



Plan Nacional
Resistencia
Antibióticos

Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance

AEMPS

AGENCIA ESPAÑOLA
DE MEDICAMENTOS
Y PRODUCTOS SANITARIOS



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DE SANIDAD, SERVICIOS SOCIALES
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agencia española de
medicamentos y
productos sanitarios



Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance

Adopted by the coordination group responsible for the preparation of the Strategic Action Plan to reduce the risk of selection and dissemination of antimicrobial resistance in their meeting of March 5, 2014.

Strategic Action Plan approved by the Interterritorial Council of the National Health System in the plenary meeting held on June 11, 2014 and by the intersectoral plenary meeting of the Ministry of Agriculture, Food and Environment held on July 8, 2014.

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Technical Coordination Group

The Coordination Group is formed by representatives of the institutions and bodies mentioned below and in accordance with that indicated in the Terms of Reference section of this plan. The different professional societies and associations will be incorporated as they participate in the preparation of the document.

Ministry of Health, Social Services and Equality, through the:

- Spanish Agency of Medicines and Medical Devices (AEMPS in Spanish).
- Spanish Agency of Consumption, Food Safety and Nutrition.
- General Directorate of Public Health, Quality and Innovation.
- General Directorate of the Basic Portfolio of the NHS and Pharmacy.
- Technical Coordination Unit of the General Secretary of Health and Consumption.

Ministry of Agriculture, Food and Environment, through the:

- General Directorate of Health of Agricultural Production.
- General Directorate of Agricultural Production and Markets.

Ministry of Economy and Competitiveness, through the:

- Carlos III Health Institute:
 - National Microbiology Centre.
 - National Epidemiology Centre.
 - Spanish Network of Infectious Pathology Investigation (REIPI in Spanish).

Ministry of Education, Culture and Sport, through the:

- Complutense University of Madrid:
 - Veterinary Science Faculty.
 - Veterinary Health Surveillance Centre.

Defense Ministry, through the:

- Central Hospital of Defense "Gómez Ulla".

Ministry of Internal Affairs, through the:

- General Subdirectorate of Prison Health.

Spanish Antibiogram Committee (COESANT in Spanish).

Scientific Societies*:

- Spanish Society of Preventive Medicine, Public Health and Hygiene (SEMPSPH in Spanish).
- Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC in Spanish).
- Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC in Spanish).
- Spanish Society of Primary Care Physicians (SEMERGEN in Spanish).
- Spanish Society of Family and Community Medicine (SEMFYC in Spanish).
- Spanish Society of General and Family Physicians (SEMG in Spanish).
- Spanish Association of Primary Care Paediatrics (AEPAP in Spanish).
- Spanish Society of Outpatient and Primary Care Paediatrics (SEPEAP in Spanish).
- Spanish Society of Primary Care Pharmacists (SEFAP in Spanish).
- Spanish Society of Hospital Pharmacy (SEFH in Spanish).
- Spanish Society of Clinical Pharmacology (SEFC in Spanish).

Collegiate Organizations*:

- General Council of Pharmaceutical Associations.
- General Council of Veterinary Associations.
- General Council of Medical Associations.
- General Council of Dentistry Associations.

Professional Associations:

- National Association of Specialists in Bovine Medicine of Spain (ANEMBE in Spanish).
- National Association of Swine Producers (ANPROGAPOR in Spanish).
- Interprofessional Association of Chicken Meat Farming of the Spanish Kingdom (PROPOLLO in Spanish).
- Spanish Association of Ovine and Goat Technology (SEOC in Spanish).

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1.

Executive summary

The European Union Council, European Parliament, European Commission and its Agencies (EMA, ECDC, HMA and EFSA) have identified the need to establish a common European strategy in order to evaluate and confront the problem of development of antimicrobial resistance. This has been expressed in different official documents such as the European Parliament Resolution of May 9, 2011, the European Commission Communication of November 17, 2011, establishing an Action Plan on Antimicrobial Resistance or the Conclusions of the European Union Council of May 29, 2012, on the impact of antimicrobial resistance and how this must be jointly addressed from human and animal health. All these documents set out a series of actions which are necessary to confront this serious problem.

In the Action Plan on Antimicrobial Resistance developed in the aforementioned European Commission Communication, 12 actions are included that are identified as vital in the fight against resistance in the Member States and that should be addressed in a period of 5 years (2011-2015). At the end of this period the Commission will publish a new report on the progress made and deficiencies at a national and EU level (expost evaluation) in the implementation of this five-year action plan.

Likewise, in the Conclusions of the European Union Council of May 29, 2012, Member States are encouraged to develop and implement strategies and action plans at national level to control the development of antimicrobial resistance, highlighting the need for both a human and veterinary perspective if these strategies are to be effective in the fight against the development and propagation of antimicrobial resistance.

On March 8, 2012, during an internal meeting called by the Ministry of Health, Social Services and Equality (MSSSI in Spanish) for the preparation of the Conference of Experts of the Danish presidency, the need to create a



working group made up of all the parties interested in this issue was manifested, which would make it possible to lay the foundations for the development of an intersectoral mechanism on antimicrobial resistance at a state level. Said meeting was attended by members of the General Directorate of Public Health, Quality and Innovation (DGSPCI in Spanish), the General Directorate of the Basic Portfolio of the NHS and Pharmacy, the Technical Coordination Unit of the General Secretary of Health and Consumption, the National Microbiology Centre of the Carlos III Health Institute (ISCIII in Spanish) and the Spanish Agency of Medicines and Medical Devices (AEMPS in Spanish).

The Spanish Agency of Medicines and Medical Devices called the first meeting on July 6, 2012, with the aim of constituting the so-called coordination group responsible for the preparation of the Strategic Action Plan to reduce the risk of selection and dissemination of antimicrobial resistance.

