the use of more broad-spectrum antimicrobials for empirical treatment.

At several hospitals, laboratory capacity was cited as the main reason why screening programmes for CRE and MRSA could not be expanded.

There is no formal referral system to a National Reference Laboratory on a national scale.

Almost all laboratories involved in EARS-Net surveillance participate in the annual EARS-Net EQA scheme. There is no national EQA scheme, although some regional EQA schemes are in place. Therefore, the accreditation systems, EQA schemes and quality control systems of laboratories differ depending on the region.

While visiting hospital laboratories, ECDC noticed that antimicrobial susceptibility testing was done by semi-automated systems (including colistin susceptibility testing). However, according to EUCAST recommendations, semi-automated systems have not been fully tested for colistin susceptibility testing, in particular for the detection of the *mcr-1* gene.<sup>i</sup>

Semi-automated systems perform very well to detect chromosomal resistance towards colistin (since minimum inhibitory concentrations (MICs) for colistin are above 4 mg/l and often higher) and will correctly detect and identify isolates in settings where resistance to colistin is endemic. However, identification of colistin hetero-resistance due to use of polymyxins, and in particular colistin, occurring in bacteria from an individual patient might be more challenging. Resistance to colistin can develop rather quickly within one single treatment course (typically within 10–14 days, but might occur earlier). Moreover, semi-automated systems might not detect isolates that carry the plasmid-borne colistin resistance genes such as *mcr-1* (since these have MICs around 4 mg/l and may be falsely reported as colistin-susceptible). Semi-automated systems can be used in situations where colistin resistance based on chromosomal genes is endemic, but should not be used for surveillance with the purpose of detecting isolates that carry plasmid-borne genes such as *mcr-1*.

EUCAST recommends using the microdilution method for colistin susceptibility testing on all carbapenem-resistant bacteria, including CRE.<sup>ii</sup>

### 3.4 Monitoring of antibiotic resistance

Italy has been participating in European surveillance of AMR (EARSS, then EARS-Net) since it first began. This level of activity has been critical for highlighting the major areas of concern.

At national level, there are two sentinel networks with voluntary participation: AR-ISS (blood and cerebrospinal fluid isolates) and MICRONET (all samples). AR-ISS is a country-wide passive sentinel surveillance system for AMR, coordinated by ISS and including around 58 hospital laboratories which collect and send routine antimicrobial susceptibility testing (AST) data to ISS. AR-ISS laboratories follow the EARS-Net protocol and participate in the EARS-Net EQA scheme. MICRONET is an electronic platform for automatic transfer of microbiology data (including AST data) from the hospital laboratory systems to a central server. At present, only 12 hospital laboratories use the MICRONET platform, which ensures real-time availability of data. Both AR-ISS and MICRONET are hosted at ISS and receive the financial support of the Ministry of Health.

As for other surveillance networks, there is an unequal, geographical distribution of the hospital laboratories that participate in AR-ISS and MICRONET which are mostly located in the northern regions. Hospital laboratories in the central and the southern regions of the country, where AMR prevalence is acknowledged to be highest, are under-represented. This, together with the very limited (approximately 15%) coverage of the country population by AR-ISS, makes it more than likely that the overall AMR situation of the country is significantly worse than currently reported by AR-ISS and by EARS-Net.

The Ministerial Circular 'Surveillance and control of infections due to carbapenemase-producing bacteria (CPE)' dated 26 February 2013 requires laboratories to notify cases of CPE bacteraemia within 48 hours to the medical direction of the hospital and/or of the local health service, which in turn has 48 hours to send the complete epidemiological and microbiological information on each case to the local health authority (Azienda Sanitaria

<sup>i</sup>[http://www.eucast.org/ast\\_of\\_bacteria/warnings/](http://www.eucast.org/ast_of_bacteria/warnings/)

<sup>ii</sup>[http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST\\_files/General\\_documents/Recommendations\\_for\\_MIC\\_determination\\_of\\_colistin\\_March\\_2016.pdf](http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/General_documents/Recommendations_for_MIC_determination_of_colistin_March_2016.pdf)[http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST\\_files/Disk\\_test\\_documents/Version\\_5/Media\\_preparation\\_v\\_5.0\\_EUCAST\\_AST.pdf](http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Disk_test_documents/Version_5/Media_preparation_v_5.0_EUCAST_AST.pdf).

Locale, ASL). Finally, the local health authority has seven days to notify this information to (a) the regional health authority, (b) the Ministry of Health and (c) the ISS. This Ministerial Circular represents a first step in the right direction. However, reporting is not enforced and the delays in reporting do not allow for timely action to provide support in controlling outbreaks and preventing further spread. From the data presented, it also appears that there is a substantial level of variability in the level of notification from various regions and laboratories. Once again, regions with the highest levels of CPE prevalence (data from other surveillance systems) paradoxically reported the lower numbers of CPE cases in response to the Ministerial Circular.

The reported CPE cases mainly relate to *Klebsiella pneumoniae*, with very few cases of *Escherichia coli*. In 2013, 718 CPE cases were reported. This number increased to 1 881 CPE cases in 2015 (probably due to more awareness and uptake of the reported cases), and 1 169 CPE cases in the first seven months of 2016.

Systems for surveillance of AMR at regional level are only in place in a few regions.

At local hospital level, surveillance of AMR in several locations that we visited tended to be unstructured and lacking focus in the key areas of interest. This suggests suboptimal training in AMR surveillance and methodology. Effective feed-back on easily understandable AMR data is acknowledged as a critical component of any AMR strategy.

### 3.5 Monitoring of antibiotic usage

Since 2000, antimicrobial consumption has been reported on annual basis by the Medicines Utilisation Monitoring Centre (OsMed) at the AIFA, mainly through the 'National Report on Medicine Use in Italy'. The report covers analyses of antimicrobial consumption in the outpatient and inpatient sectors. This is part of the overall monitoring of prescribed medicines and is legally supported. National coverage for prescribed antibiotics is 98%.

The annual OsMed report defines 'sell-out' data as the information (disaggregated per single package, per region and per month) on medicines sold by community pharmacies and charged to the Servizio Sanitario Nazionale (Italy's national health system). The report also defines 'sell-in' data as the information on medicines bought by community pharmacies from wholesalers. Therefore, it is possible to determine the out-of-pocket amount spent for medicines privately purchased by citizens through the community pharmacies by subtracting the amount spent for 'sell-out' from that spent for 'sell-in'. Out-of-pocket expenditure comprises class C medicines (not reimbursed), over-the-counter (OTC) medicines and medicines that do not need a medical prescription (mostly topical antibiotics), and patient co-payments for class A and class H medicines (that need a prescription). There is no specific information on antibiotic consumption from direct sales to patients without a prescription (over-the-counter sales), which is prohibited in Italy.