It was agreed in this meeting that there was a need to prepare a joint national strategic plan encompassing both human and veterinary medicine in order to reduce the risk of selection and dissemination of antimicrobial resistance.

Said plan has already been developed and was adopted by the group in their meeting of March 5, 2014, in fulfilment of the European Commission Communication of November 17, 2011, in which Member States are requested to prepare an Action Plan on Antimicrobial Resistance, as well as the Conclusions of the European Union Council of May 29, 2012, in which a joint approach is urged.

The plan is structured around six strategic lines common to both human and veterinary health, these in turn, being subdivided into measures and specific actions.

2.

Introduction

Since the introduction of antibiotics in clinical practice in the 1940s, these have become essential in the treatment of bacterial infectious processes in both humans and animals¹. The development of **antimicrobial resistance (hereafter AMR)**, especially the appearance and dissemination of multiresistant bacteria and the lack of alternative treatments, are two of the biggest public and animal health problems that must be faced at the present time.

Although there are many factors that facilitate the selection and dissemination of antibiotic resistance², the inappropriate or indiscriminate use of antibiotics is one of the main factors that contribute to this phenomenon³, together with deficient control of the bacterial infection. Not only is AMR a serious health problem in Europe but also at a global level, given that it affects different sectors such as human health, animal health, agriculture, the environment and trade.

There are significant differences in the rates of antibiotic consumption among different countries. In human health, according to a study of the *European Centre for Disease Prevention and Control (ECDC)*⁴, it is estimated that on any given day, around 30% of the patients admitted in European hospitals receive at least one antimicrobial agent. This study shows that Spain is above the European average, with an estimated figure of 46%, which places us in the fifth position in respect of antibiotic consumption in Europe at a hospital level (Figure 1).

On the other hand, 90% of antibiotic consumption occurs in primary care⁵, where one third of the doctor's visits are related to infectious diseases and, of these, a little more than half are related to infections of the respiratory tract⁶. An OCDE report showed that Spain has relatively similar figures to the rest of the OCDE countries with regard to the prescribed volume of antibiotics. However, this was not the case in the prescription of cephalosporins and quinolones, where Spain exceeded the rest of the OCDE countries⁷.

Patients receiving antimicrobials (%)

- <30
- 30 a <35
- 35 a <40
- 40 a <45
- >/= 45
- Not included

Non visible countries:

- Lienchtenstein
- Luxembourg
- Malta

Figure 1. Prevalence of antibiotic use (% of patients receiving at least one antimicrobial agent) in European hospitals, according to country (adapted from ECDC PPS 2011-2012) (2)

Antibiotic use would therefore appear to be excessive and frequently inappropriate in both primary and hospital care. In human health, the implementation of inappropriate treatments occurs in percentages approaching or exceeding 50% of the antibiotic use, both in the hospital setting and in primary care⁸.

In animal health, the antibiotic consumption data of 2011 places us in the third position of the European Union (EU)*.

Sales of different classes of antimicrobials for use in food-producing species, including horses, expressed in mg / PCU per country, for 25 countries in 2011

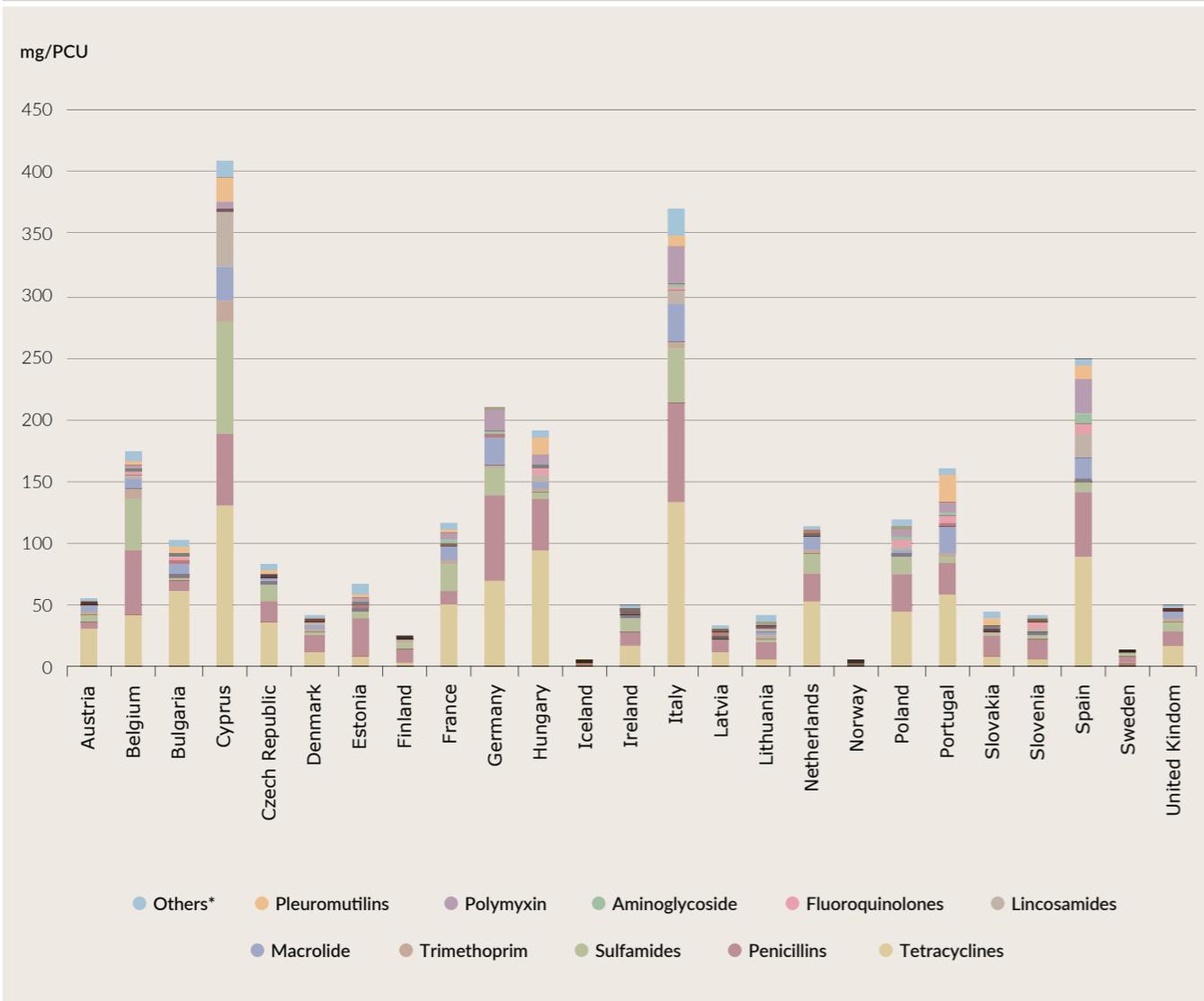


Figure 2. Sales of Veterinary Antimicrobial agents in 25 EU/EEA countries in 2011; www.ema.europa.eu/ema

This inappropriate use has very serious consequences, given that it increases the morbidity and mortality of infectious processes

At the end of the twentieth century, the main problems of resistance in our country were caused by Gram positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) at a hospital level and *Streptococcus pneumoniae* resistant to penicillin and macrolides at a community level

In this sector the main use of antibiotics is in oral form for mass treatment.

The tremendous intrinsic complexity of decisions in antibiotherapy, sparse microbiological information and insufficient knowledge of infectious diseases have been identified as being able to lead to a bad selection or duration of antibiotic treatments, thus resulting in inappropriate use. Finally, there is no common system of electronic prescription either in human or veterinary medicine that allows greater control of their use, which itself presents problems of control and facilitates the appearance of AMR.

This inappropriate use has very serious consequences, given that it increases the morbidity and mortality of infectious processes, contributes to dissemination of AMR and increases the frequency of related adverse effects (e.g. diarrhoea caused by *Clostridium difficile*, nephrotoxicity, etc.), thus increasing unnecessarily the cost of health care.

At the end of the twentieth century, the principal problems of resistance in our country were caused by Gram positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) at a hospital level and *Streptococcus pneumoniae* resistant to penicillin and macrolides at a community level. Far from disappearing, these problems currently persist with a prevalence of around 25-30% of the total of both isolated pathogenic agents. Other Gram positive bacteria such as *Enterococcus* spp. resistant to glycopeptides are beginning to gain relevance over the last decade. However, without doubt, the greatest increasing threat in our time is determined by the Gram-negative bacteria, capable of accumulating resistance to all (pandrug resistance, PDR) or almost all the available antibiotics (extensive drug resistance, or XDR)¹⁰, especially *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

Enterobacteriaceae are one of the main families of microorganisms that cause infections at both a hospital and community level. Resistance to third generation cephalosporins mediated mainly by the production of extended spectrum beta-lactamase (ESBL), is a growing problem in *Escherichia coli* and *Klebsiella pneumoniae*. With regard to this *E. coli*, national studies conducted in 2000 and 2006 show an 8-fold increase in its prevalence (from 0.5% to 4%). In 2003, 5.5% of the invasive strains of *E. coli* in Spain were ESBL producers, increasing to 13.6% in 2012¹¹.

Nevertheless, the greatest current threat is the growing dissemination in our country of carbapenemase-producing *Enterobacteriaceae*, enzymes capable of carbapenem inactivation, the last available step in the treatment of many bacterial infections. The health consequences of these AMR are overwhelming given that the mortality of the invasive infections caused by these microorganisms is 40-60%. The isolation of this type of microorganisms was testimonial until 2009, but the latest available data indicate that their

In the last 2-3 years we are witnessing increasingly frequent descriptions of important nosocomial outbreaks caused by these bacteria and a progressive increase of sporadic infections

It is estimated that more than 25,000 deaths annually in the EU are due to multiresistant bacteria

prevalence could already exceed 1%. In Spain, the situation is changing rapidly. In the last 2-3 years we are witnessing increasingly frequent descriptions of important nosocomial outbreaks caused by these bacteria and a progressive increase of sporadic infections. According to data of the Resistance Surveillance Programme of the National Microbiology Centre (CNM in Spanish), the number of cases of carbapenemase-producing *Enterobacteriaceae* reported increased from 15 in 2009 to 237 in 2012. This increase was mainly due to the dissemination within and among hospitals of a limited number of clones of OXA-48 carbapenemase-producing *K. pneumoniae*. In the same period, the number of hospitals reporting cases increased from 6 in 2009 to 30 in 2012¹².

At the beginning of the twenty-first century, the incidence of nosocomial infections due to multiresistant strains (resistance to at least three antibiotic families or MDR) of *P. aeruginosa* was not infrequent but was still not considered to be a serious problem. In 2008, more than 30% of the strains causing bacteraemic infections in Spanish hospitals were already MDR, and up to 10% of these presented XDR¹⁰ profiles.

In the year 2000, the percentage of strains of *A. baumannii* resistant to carbapenems in Spanish hospitals exceeded 40%; in a comparative study carried out in 2010 this figure had doubled, reaching 80%. Moreover, the data from this last national study showed that 94% of the strains of *A. baumannii* in our country are MDR, 86% are XDR and 2% are resistant to all the available antibiotics (pandrug-resistant or PDR).