The AIFA monitors all medicinal products purchased by public health services such as local health units (Azienda Sanitaria Locale, ASL) and hospitals, on a daily basis for inpatient and outpatient distribution. However there is currently no information on patient diagnosis (primary care) or patient case-mix (hospitals) for antimicrobial consumption data.

At regional level, data are available at prescriber level, which enables a detailed assessment of prescribing practices. In most hospitals visited, reasonably detailed consumption data were available, although these did not refer to recent years. Both in the community as well as in hospitals, this data can be used for data mining and to inform antibiotic stewardship activities.

The AIFA has developed a database and indicators on consumption of medicines and the appropriateness of prescriptions. Patient-level data include the date and type of admission and discharge from hospital, primary and secondary diagnosis (ICD-9), procedures (ICD-9), Diagnoses Related Group (DRG) and reimbursement per hospital stay (hospital discharge records), and can be consulted at ASL, regional and patient level. This database represents 63.8% of the Italian population, geographically evenly distributed, with 48 institutions (40 ASLs and eight regions) contributing to the database.

### 3.6 Antibiotic usage and treatment guidance

'Over the counter' antibiotics are not available in Italy, yet there is the impression that a certain amount of antibiotics are sold without prescription. ECDC did not get the impression that this practice was applied by clinical doctors. The AIFA also mentioned a telephone line (FarmaciLine) that was not referred to again during the visit. Most medical doctors mentioned the use of guidelines issued by the medical societies but paediatricians, general practitioners (GPs) and some of the hospital doctors that ECDC met wished to see more guidelines. It was also not clear whether there was a system to ensure a regular update of existing guidelines. The National Health Institute does not issue guidelines.

The consumption of antimicrobials is very high in Italy. In primary care, there is an emphasis on prescribing broad-spectrum antibiotics, especially amoxicillin-clavulanic acid, quinolones and cephalosporins – including those



administered parenterally. Antibiotics (e.g. gentamicin) which are normally restricted to hospitals were found to be commonly used in community practice. Hospital data suggest even higher consumption; in one hospital we visited the average level of antibiotic use was even higher than that of the average intensive care unit in a northern European hospital. Prescribing is heavily skewed towards broad-spectrum antimicrobials, including carbapenems, polymyxins and other critically important antimicrobials.

Local guidelines seem in general to be present but are not based on local epidemiological data in primary care. Furthermore, for hospitals microbiological data is partly missing on admission for treatment of community acquired infections.

Compliance with guidelines is hard to establish due to the lack of database systems providing information on indication, prescription and other relevant information on the appropriateness of use.

It is not clear whether the guidelines had defined standardised criteria.

GPs and paediatricians seem to be using StrepA near-patient kits, but the exact amount used was not measured. In general, more diagnostic tools were requested to support and facilitate decision-making when treating infections.

One hospital reported that more than 70% of blood cultures were taken before the start of empirical treatment. However, inappropriate treatment was reported in up to 60% of the cases, either because the chosen antibiotic was not adjusted after microbiology results, including the antimicrobial susceptibility profile, became available or because the duration of treatment was incorrect.

### 3.7 Infection control

At national level, several projects have been undertaken over the past decade related to hand hygiene; surveillance of surgical site and intensive care infections; MRSA and CPE control. In the hospitals that we visited, the components of an effective infection prevention and control (IPC) infrastructure were in place including presence of an Infection Control Committee, as required by Italian law, chaired by a senior member of the administration. Full time infection control nurses (ICNs) were also in place but not always at a ratio of about one ICN full time employee (FTE) per 300 beds.

Doctors providing support to the IPC teams were also present in all hospitals visited. However, in most cases, the time that they could allocate to IPC activities was far less than the international benchmark of one IPC doctor FTE per 1 000 beds. Their actual day-to-day involvement in IPC was also very variable. In only one hospital that we visited was there a doctor dedicated solely to 'hands-on' IPC and antibiotic stewardship on a full-time basis. Not surprisingly, this was the hospital with by far the best AMR outcomes.

Even in hospitals reporting high CPE prevalence, the basic materials required for IPC were present. Alcohol hand rub was found in all hospitals, as well as the necessary personal protective equipment. However, it was quite evident that safety culture for effective IPC varied considerably in these hospitals. Posters and visual reminders were either absent or barely evident. Similarly, isolation signs were often absent, making it difficult for visiting doctors to know which patients were isolated and for what reason, and for relatives to know about precautionary measures.

Most personnel seemed unaware of basic hand hygiene principles. Some personnel, including core IPC personnel (nurses) were wearing jewellery on their hands and arms.

Alcohol rub bottles were often placed in relatively inaccessible locations where it was unrealistic to expect them to be routinely used. This conclusion was supported by information on the low levels of alcohol rub consumption in these hospitals.

Compliance with IPC practices was never systematically assessed by documented process audits (e.g. of hand hygiene, contact precautions and use of personal protective equipment). Key sentinel events such as MRSA bacteraemia were rarely investigated through root cause analysis, meaning that the aetiological factors behind these infections remain unknown and effective intervention is therefore unlikely.

On the other hand, the hospital with significantly improved AMR outcomes showed comprehensive initiatives and, above all, concrete evidence of teamwork across many disciplines and professions.

### 3.8 Educational programmes on AMR

In Italy, there are many educational or training initiatives on AMR, but few are centralised or coordinated.

For undergraduate medical students, AMR and antibiotics may be mentioned in several parts of the curriculum, but not necessarily as a specific topic; coverage depends on the awareness and willingness of each university.

There are no specific or routine post-graduate courses on AMR and antibiotics for medical doctors.

Similarly, there are no regular educational programmes on AMR and antibiotics for other healthcare workers. In some hospitals, personnel were trained when starting work at the hospital or at regular intervals.

Information was not available on the proportion of material concerning antibiotics provided or sponsored by the pharmaceutical industry.

### 3.9 Public information related to AMR

Each year since 2008, Italy has participated in European Antibiotic Awareness Day (EAAD) with activities coordinated by the Ministry of Health, and is using the day to promote its activities.