Therefore, the data that urge taking action to fight against the selection and propagation of AMR are numerous, among which we must highlight:

The rapidity of the propagation of AMR between countries and continents, facilitated by increased trade and travel, make it a global problem that affects public and animal health.

The infections caused by resistant microorganisms that do not respond to traditional antibiotics, leading to a prolongation of the disease and even the death of the patient. It is estimated that more than 25,000 annual deaths in the EU are due to multiresistant bacteria².

We are facing bacterial infections at risk of becoming clinically uncontrollable, taking us back to the age before antibiotics in both human and veterinary medicine.



When the microorganisms are resistant to first-line antibiotics, more expensive therapies are usually used. The longer duration of the disease and treatment, often in hospitals, increases health care costs and the financial burden of families and society. It is estimated that the added costs in the EU are approximately an extra 1,500 million Euros for hospital care².

The achievements of modern medicine are put at risk by AMR. Without effective antibiotics for the care and prevention of infections, the success of treatments such as organ transplants, cancer, chemotherapy and major surgery would be compromised.

Animals are the reservoir of certain microorganisms that can be transferred to humans (zoonosis). Antibiotics are essential tools for their treatment and control.

Animal health is fundamental for the procurement of “healthy and safe” food for human consumption. Without effective antibiotics for the treatment of infections in animals the provision of these foods is at risk.



There is a general consensus on the need to improve antibiotic use. However, this has not led to the adoption of general measures and with the necessary coordination to enhance the possibilities of success. For example, at a hospital level, the results of a national survey conducted in 2011 indicate that only 40% of the hospitals surveyed carried out activities of monitoring and improvement of antibiotic use¹³. As has been mentioned before, given that most antibiotic use is in the community environment, rational use in this sector should be considered a priority⁶. In veterinary medicine, a survey has been carried out on the influencing factors in prescription and the use of susceptibility tests among the Member States. The results were quite different among the different States but, generally, the susceptibility tests are carried out when there has been a treatment failure. The responses not only indicate the need to improve the use of the aforementioned tests, but also to improve the availability of more rapid and cheaper diagnostic tests and the monitoring of resistance¹⁴.

The solutions are not easy. Nevertheless, there is a high degree of scientific evidence showing that the interventions which can be carried out to improve antibiotic use reduce antibiotic pressure and contribute to the control of resistance. As an example, the results of a recent study¹⁵, whose aim was a prospective evaluation of the appropriateness of prescriptions and antibiotic consumption during one year, indicate that following the implementation of an institutional programme for the optimisation of antimicrobial treatment, the proportion of inappropriate prescriptions was reduced significantly (from 53% to 26.4%) and also antibiotic consumption [from 1,150 defined daily doses (DDD) for each 1,000 hospital stays in the first quarter it passed to 852 DDD in the last quarter]. This reduction in consumption because of appropriate antibiotic use signified a total decrease of 42% in the direct costs of antibiotic medication, which led to an estimated cost savings of more than 1 million Euros (1,012,560 €). Therefore, the implementation of an institutional programme for the optimisation of antimicrobial treatment raises the level of knowledge of antibiotics in the hospital, improves inappropriate prescription, has a direct impact on the patient's clinical evolution and is cost-effective.

In primary care, it has been observed that delayed prescribing of antibiotics and availability of rapid diagnostic methods in doctor's visits help to accomplish a more rational use of antibiotics and to reduce their unnecessary prescription, above all in respiratory infections⁶.

The interventions are diverse and must be adapted to the environment, since they cannot be the same for such disparate environments like hospitals, primary care or in the veterinary field, production animals or pets.

The recommendations of the World Health Organisation (WHO) and the European Commission (EC) indicate that to be successful in the fight against AMR a global and multidisciplinary approach is required

The recommendations of the World Health Organisation (WHO) and the European Commission (EC) indicate that to be successful in the fight against AMR a global and multidisciplinary approach is required. This would include all the agents involved such as healthcare professionals with the capacity to prescribe medicines (physicians and veterinarians), pharmacists, clinical pharmacologists, microbiologists, professionals dedicated to preventive medicine, nursing professionals, as well as those dedicated to the vigilance and study of AMR, professionals with activities in the veterinary field, social entities who facilitate the dissemination of messages to the public and very importantly, responsible persons of the State Administration with the capacity to implement these control strategies.

In the joint approach to AMR it is the Public Administrations that are responsible for the preparation and implementation of health and food safety policies which foster the appropriate use of medicines. Nevertheless, only the collaboration and effort of multiple disciplines, working at a local as well as national and international level, can ensure the achievement of an optimal level of human and animal health.

Actions such as appropriate prescription, notification of the existence of AMR to the vigilance network, rapid identification of mechanisms of resistance and epidemic clones, encouragement of good professional practice and the promotion, fomentation and dissemination of the study and research of AMR are vital to achieve optimal use of antibiotics.

Awareness of the seriousness of this situation has led different international bodies, such as the United Nations Food and Agriculture Organisation (FAO), the World Organisation of Animal Health (OIE) and the WHO to publish numerous documents, reports, reflections and guidelines designed to promote the prudent use of antibiotics in both human and animal medicine. Likewise, in the EU-USA Summit meeting on November 3, 2009, under the Swedish presidency of the EU Council, the decision was made to create a transatlantic working group to exchange areas of knowledge, exchange of information, coordination and cooperation in the field of antimicrobial resistance (*Trans Atlantic Taskforce on Antimicrobial Resistance*, TATFAR) in which the then Ministry of Health, Social Services and Equality and the Carlos III Health Institute participated. The objective of this working group is to intensify cooperation for the appropriate use of antibiotics in human and animal health, prevent infections caused by resistant bacteria and develop strategies to improve the development of new antibiotics¹⁶.