In 2008, the Ministry of Health, AIFA and ISS conducted a fully coordinated national awareness campaign to promote responsible use of antibiotics by the general public, with a website and a call centre managed by AIFA.

Since 2009, there have been annual communication campaigns organised by AIFA on traditional and social media. Since 2009, the Ministry of Health has also managed some dedicated web pages on its website.

There are some ongoing regional awareness campaigns in several regions, but little coordination at national level.

Italy is a partner in the e-Bug project, the European antibiotic and hygiene web-based teaching resource for junior and senior school children and young adults. The e-Bug material could be particularly interesting as it is already available in Italian and could be made available to schools.

Indicators for the national communication campaign (following the implementation of the national AMR strategy) have been developed as part of the training module on deploying national prudent antibiotic use campaigns developed by the Karolinska Institutet (Sweden) for ECDC.

Nevertheless, according to the Eurobarometer 445 survey (April 2016), the level of knowledge of AMR among the Italian general population was among the lowest in Europe, and the level of awareness on misuse of antibiotics was the lowest.

### 3.10 Marketing related issues

Independent (i.e. not supported by industry) drug information is available. AIFA is available by phone or email for questions from the public and healthcare workers. Local authorities can check the prescription habits of individual GPs. Prescriptions can have a negative influence on the salary if excessive or unjustified expenses are incurred.

Personal gifts from industry to physicians are illegal; however, pharmaceutical representatives were described as having constant and rather poorly regulated access to doctors. It would seem that the pharmaceutical industry has significant influence on prescribing habits.



## 4 Conclusion and recommendations

### 4.1 Conclusions

Observations from this ECDC visit confirm that the AMR situation in Italian hospitals and regions poses a major public health threat to the country. The levels of carbapenem-resistant *Enterobacteriaceae* (CRE) and *Acinetobacter baumannii* have now reached hyper-endemic levels and, together with methicillin-resistant *Staphylococcus aureus* (MRSA), this situation causes Italy to be one of the Member States with the highest level of resistance in Europe.

During conversations in Italy, ECDC often gained the impression that these high levels of AMR appear to be accepted by stakeholders throughout the healthcare system, as if they were an unavoidable state of affairs.

The factors that contribute negatively to this situation seem to be:

- Little sense of urgency about the current AMR situation from most stakeholders and a tendency by many stakeholders to avoid taking charge of the problem;
- Lack of institutional support at national, regional and local level;
- Lack of professional leadership at each level;
- Lack of accountability at each level;
- Lack of coordination of the activities between and within levels.

If the current trends of carbapenem resistance and colistin resistance in gram-negative bacteria such as *Klebsiella pneumoniae* and *A. baumannii* are not reversed, key medical interventions will be compromised in the near future. Untreatable infections following organ transplantation, intensive care or major surgical interventions are now a significant possibility in many Italian hospitals.

ECDC believes that the first step towards halting and reversing the current multidrug-resistant microorganism (MDRO) situation is to strengthen the current systems and introduce appropriate measures to reduce unnecessary antibiotic use (in communities and hospital) along with improved infection control.

Such corrective actions need to be taken at the following levels: national, regional and local (hospital).

There needs to be a greater sense of urgency about the current AMR situation at all levels and among all the stakeholders in the country. This also includes the need to establish clear definitions of the responsibility of each stakeholder. During all the meetings held as part of the visit, ECDC was impressed by the enthusiasm and dedication of the many professionals who can contribute to this effort. These people represent an asset to the country and an opportunity to address or even reverse the current AMR situation.

AMR is a national and cross-regional challenge, especially because the movement of patients (and resistant bacteria) is not restricted by regional borders. Therefore there is a significant risk that, with a regional framework such as that in Italy, it may not be possible to achieve cohesive and standardised action nationwide when dealing with a threat such as AMR. For this reason, a comprehensive coordinated response is required that ensures central coordination, supervision and auditing of the progress being made in the regions, especially those with higher prevalence.

It is vital that the examples of good practice that we observed during our visit in some regions/hospitals across the country are extended to all the other areas, especially those with the highest levels of AMR. ECDC believes that this will not be possible without strong and coordinated activities at central level, which will result in concrete actions at regional and local level.

### 4.2 Recommendations

Based on these observations, ECDC's team recommends the following actions:

**Designate AMR as a national public health threat.** The Ministry of Health should formally designate AMR as a national public health threat that affecting all regions. This state of affairs requires prioritisation of resource allocation and short/long term planning.

**National Action Plan.** The National Action Plan offers an opportunity to design an effective roadmap to achieve these goals. It should be finalised and strengthened as a matter of urgency by including actions, indicators and targets, with measurable outcomes and much shorter deadlines for its operational implementation.

**Learn lessons from the recent national vaccination initiative.** In the same manner, key performance indicators and targets for AMR should be identified and incorporated into the minimum levels of assistance.

**Estimate costs for activities at both national and regional level** to make available the appropriate budgets.

The regions with the greatest AMR challenges also tend to be those subjected to the repayment plan. Despite the financial situation, investment into antibiotic stewardship and infection prevention and control has been proven to be cost-effective and will (relatively quickly) result in savings that exceed the amount invested. Financial deficits should not therefore be a barrier to implementation of the National Action Plan and its activities.

**Intersectoral Coordinating Mechanism.** The Intersectoral Coordinating Mechanism under the Ministry of Health should have a clear mandate that goes beyond completion of the National Action Plan, and receive financial support for its activities.

**Appointment of regional AMR specialists.** Each region should formally appoint an expert with specialist knowledge of AMR control and clear terms of reference responsible for initiating and coordinating the necessary AMR prevention and control activities. These trained specialists should meet quarterly in an inter-regional assembly to share good practices and support one another.

**Central supervision.** The heterogeneity of the regional system requires a level of supervision coordinated at a central level. This could take the form of a team of auditors or peer-reviewers who would regularly visit the regions to assess and check that activities are implemented at regional level according to the National Action Plan.

**Milestones linked to financial incentives.** The achievement of agreed milestones should be linked to financial incentives in order to acknowledge progress and motivate further improvement. Achievement of milestones should be publicised to retain focus and initiative.

At central level, these initiatives are sufficiently significant to justify setting up an adequately resourced team within the Ministry of Health dedicated solely to tackling AMR. This will allow a consistent and uninterrupted level of activity as well as the development of an effective system that provides guidance and audits progress in the regions. The team would also coordinate national and regional public awareness campaigns.

**Improve central collection of surveillance data.** The surveillance data on AMR and antimicrobial use that is collected centrally needs to be improved. This can be done by improving the geographical representativeness and timeliness of the MICRONET system. In addition, notification of new cases of CRE and MRSA bacteraemia should become mandatory and be undertaken through a simple online reporting system that automatically transmits the information in real time both to the regional and central coordinating entities.

**Tackle unaccredited microbiology laboratories.** The substantial number of unaccredited microbiology laboratories should be tackled by introducing a programme of minimal accreditation criteria for laboratories that perform analysis of microbiological samples. This intervention would ensure quality results and maximise the effectiveness of the subsequent antibiotic treatments.

**Agree minimal structural indicators** for effective infection prevention and control and antimicrobial stewardship at hospital level, linked to bed occupancy and type of care provided. This will ensure that the necessary staff are involved at local level. Clear job descriptions and responsibilities should be included.

**Increase the number of hospital professionals specialising in infection prevention and control** and antimicrobial stewardship and the resources for training them.

**Publish national guidelines on the use of antibiotics.** Italy would benefit greatly from developing and publishing national guidelines with general principles on the use of antimicrobial agents in human medicine.

**Check the appropriateness of antibiotics dispensed at pharmacies.** In all regions of the country the appropriateness of the antibiotics dispensed at community pharmacies should be checked to establish whether and to what extent antibiotics are being sold over-the-counter without medical prescriptions.

**Organise a national antibiotics awareness campaign.** Given the Italian population's low level of awareness concerning antibiotics and AMR, Italy would also benefit greatly from the organisation of a national antibiotic awareness campaign on the prudent use of antibiotics. In addition, national communication strategies on the prudent use of antibiotics would benefit from a higher level of cooperation in the regions.

## 5. Annexes

### 5.1 Country visit team and people met during ECDC country visit to Italy to discuss AMR issues

#### ECDC country visit team

- Dominique L. Monnet, Head of Antimicrobial Resistance and Healthcare-associated Infections (ARHAI) Programme, ECDC, Stockholm, Sweden
- Alessandro Cassini, Expert for Antimicrobial Resistance and Healthcare-associated Infections, ECDC, Stockholm, Sweden
- Michael A. Borg, External expert, National Focal Point for AMR, Malta
- José Miguel Cisneros, Clinical Unit of Infectious Diseases, Microbiology and Preventive Medicine, Infectious Diseases Research Group, Institute of Biomedicine of Seville (IBiS), University of Seville/CSIC/University Hospital Virgen del Rocío, Seville, Spain
- Ute Wolff Sönksen, Clinical Microbiology specialist, National Focal Point for AMR and for Antimicrobial Consumption, Bacteria, Parasites & Fungi, Statens Serum Institut, Copenhagen, Denmark
- Giovanni Mancarella, External Communication Unit, ECDC, Stockholm, Sweden (only 9 January 2017)

#### Those met during country visit

##### Monday 9 January 2017

**Meeting with national authorities: Ministry of Health (Directorate General Prevention, Directorate General Hygiene, Food Safety and Nutrition, Directorate General Health Programming, Directorate General Animal Health and Veterinary Medicines), AIFA (Italian Medicines Agency), ISS (National Public Health Institute) and representatives of regional health authorities.**

**Meeting with Intersectoral Coordination Committee - ICM (i.e. PNCAR Group working on the National Plan to tackle AMR) and scientific societies**

##### Ministry of Health, Rome

- Antonella Agodi, University of Catania, Sicily Regional Health Authority, Italian Society of Hygiene, Preventive Medicine and Public Health (SItI)
- Stefano Angotzi, General Secretariat, Ministry of Health
- Silvio Brusafferro, University of Udine, Friuli Venezia Giulia Regional Health Authority, alternate National Focal Point for Healthcare-associated Infections
- Silvia Cammarata, Italian Medicine Agency (AIFA)
- Loredana Candela, DG Animal Health and Veterinary Medicines, Ministry of Health
- Fortunato D'Ancona, National Public Health Institute (ISS) and DG Prevention, Ministry of Health, alternate National Focal Point for Antimicrobial Resistance
- Antonino Di Caro, Head of Laboratory services, National Institute for Infectious Diseases 'Lazzaro Spallanzani'
- Mauro Dionisio, DG Health Programming, Ministry of Health
- Giuseppe Facelli, General Secretariat, Ministry of Health
- Silvia Forni, Quality of Care, Tuscany Regional Health Authority
- Paolo Foggi, Italian Medicine Agency (AIFA)
- Rosa Gagliani, DG Animal Health and Veterinary Medicines, Ministry of Health
- Raniero Guerra, Director General for Prevention, Ministry of Health
- Lucia Guidotti, DG Health Programming, Ministry of Health
- Stefania Iannazzo, DG Prevention, Ministry of Health
- Francesco Paolo Maraglino, DG Prevention, Ministry of Health
- Marcello Meledandri, Director of Microbiology, San Filippo Neri Hospital and Trust
- Maria Luisa Moro, Director, Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-associated Infections
- Annalisa Pantosti, National Public Health Institute (ISS), National Focal Point for Antimicrobial Resistance
- Cesira Pasquarella, University of Parma, Italian Society of Hygiene, Preventive Medicine and Public Health (SItI)
- Sandra Petraglia, Italian Medicine Agency (AIFA)
- Patrizio Pezzotti, National Public Health Institute (ISS)
- Francesca Roberti, DG Animal Health and Veterinary Medicines, Ministry of Health
- Paola Scognamiglio, National Institute for Infectious Diseases 'Lazzaro Spallanzani'

### Via videoconference, Ministry of Health, Rome

- Tolinda Gallo, Friuli Venezia Giulia Regional Health Authority
- Francesco Luzzaro, Italian Society of Clinical Microbiologists
- Giustino Parruti, Abruzzo Regional Health Authority
- Rosa Prato, Puglia Regional Health Authority
- Roberto Raso, Piemonte Regional Health Authority
- Francesca Simion, Veneto Regional Health Authority
- Marco Tinelli, Italian Society of Infectious and Tropical Diseases
- Francesca Zanella, Veneto Regional Health Authority