Furthermore, the EU Council, the European Parliament, the Commission and its Agencies [European Medicines Agency (EMA), ECDC and the European Food Safety Authority (EFSA)] have identified the need of a European

The objective of this working group is to intensify cooperation for the appropriate use of antibiotics in human and animal health

strategy to evaluate and confront the problem. This has been manifested in different official documents such as the European Parliament Resolution, of May 12, 2011, the European Commission Communication, of November 17, 2011, establishing an Action Plan on Antimicrobial Resistance¹⁷, or the conclusions of the European Union Council, of June 22, 2012¹⁸, on the impact of antimicrobial resistance and the need for a joint approach from both human and animal health. These documents recommend a list of necessary actions to confront this serious problem.

In the Action Plan on Antimicrobial Resistance developed in the aforementioned European Commission Communication, 12 actions that are identified as key points in the fight against resistance in the Member States and that should be developed within a period of five years (2011-2015) are included. At the end of this period the Commission will publish a new report on the progress made and the deficiencies at a national and EU level (ex post evaluation).

Likewise, in the conclusions of the European Union Council, of June 22, 2012, Member States are requested to prepare and implement strategies or action plans to control the development of AMR at a national level.

In these last conclusions the need of a joint human and animal perspective is emphasised so that the fight against the development and dissemination of antibiotic resistance is really effective.

On March 8, 2012, during an internal meeting called by the Ministry of Health, Social Services and Equality (MSSSI in Spanish) for the preparation of the Conference of Experts of the Danish presidency, the possibility of creating a working group made up of all the parties interested in this issue was raised, which would make it possible to lay the foundations for the development of an intersectoral mechanism on AMR at a state level. The meeting was attended by members of the General Directorate of Public Health, Quality and Innovation (DGSPCI), the General Directorate of the Basic Portfolio of the NHS and Pharmacy, the Technical Coordination Unit of the General Secretary of Health and Consumption, the National Microbiology Centre of the Carlos III Health Institute (ISCIII in Spanish) and the Spanish Agency of Medicines and Medical Devices (AEMPS in Spanish). Subsequently, given the inclusive nature of the Plan regarding human and veterinary health, different technical dependencies of the Ministry of Agriculture, Food and Environment joined the group.



With these concerns in mind and based on this approach, on July 6, 2012, the Spanish Agency of Medicines and Medical Devices called the first meeting of the Working Group, hereafter «Coordination Group», thus mobilising the professionals involved in the launching of a strategic action plan for the reduction of the risk of resistance centered on antibiotics, whose aim is to comply with the European Commission Communication and develop a future **Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance**. The Spanish Agency (AEMPS), which reports to the General Secretary of Health and Consumption, is the coordinator of this Action Plan.

Thus, the components of said Coordination Group were identified and agreed upon in the first meeting and the «Terms of Reference» (ToR) that would be the basis for the development of aforementioned Plan were prepared.

The ToR and the proposal to develop the Strategic Action Plan were presented to the General Secretary of Health and Consumption and the General Secretary of Agriculture and Food for approval.

3.

Terms of reference

3.1 GENERAL OBJECTIVE

To prepare a **Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance covering both human and veterinary medicine, so as to reduce the risk and dissemination of AMR.**

Said plan shall fulfil the European Commission Communication, of November 17, 2011, in which Member States are requested to prepare an action plan on antibiotic resistance, as well as the Conclusions of the EU Council, of June 22, in which a joint approach is encouraged.

This European Commission Communication, in point 29, asks Member States to prepare and implement strategies or action plans at a national level that develop the following aspects:

Prepare and apply national recommendations on the treatment of persons or animals with antibiotics that guarantee responsible and rational use.

Limit the use of critically important antibiotics to those cases in which the microbiological diagnosis and susceptibility tests have determined that no other antimicrobial agent would be effective.

Limit prophylactic use of antibiotics to cases with clearly defined clinical needs.



Foster treatments with antibiotics based on microbiological diagnosis and on the carrying out of antibiograms.

Identify, boost and support at a national level vigilance and follow-up networks of antibiotic resistance in pathogenic, zoonotic and indicator bacteria, as well as the network of collection of data on antibiotic consumption in persons and animals.

Promote effective surveillance systems that cover the sectors of both human and animal health, with the aim of having a timely data collection, and that these data can be compared between sectors and Member States.

Identify and boost alternative and/or complementary measures of prevention and treatment of bacterial infections in both human and animal health.

Promote animal health through the prevention of diseases and the improvement of hygiene measures and as a result, favour the reduction in the need for antibiotics.

Prevent and control infections related to health care (HAI).

Develop a strategic plan for communication, training and education.

Promote the effective application of national legislation that impedes illegal dispensing of antibiotic agents in the sectors of both human and animal health.

3.2 PARTICIPATING INSTITUTIONS AND BODIES

Ministry of Health, Social Services and Equality, through the:

- Spanish Agency of Medicines and Medical Devices
- Spanish Agency of Consumption, Food Safety and Nutrition
- General Directorate of Public Health, Quality and Innovation
- General Directorate of the Basic Portfolio of the NHS and Pharmacy
- Technical Coordination Unit of the General Secretary of Health and Consumption
- Coordination Centre for Health Alerts and Emergencies

Ministry of Agriculture, Food and Environment, through the:

- General Directorate of Health in Agricultural Production
- General Directorate of Agricultural Production and Markets

Ministry of Economy and Competitiveness, through the:

- Carlos III Health Institute:
 - National Microbiology Centre
 - National Epidemiology Centre
 - Spanish Network of Infectious Pathology Investigation (REIPI in Spanish)

Ministry of Education, Culture and Sport, through the:

- Complutense University of Madrid:
 - Veterinary Science Faculty
 - Veterinary Health Surveillance Centre

Defense Ministry, through the:

- Central Hospital of Defense "Gómez Ulla"

Ministry of Internal Affairs, through the:

- General Subdirectorate of Prison Health

Spanish Antibiogram Committee (COESANT in Spanish).