### Meeting with representatives of general practitioners, pediatricians and pharmacists

#### Ministry of Health, Rome

- Domenico Crisarà, Italian Federation of General Practitioners
- Adima Lamborghini, Italian Federation of Pediatricians
- Walter Marrocco, Italian Federation of General Practitioners
- Alessandro Patrizi, Italian Federation of Pharmacists
- Silvestro Scotti, Italian Federation of General Practitioners
- Alberto Villani, Italian Society of Paediatrics

## Tuesday 10 January 2017

**Meeting with executives and professionals involved in the regional programme for the control of AMR. Presentation and discussion of recent intersectoral AMR initiatives by the Directorate General 'Health Protection and Coordination of the Regional Healthcare System'. Brief presentation on programmed interventions for 2017-18.**

#### Campania Region offices, Naples

- Aurelio Bouché, Campania Region
- Enrico Coscioni, Senior Health Advisor, Campania Region
- Federica D'Agostino, biostatistician, University of Naples 'Federico II'
- Fortunato D'Ancona, National Public Health Institute (ISS) and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance
- Ugo Piscopo, IT specialist, Campania Region
- Antonella Guida, General Directorate for Health and Coordination of the Regional Health Service, Campania Region
- Luciano Sagliocco, Epidemiologist, Campania Region
- Bruno Sarnelli, General Directorate for Health and Coordination of the Regional Health Service, Campania Region
- Silvestro Scotti, President of Italian Federation of General Practitioners, President of Regional Board of Medical Doctors
- Giuseppe Signoriello, Professor of Biostatistics, University of Naples 'Federico II'
- Ugo Trama, Pharmacist, 'Napoli I Centro' Local Health Centre (ASL)

### Meeting with the Strategic Directorate of the Monaldi Hospital Trust.

**Meeting with hospital staff involved in initiatives to control AMR: medical doctors from the Medical Directorate, infectious disease specialists, pharmacists, microbiologists, nurses responsible for controlling healthcare-associated infections.**

**Visit of ICU and areas of critical care: reanimation and extracorporeal membrane oxygenation (ECMO), cardiac surgery, respiratory pathophysiology and rehabilitation. Visit of the clinical microbiology laboratory.**

#### Monaldi Hospital Trust, Naples

- Rossella Alfano, Hygiene and public health doctor, Monaldi Hospital
- Antonio Corcione, Head of critical care, Monaldi Hospital
- Adriano Cristinziano, Head of hospital pharmacy, Monaldi Hospital
- Valeria Crivaro, Deputy Director, Health Directorate, Monaldi Hospital
- Diego Cuccurullo, Surgeon, Monaldi Hospital
- Susanna Cuccurullo, Microbiologist, Monaldi Hospital
- Fortunato D'Ancona, National Public Health Institute (ISS) and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance
- Emanuele Durante Mangoni, Head of Infectious disease, Monaldi Hospital

- Giuseppe Fiorentino, Director of Respiratory Diseases, Monaldi Hospital
- Mariella Galdo, Pharmacy, Monaldi Hospital
- Giuseppe Longo, Director General, Monaldi Hospital
- Giuseppe Matarazzo, Director, Health Directorate, Monaldi Hospital
- Patrizia Murino, Director Cardio-respiratory Unit, Monaldi Hospital
- Liliana Pagano, HAI prevention nurse, Monaldi Hospital
- Germano Perito, Director of Administration, Monaldi Hospital
- Bruno Sarnelli, General Directorate for Health and Coordination of the Regional Health Service, Campania Region

**Meeting with managers of the pharmaceutical services and those responsible for surveillance: monitoring antibiotic prescriptions in community medicine through analysis of indicators related to drug use and GP prescription profiles.**

#### **Local Health Centre (Azienda Sanitaria Local, ASL) 'Napoli 1 Centro'**

- Simona Criezzola, Pharmacist, ASL Napoli I Centro
- Fortunato D'Ancona, National Public Health Institute (ISS) and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance
- Claudia De Marino, Pharmacist, ASL Napoli I Centro
- Carmen Ruotolo, Quality management, ASL Napoli I Centro
- Antonio Sardù, General Practitioner, ASL Napoli I Centro
- Bruno Sarnelli, General Directorate for Health and Coordination of the Regional Health Service, Campania Region
- Antonio Stellato, Director, ASL Napoli I Centro.

### **Wednesday 11 January 2017**

**Meeting with regional/local groups and presentation of regional/local activities to prevent and control AMR: regional activities, ICA control, regional guidelines, surveillance systems, best practices, multidisciplinary approach at regional level.**

#### **Emilia-Romagna Region offices, Bologna**

- Viviana Accorsi, IT specialist, Regional Health Agency Emilia-Romagna
- Rossella Buttazzi, Regional Health Directorate
- Simona Di Mario, Pediatrician, Regional Health Directorate
- Giuseppe Diegoli, Veterinary services, Regional Health Directorate
- Andrea Donatini, Regional Health Directorate
- Cecilia Fabiano, Regional Health Agency Emilia-Romagna
- Carlo Gagliotti, Regional Health Agency Emilia-Romagna
- Cristina Lelli, IT specialist, Regional Health Agency Emilia-Romagna
- Andrea Mattivi, Prevention service, Regional Health Directorate
- Alessandro Milani, IT specialist, Regional Health Agency Emilia-Romagna
- Viviana Miraglia, Veterinary services, Regional Health Directorate
- Maria Luisa Moro, Director, Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-associated Infections
- Annalisa Pantosti, National Public Health Institute (ISS), National Focal Point for Antimicrobial Resistance
- Enrico Ricchizzi, Regional Health Agency Emilia-Romagna
- Alberto Ricciardi, Regional Health Agency Emilia-Romagna
- Grazia Tura, Head nurse, Romagna Local Health Centre (ASL).

**Meeting with the Strategic Directorate of the University Hospital of Modena.**

**Meeting with hospital staff involved in initiatives to control AMR: medical doctors from the Medical Directorate, infectious disease specialists, pharmacists, microbiologists, nurses responsible for controlling healthcare-associated infections.**

**Visit of ICU and areas of critical care. Visit of the clinical microbiology laboratory.**

#### **Modena University Hospital, Modena**

- Patrizia Albinelli, General Directorate, Modena University Hospital
- Monica Barbieri, General Directorate, Modena University Hospital
- Andrea Bedini, Infectious diseases, Modena University Hospital
- Mauro Codeluppi, Infectious diseases, Modena University Hospital
- Erica Franceschini, Infectious diseases, Modena University Hospital
- Annarita Garzia, General Directorate, Modena University Hospital

- Carlo Gagliotti, Regional Health Agency Emilia-Romagna
- Cosetta Iavazza, Quality control, Modena University Hospital
- Mauro Mancini, Pharmacy, Modena University Hospital
- Maria Luisa Moro, Director, Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-associated Infections
- Cristina Mussini, Director of Infectious diseases, Modena University Hospital
- Gabriella Orlando, Infectious diseases, Modena University Hospital
- Annalisa Pantosti, National Public Health Institute (ISS), National Focal Point for Antimicrobial Resistance
- Cinzia Puzzolante, Infectious diseases, Modena University Hospital
- Patrizia Scannavini, General Directorate, Modena University Hospital
- Luca Sircana, Director of Health Directorate, Modena University Hospital
- Elena Vecchi, Health Directorate, Modena University Hospital
- Claudia Venturelli, Microbiology, Modena University Hospital.

## Thursday 12 January 2017

**Meeting with Health Director, meeting with personnel in charge of AMR prevention and control. Visit of intensive care unit, medical and/or surgical ward and clinical microbiology laboratory.**

### San Filippo Neri Hospital and Local Health Centre 'ASL Roma 1' - Rome

- Daniela Batticiocca, Head Nurse, Prevention of HAIs, San Filippo Neri
- Franco Cerquetani, Hospital health Directorate, San Filippo Neri
- Silvana Chiaradia, Hospital health Directorate, San Filippo Neri
- Patrizia Chierchini, Director of Health Directorate, San Filippo Neri
- Francesco Cortese, Emergency surgery and infectious disease specialist, San Filippo Neri
- Giancarlo Di Battista, Head of Neurology, San Filippo Neri
- Stefano Mancini, Head of General Surgery, San Filippo Neri
- Marcello Meledandri, Head of Microbiology, San Filippo Neri
- Carlo Monaco, Head of Anesthesiology, San Filippo Neri
- Roberta Pavan, Head of Pharmacy, San Filippo Neri
- Claudio Pisanelli, Pharmacy, San Filippo Neri
- Luigi Polidori, Urology, San Filippo Neri
- Maddalena Quintili, Risk manager, San Filippo Neri
- Antonella Rao, Infection control nurse, San Filippo Neri
- Adelina Sanna, Infection control nurse. San Filippo Neri
- Denise Schembri Witmayer, anaesthesiologist, San Filippo Neri.

**Meeting with Health Director, meeting with personnel in charge of AMR prevention and control.**

### National Institute for Infectious Diseases (INMI) 'Lazzaro Spallanzani' - Rome

- Marta Blanca, Director of General Directorate, INMI 'Lazzaro Spallanzani'
- Antonino Di Caro, Head of Laboratory services, INMI 'Lazzaro Spallanzani'
- Delia Goletti, Head of Translational Research, INMI 'Lazzaro Spallanzani'
- Giuseppe Ippolito, Scientific Director, INMI 'Lazzaro Spallanzani'
- Patrizia Magrini, Director of Health Directorate, INMI 'Lazzaro Spallanzani'
- Silvia Morachelli, Pharmacist, INMI 'Lazzaro Spallanzani'
- Fabrizio Palmieri, Respiratory and post-acute unit, INMI 'Lazzaro Spallanzani'
- Nicola Petrosillo, Head of Infectious Diseases Unit, INMI 'Lazzaro Spallanzani'
- Vincenzo Puro, Risk management and regional surveillance, INMI 'Lazzaro Spallanzani'
- Paola Scognamiglio, Regional Surveillance Centre, INMI 'Lazzaro Spallanzani'.



## Friday 13 January 2017

### Preliminary report from the ECDC team to the Director General for Prevention

#### Ministry of Health, Rome

- Raniero Guerra, Director General for Prevention, Ministry of Health
- Stefania Iannazzo, DG Prevention, Ministry of Health
- Francesco Paolo Maraglino, DG Prevention, Ministry of Health

**Preliminary report from the ECDC team to representatives of the Ministry of Health (Directorate General Prevention, DG Hygiene and Food Safety and Nutrition, DG Health Programming, DG Animal Health and Veterinary Medicines), AIFA (Italian Medicine Agency), ISS (National Public Health Institute), representatives of Regional health Authorities, Intersectoral Coordination Committee - ICM (i.e. PNCAR Group working on the National Plan to tackle AMR) and scientific societies.**

#### Ministry of Health, Rome

- Loredana Candela, DG Animal Health and Veterinary Medicines, Ministry of Health
- Fortunato D'Ancona, National Public Health Institute (ISS) and Ministry of Health, alternate National Focal Point for Antimicrobial Resistance
- Lucia Guidotti, DG Health Programming, Ministry of Health
- Stefania Iannazzo, DG Prevention, Ministry of Health
- Francesco Paolo Maraglino, DG Prevention, Ministry of Health
- Marcello Meledandri, Director of Microbiology, San Filippo Neri Hospital and Trust
- Annalisa Pantosti, National Public Health Institute (ISS), National Focal Point for Antimicrobial Resistance
- Vincenzo Puro, Risk management and regional surveillance, INMI 'Lazzaro Spallanzani'
- Paola Scognamiglio, National Institute for Infectious Diseases 'Lazzaro Spallanzani'.

#### Via videoconference, Ministry of Health, Rome

- Antonella Agodi, University of Catania, Sicily Regional Health Authority, Italian Society of Hygiene, Preventive Medicine and Public Health (SItI)
- Silvio Brusaferrò, University of Udine, Friuli Venezia Giulia Regional Health Authority, alternate National Focal Point for Healthcare-associated infections
- Silvia Cammarata, Italian Medicine Agency (AIFA)
- Roberto Carloni, Liguria Regional Health Authority
- Paolo Foggi, Italian Medicine Agency (AIFA)
- Tolinda Gallo, Friuli Venezia Giulia Regional Health Authority
- Francesco Luzzaro, Italian Society of Clinical Microbiologists
- Elena Mazzolini, Veterinarian services, Friuli Venezia Giulia Regional Health Authority
- Maria Luisa Moro, Director, Emilia-Romagna Regional Health Agency, National Focal Point for Healthcare-associated Infections
- Giustino Parruti, Abruzzo Regional Health Authority
- Cesira Pasquarella, University of Parma, Italian Society of Hygiene, Preventive Medicine and Public Health (SItI)
- Sandra Petraglia, Italian Medicine Agency (AIFA)
- Rosa Prato, Puglia Regional Health Authority
- Roberto Raso, Piemonte Regional Health Authority
- Francesca Simion, Veneto Regional Health Authority
- Marco Tinelli, Italian Society of Infectious and Tropical Diseases
- Francesca Zanella, Veneto Regional Health Authority.