Scientific Societies*:

- Spanish Society of Preventive Medicine, Public Health and Hygiene (SEMPSPH in Spanish)
- Spanish Society for Clinical Microbiology and Infectious Diseases (SEIMC in Spanish)
- Spanish Society of Primary Care Physicians (SEMERGEN in Spanish)
- Spanish Society of Family and Community Medicine (SEMFYC in Spanish)
- Spanish Society of General and Family Physicians (SEMG in Spanish)
- Spanish Association of Primary Care Paediatrics (AEPAP in Spanish)
- Spanish Society of Outpatient and Primary Care Paediatrics (SEPEAP in Spanish)

- Spanish Society of Primary Care Pharmacists (SEFAP in Spanish)
- Spanish Society of Hospital Pharmacy (SEFH in Spanish)
- Spanish Society of Clinical Pharmacology (SEFC in Spanish)

Collegiate Organizations*:

- General Council of Pharmaceutical Associations
- General Council of Veterinary Associations
- General Council of Medical Associations
- General Council of Dentistry Associations

Professional Associations :

- AECA-WPSA: Spanish Association of Poultry Science
- AMVAC: Madrid Association of Veterinarians for Pets
- ANAPORC: National Association of Scientific Swine Production
- ANEMBE: National Association of Specialists in Bovine Medicine of Spain
- ANPROGAPOR: National Association of Swine Producers
- APROMAR: Business Association of Marine Aquaculture Producers of Spain
- FEADSA: Spanish Federation of Health Protection Groups for Aquaculture
- ASEMAZ-ASA: Association for Animal Health
- ASEPRHU: Spanish Association of Egg Producers
- INPROVO: Interprofessional Association of eggs and its products
- ADESCU: Spanish Association of Rabbit Breeding
- ASFAC: Catalan Association of Feed Manufacturers
- AVEDILA: Association of Spanish Veterinary Specialists in Laboratory Diagnosis
- AVESA: Association of Veterinary Specialists in Food Security
- CESFAC: Spanish Confederation of Animal Feed Manufacturers
- CReSA: Foundation Centre for Research in Animal Health
- FEDEROVO: Spanish Federation of Producers of Eggs and Egg-derived Products
- FENIN: Spanish Federation of Healthcare Technology Companies
- NEIKER: Public Centre for Agricultural Research of the Basque Government
- PROPOLLO: Interprofessional Association of Chicken Meat Farming of the Spanish Kingdom
- SEOC: Spanish Association of Ovine and Goat Technology
- SOCIVEST: Society of Veterinary Science for Community and Public Health
- VET+I: Spanish Technological Platform for Animal Health

* The different professional societies and associations will be incorporated as they participate in the preparation of the document.

3.3 PRIORITY AREAS OF THE PLAN

The Plan is structured around six priority areas which are set out schematically in the following figure:



Figure 3. Priority areas of the plan

3.4 WORKING METHOD

3.4.1.

Two Coordination Groups have been formed, one composed of representatives of the official institutions and bodies included in point 3.2, and another composed of representatives of the different Autonomous Communities.

3.4.2.

The Coordination Groups meet regularly, at least twice a year.

3.4.3.

Each Coordination Group evaluates and adapts the different work proposals and strategies encompassed by the Annual Report.

3.4.4.

Each Coordination Group is able to request collaboration in specific aspects from the persons or institutions they deem necessary to guarantee the appropriate development of their work.

3.4.5.

The meetings of the subgroups may be face-to-face or online using telematic technology.

4.

3.4.6.

A working group for each measure has been constituted. Each subgroup shall follow the method of work described below:

- Identify already existing data in this field, actions that have already been implemented and stakeholders in the development of said actions.
- Identify the areas/aspects that are necessary to implement since they have not yet been initiated.
- Identify the areas/aspects that need to be improved because their development has not produced the expected results.
- Design and propose specific strategic lines.
- Bearing in mind these strategies, develop a calendar which includes a roadmap of actions, their methods of implementation, execution time (short, medium and long-term), the degree of priority and the person/persons responsible for each one.
- Design an assessment procedure to verify the level of fulfilment of the objectives.

3.4.7.

The Group shall ensure the continuous updating of the Plan.

Strategies to reduce the risk of selection and dissemination of antibiotic resistance

The objective of the plan is to develop a series of necessary strategic lines and actions to reduce the risk of selection and dissemination of AMR and subsequently, reduce its consequences for the health of animals and humans, thus conserving the existing therapeutic arsenal in a sustainable manner. Said plan will fulfil the European Commission Communication, of November 17, 2011, in which Member States are asked to prepare an action plan on antibiotic resistance, as well as the Conclusions of the EU Council, of June 22, in which a joint approach is urged.

The strategic lines and actions proposed for development are based on several aspects which underpin the whole Plan.

Firstly, they have been designed taking into consideration the fact that **the selection and dissemination of AMR is a complex and multifactorial problem with multiple victims**. Given this complexity, the implementation of isolated or badly coordinated measures is not effective and the establishment of programmes at a national or supranational level, with well coordinated multi-sectoral responses, is essential to confront control of the risk derived from the appearance of resistance with possibilities of success.



Among those affected by this threat, but who are also responsible for combating it and therefore participants in the Plan, are:

Society as a whole, and in particular patients and their family members who need to understand that antibiotics do not cure all diseases and that their incorrect use could compromise their efficacy when they are really needed.