## 5.2 Assessment tool for ECDC country visits to discuss antimicrobial resistance (AMR) issues

The mechanisms behind emerging AMR are complex. However, two main issues that stand out offering opportunity for control efforts are: the use of antibiotics and the epidemiological spread of resistant microbes.

The complexity of the problem makes it difficult to grade which interventions are most successful. Where interventions have been introduced few of them have been evaluated. This may partly be because few systematic interventions have been used.

The Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) lists a number of areas that have an impact on controlling AMR. Most of the following tentative indicators are based on the Council Recommendation. Some are based on experience from different countries. These indicators are either structure- or process-related. Outcome indicators are collected by dedicated surveillance networks.

### 1. Development of an Intersectoral Coordinating Mechanism (ICM)

Due to the complexity of the issue there is a need for coordination to make an interventional strategy work. There is also a need for close cooperation from fields such as epidemiology, microbiology clinical medicine, infection control, veterinary medicine, pharmacology and behavioural sciences. It also requires cooperation from practitioners working in different medical specialities as well as government departments and healthcare providers.

In the Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) and the World Health Organization (WHO) Global Strategy for Containment of Antimicrobial Resistance (WHO/CDS/CSR/DRS/2001.2) the establishment of a coordinating group is regarded as essential.

Member States have different administrative organisations. There should be a group at the highest administrative level where representatives from regulatory bodies and professionals from the different sectors coordinate.

### Tentative indicators for 1

#### Structures

- Multidisciplinary composition
- Regular meetings
- Minutes from meetings
- National strategy plan available
- Defined governmental mandate
- Financially supported by government.

#### Functions

- Coordinates analysis of consumption and plans and supports interventions
- Proposes national objectives and policies
- Proposes, plans and supports interventions
- Provides policymakers, media and public with continues updated and structured data
- Provides support to local working groups.

### 2. Organised multidisciplinary and multisectoral collaboration at local level

One of the main elements for control strategies is to lower the selective pressure of antibiotics by restricting usage to appropriate indications. There is much evidence showing that antibiotics are overused. Prescribers need to be well acquainted with the AMR problem and the rational of using antibiotics appropriately.

A non-regulatory intervention that has had some influence on prescribing habits is a local activity whereby practising physicians discuss local data on consumption and bacterial resistance patterns, supported by epidemiologists, pharmacists and infection control. This proves to be an appropriate opportunity to revise local usage patterns, develop local guidelines (based on national guidelines) and organise local meetings with prescribers to promote rational use of antibiotics. In addition, topical issues can be discussed, such as problems related to MRSA or *Clostridium difficile* 027.

Practising doctors have limited time available. It is essential that there is a good collaboration with and support from the national/regional group to provide background data and help with scientific updates.



## Tentative indicators for 2

### *General*

#### **Structures**

- Are there local activities in some places?
- Are there nationally disseminated local activities?
- Are activities in hospitals and primary healthcare coordinated at the local level?

### *Primary health care*

#### **Structures**

- Are there local activities in primary health care?
  - If yes:
  - Mostly multidisciplinary
  - Private practitioners are taking part
  - Have access to local surveillance data on AMR
  - Have access to local antibiotic consumption data
  - Have public funding
  - Meet regularly.

#### **Functions**

##### **Primary areas of work are:**

- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions
- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

### *Hospitals*

#### **Structures**

- Are there local activities in hospital health care?
  - If yes:
  - Mostly multidisciplinary
  - Have access to local surveillance data on AMR
  - Have access to local antibiotic consumption data
  - Have public funding
  - Meet regularly.

#### **Functions**

##### **Primary areas of work are:**

- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions
- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

## 3. Laboratory capacity

Laboratory capacity is essential for many reasons:

- To be able to follow trends in antimicrobial resistance;
- To discover newly emergent resistant strains;
- To enable prescribers to make informed antibiotic choices. For this there is a need for timely feedback to clinicians.

It is important to characterise isolates that may have clinical importance. Often this cannot be done in all laboratories so a referral system to specialised laboratories should exist.

All laboratory work should be quality assessed regularly.

## Tentative indicators for 3

### General

#### Structures

- How many diagnostic laboratories are appropriately equipped for microbiological diagnostic work (minimum requirement: performance of gram-stain, aerobic culture and antimicrobial susceptibility testing)?
- What proportion of microbiological laboratories have at least one specialist clinical/medical microbiologist?
- Is there a formal referral structure to reference laboratories supported by public (alternatively through insurance system or equivalent) funding?
- Does a national external quality assessment scheme exist?
- Does an accreditation system exist for microbiological laboratories that requires regular QC and EQA?

### Hospitals

#### Functions

- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 12 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 24 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides species identification of blood culture isolates to the submitting clinician?
- Who pays for the analysis of samples sent in?

### Out patients

#### Functions

- What proportion of general practitioners can submit clinical specimen for microbiological investigation to an appropriately equipped microbiological laboratory within 12 hours?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) to the submitting clinician within the first 24 hours of receiving diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- Who pays for sent in sample analysis?

## 4. Monitoring of antibiotic resistance

Resistance patterns should regularly be followed. This should be done using a standardised method. The method should be quality assessed on a regular basis.

To be able to guide prescribers in prudent usage of antibiotics, surveys of different clinical conditions should be carried out to define which pathogens and their susceptibility profiles for antibiotics. The resistance pattern may vary from area to area so local monitoring may be needed.

Data should be gathered nationally and internationally to follow long term trends.

### Tentative indicators for 4

- Local, time limited studies have been performed
- Local continuous, monitoring is done in a few laboratories
- Are duplicates excluded?
- National monitoring with standardised methodology on clinically and epidemiologically relevant bacterial pathogens is on-going
- Country wide local monitoring with standardized methodology in communities and hospital unites is on-going
- Data from hospitals and out-patient settings are treated separately
- Data collection is financially supported by government
- Regular surveys of resistance patterns for pathogens in population based syndromes are performed
- Regular feedback of resistance patterns to prescribers and local groups is given.