Livestock farmers and owners or animal caregivers, who need to know the danger that this threat presents for society, the environment and the health of the animals under their care.

Primary and hospital care professionals, clinical veterinarians, pharmacists, nursing professionals and all those involved in health care and the rational use of medicines, who should use the available resources appropriately.

Institutions and bodies which are able to contribute to the formulation of recommendations for physicians and veterinarians and provide tools for help in prescription.

Institutions and bodies (universities, scientific societies, and professional associations) involved in the programmes of pre- and post-graduate training of healthcare professionals.

Investigators and pharmaceutical companies that must strive to develop new antibiotics or alternatives to these and acquire a deeper understanding of the phenomenon of resistance.

We are all part of a great ecosystem and any measure adopted in antibiotic policy will have some repercussion on said ecosystem

Communication experts who work to inform of decisions regarding public and animal health in the field of antibiotic use and the fight against AMR.

The Ministries of Health, Social Services and Equality and Agriculture, Food and Environment, responsible for the political momentum and consistency of action, the Ministry of Economy and Competiveness through the Carlos III Health Institute, the Ministry of Education, Culture and Sport, as well as any other national or regional body with responsibility in this matter who, given their competence and capacity, are able to adopt measures aligned with the Plan.

Secondly, and subsequent to the first point, **the Plan has a joint focus from the sectors of both human and animal health.** This has made it necessary to fit different actions of human or animal health, which are clearly differentiated and with different degrees of development in either area, within the same strategic line. However, this has been considered preferable for reasons of making this joint perspective more visible given that there are less and less barriers for the transference of resistance genes between microorganisms, the transference of microorganisms from animals to humans or humans to animals, as well as the transference of microorganisms between individuals. We are all part of a great ecosystem and any measure adopted in antibiotic policy will have some repercussion on said ecosystem. Therefore, a joint effort must be made on the part of veterinarians, physicians, pharmacists, health authorities and the pharmaceutical industry to address this problem in a comprehensive manner, and adopt appropriate measures that permit, as far as possible, the problem of antibiotic resistance to be controlled, since this is able to compromise the treatment of infectious processes of bacterial origin in both persons and animals.

Thirdly, **the plan is necessary due to the magnitude of the AMR problem.** Without doubt this has become one of the main threats for public health, with a tremendous clinical, epidemiological and microbiological impact globally. There are a certain number of microorganisms that have acquired a great variety of resistance mechanisms to numerous antibacterials, which currently permits them to evade practically all of the therapeutic options available.



To confront this threat it is necessary that all the sectors involved are mobilised towards a common objective that conciliates individual and collective aspects, so as to conserve a valuable commodity like antibiotics which is difficult to renew.

Fourthly, the insufficient capacity demonstrated by the health system to adopt solutions spontaneously. Since 2008, only two new antibacterial medicinal products have been authorised in Europe (ceftaroline y fidaxomicin). At the present time, there are only seven parental medicinal products in clinical development for the treatment of infections caused by MDR bacteria. The number of new antibacterial agents in phase II or III development continues to be alarmingly low. The most disturbing feature is the almost total absence of candidates able to be converted into medicinal products that are potentially active against carbapenemase-producing Gram-negative bacteria.

Finally, **the Plan should bear in mind the actions that are already underway** at both a national and international level in the fields of veterinary and human health. In fact, quite a number of actions proposed are part of national and international actions already underway. Among these, it is necessary to mention the working party on Microbacterial Resistance of the Codex Alimentarius Commission (with representatives from the OIE, FAO and WHO), the Decision 1082/2013/EU on serious cross-border threats, which specifically includes antimicrobial resistance, the actions spearheaded by the EU for the vigilance, follow-up and data collection or the prevention of diseases communicable to humans - zoonoses (Directive 99/2003/EC and Regulation 2160/2003), among others, for example, the close collaboration between the Spanish Agency of Medicines and Medical Devices and the Ministry of Agriculture, Food and Environment in the Network of Veterinary Vigilance of Antibiotic Resistance (VAV), or the actions of the Ministry of Health, Social Services and Equality and the regional governments in their hand washing and bacteraemia, pneumonia and resistance “zero” programmes.

The duration of this national Plan is five years (2014-2018), which provides sufficient temporary framework to objectify and prioritise the needs, as well as carrying out the foreseen actions. The Plan has an assessment report at the end of each year, which will allow different activities to be modified and/or prioritised on the basis of the analysis of the obtained results. In this regard, the flexibility of the Plan provides for the possibility of the action scheme being revised in accordance with the results of the annual assessment reports, as well as for updating derived from modifications that are produced in the health, scientific, judicial or organisational fields.

5.

Presentation of Strategic Lines

Six common strategic lines that correspond to the priority areas identified in the terms of reference (Figure 4) are proposed for human and veterinary health in order to achieve the objective of the Plan. Each of these strategic lines is subdivided into measures and each of these measures into specific actions.

Strategic Action Plan to reduce the risk of selection and dissemination of antibiotic resistance

<p>I. Surveillance of antibiotic consumption and antimicrobial resistance</p>	<p>II. Control of bacterial resistance</p>	<p>III. Identification and spearheading of a lternative and/or complementary measures of prevention and treatment</p>
<p>IV. Defining research priorities</p>	<p>V. Training and information for healthcare professionals</p>	<p>VI. Communication and raising awareness in the population as a whole and in population subgroups</p>

Figure 4. Strategic lines of the Strategic Action Plan



The Plan consists of twenty measures and seventy-four actions in total. Given the degree of development required by each of these according to their field of action, there are specific actions for human health, others that are specific for animal health and others which are common to both human and animal health.