## 5. Monitoring of antibiotic usage

As antibiotic usage is the driving force for emerging resistance it is important to monitor usage. Therefore, reliable surveillance systems of antibiotic consumption are essential to complement antibiotic resistance data and develop instruments for assessing effective strategies to foster appropriate antibiotic use in all European countries.

Current antibiotic use surveillance systems are mostly monitoring trends and shifts in usage patterns. However, to deepen our understanding of antibiotic prescribing, more detailed information is needed on patients' age and gender, the prescriber, the indication and pathogen. Although prescriber data are felt as sensitive, this kind of data can be used for the self-assessment. Aggregated data may be used for local group discussions.

### Tentative indicators for 5

- Are valid national data on outpatient antibiotic use available?
- Are valid national (or at least representative sample) data on hospital antibiotic use available?
- Is collection of data on antibiotic use legally supported?
- Is data collection financially supported by the government?
- Are data available per prescriber/ clinical diagnosis/micro-organism?
- Is there regular feedback of prescription patterns to prescribers?
- Are anonymous data fed back to local groups?

## 6. Antibiotic utilisation and treatment guidance

Antibiotics should be used properly. 'Proper use' is a difficult term both in human and veterinary medicine. There is still a need to find some common view on what is 'proper'. Guidelines are a way of agreeing locally or nationally.

Antibiotics allow treatment of serious bacterial infections. The largest volume of antibiotics is prescribed in ambulatory care. This use is increasingly recognised as the major selective pressure driving resistance, which in turn makes them ineffective. Therefore antibiotics should be used appropriately - i.e. (no) antibiotics for those who will (not) benefit from the treatment. In addition, unnecessary use of antibiotics requires more resources, motivates patients to re-consult and exposes them to the additional risk of side effects, whereas under-prescribing could be associated with higher risk of complications of untreated infections.

A 'proper' level of usage is difficult to define. The levels are mostly for following trends and shifts in usage patterns. With these data related to other data there might be a way of defining a 'proper' range of usage. One benchmark value at European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. Individual countries should position themselves and define their own benchmark. This should be based on the epidemiology of infectious diseases and national guidelines. A range of acceptable antibiotic use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Most guidelines define treatment for specific diagnosis. This means that the diagnosis has to be made correctly before guidelines are applicable.

That also means that antibiotic usage must be directed by medical diagnosis and decisions. This is why systemic antibiotics are prescription-only medicines in the European Union.

### Tentative indicators for 6

- Availability of OTC (over-the-counter) antibiotics
- Availability of national treatment guidelines
- Availability of locally adapted treatment guidelines
- Has the compliance to guidelines been assessed?
- Defined standardised criteria for clinical diagnosis
- What is the rate of laboratory diagnostics use before deciding on use of antibiotics for sore throat (% of patients)?
- What is the rate of blood cultures before use of antibiotics for perceived bacteremia with sepsis (% of patients)?

## 7. Infection control

Healthcare and hospitals in particular have historically been a major source of spread for epidemics. This has been shown for a wide variety of microbes – for example smallpox and early outbreaks of Lassa fever. A recent well-known example is SARS. Another very well-known bacterium that spreads in healthcare settings is MRSA.

All hospitals have defined procedures and hygienic principles although these may not always be based on the latest scientific knowledge. Implementation of guidelines and adherence to procedures is another problem. Surveys have shown that adherence to infection control guidelines many times is poor.

More and more people with complicated medical conditions are given home-based care. Many of them are elderly. Such patients may have indwelling catheters, a lower immunity and often use antibiotics. Infection control guidelines are difficult to follow in a home setting and many of the care staff have little or no training in infection control. Increasingly MRSA is reported to also be a problem in these settings.

### Tentative indicators for 7

#### *General*

- Is there a national committee on issues related to infection control?

#### *Hospitals*

- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Guidelines for hygienic procedures including standardized barrier precautions in >90% of hospitals
- Specific guidelines for MRSA in >90% of hospitals
- At least one infection control nurse/doctor per hospital
- Time allocated for infection control?
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in ICUs? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in surgical wards? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in internal medicine wards? (% of hospitals)
- Are there legal requirements for infection control system in hospitals?
- Is implementation of infection control practice regularly evaluated?

#### *Health care settings outside hospitals*

- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Alcohol-based hand disinfection available in >90% of outpatient clinics
- Alcohol-based hand disinfection available in >90% of health care settings for elderly
- Guidelines for infection control are available for elderly and long term care staff
- Implementation of infection control practice in elderly and long term care is regularly evaluated.

## 8. Educational programmes on AMR

Understanding the problem with AMR is the basis for having an impact with interventional programmes. This can partially be achieved with educational programmes. Educational programmes should be an integrated part of undergraduate studies. All healthcare-related professionals need to have an understanding of the AMR problem.

‘Education’ in the context of AMR is more than just pharmacology of antibiotics or resistance patterns in microbes. It encompasses the relationship between microbes, antibiotics and the epidemiology of resistant strains. It describes the complex interrelation between all aspects brought up in this document.

Regular, repetitive, independent educational material best provided by locally-based colleagues in discussion groups seems to be one of the better success factors.

### Tentative indicators for 8

- Doctors have in their curriculum AMR as undergraduate course
- Hospital health care workers have some education on AMR
- Community health care workers have some education on AMR
- Specific post-graduate courses for doctors in antibiotic resistance are provided
- Regular educational programmes in antibiotic resistance are provided for health staff
- It is compulsory for all prescribers to take part regularly in a session on AMR
- <60% of information on AMR is industry sponsored.

## 9. Public information related to AMR

Many prescribers blame patients for demanding antibiotics irrespective of their condition. This can only be changed if the public is well informed about what antibiotics can and cannot do. Hence, educational activities for the wider public are important.

### Tentative indicators for 9

- No information provided
- Topic sometimes covered in media
- Some material for media and/or internet from official sources
- Occasional national campaigns
- Repeated, structured national campaigns
- Regular, structured information provided by professional bodies
- Public perception assessed.

## 10. Marketing related issues

Economics also have an impact on prescribing habits, irrespective of diagnosis or best practice. This should be discouraged.

### Tentative indicators for 10

- Independent (not industry supported) drug information is available
- Ethical guidelines for interrelation between physicians and industry are in place
- Physician's prescriptions do not influence on physician's salary
- Personal gifts from industry to physicians are illegal.

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