A coordinator (who is part of the Coordination Group) and a series of institutions, bodies, societies or participating groups are identified for each group of measures or actions. This subgroup will be responsible for developing each assigned measure or action, generating development indicators and proposing specific actions to the Coordination Group.

5.1 STRATEGIC LINE I Surveillance of antibiotic consumption and antimicrobial resistance

This strategy is directed towards strengthening the surveillance networks that are already underway, extending their aims and range wherever appropriate, as well as implementing those networks which have not yet been initiated. It is a question of establishing solid surveillance networks in order to improve knowledge of antibiotic use and consumption and the development of resistance to these, which will permit us to implement measures directed towards its control.

The strategic line consists of four important measures (Figure 5) which include the monitoring of antibiotic consumption, control of the use of critical antibiotics, strengthening of the resistance surveillance systems and participation in European and International projects on vigilance of antibiotic consumption and antimicrobial resistance.

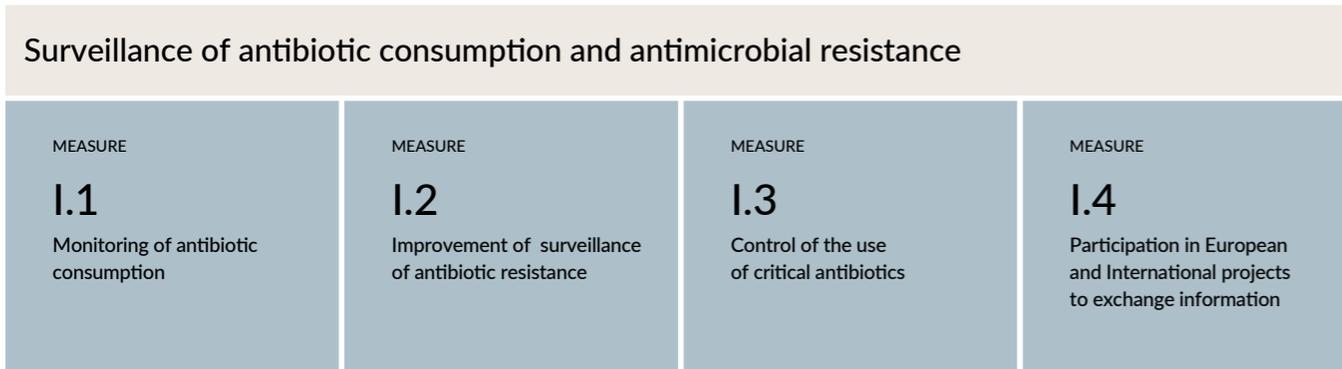


Figure 5. Strategic Line I



MEASURE

I.1

Monitoring of antibiotic consumption

Monitoring antibiotic consumption is essential to understand the pressure their use exerts on the appearance of resistance. In the field of animal health it is fundamental to improve the tools available so as to obtain data on antibiotic consumption according to animal species. In the field of human health there is a surveillance network of consumption in primary care but there is no similar existing network at a hospital level.

HUMAN HEALTH

ACTIONS

- I.1.1. Improve data collection on antibiotic consumption in the community and hospitals.
- I.1.2. Ensure the exploitation and analysis of data at a local, regional and national level and information feedback.

ANIMAL HEALTH

ACTIONS

- I.1.3. Improve the vigilance systems of antibiotic sales, including data at a distribution level.
- I.1.4. Development and implementation of the electronic prescription and of telematic control systems of treatments linked to exploitation
- I.1.5. Ensure the exploitation and analysis of data at a local, regional and national level and information feedback.



MEASURE

1.2

Improvement of surveillance of antibiotic resistance

In Spain, there are different surveillance networks in operation that permit availability of data on the prevalence and evolution of zoonotic, comensal and pathogenic bacteria. In human health it is necessary to promote the creation of an antimicrobial resistance surveillance system that, in addition to early detection and response in situations of risk, allows us to focus on and improve programmes directed towards the control and reduction of resistance, taking into account its temporary evolution and geographic variability.

Associated with this surveillance system it could be beneficial to promote a structure of reference centres/laboratories that guarantee quality and comparability of the analysed samples. The Carlos III Health Institute should be responsible for organising this system as the official scientific-technical support body of the State and Regional Government health departments in accordance with Law 14/1986, of April 25, and as the body responsible for the management of the National Surveillance Network.

At present, bacteria with special problems of multiresistance, with extended resistance and pan-resistance according to the ECDC definitions, are sent on a discretionary basis to the Official Resistance Surveillance Programme of the National Microbiology Centre. Another essential function of the programme is the study of hospital and community outbreaks at a local, regional and national level as well as the study of multiresistant bacteria isolated from healthy carriers in the population.

It is mandatory to inform the National Epidemiology Centre of infections caused by certain pathogens. At a regional level there are microbiological information systems that have demonstrated their effectiveness and for these it is vital to improve interaction at a national level.



MEASURE

1.2

Improvement of surveillance of antibiotic resistance

→ It is fundamental to consolidate and/or improve existing surveillance systems, extending the objectives and scope of these programmes wherever appropriate. Likewise, it is necessary to implement homogeneously into these systems the criteria of the European Committee of Antimicrobial Susceptibility Testing (EUCAST) in the collection of resistance data using the epidemiological vigilance points (ECOFF) and the critical susceptibility points (clinical breakpoints).

This will firstly permit the obtaining of homogeneous AMR data, with special reference to resistance in expanding zoonotic and indicator bacteria, secondly, the crossing of resistance and consumption data in the fields of both human and animal health and lastly, the diffusion of the data and their understanding in order to take specific measures if necessary.

HUMAN HEALTH

ACTIONS

1.2.1. Strengthen AMR data collection, with special analysis of expanding AMR.

1.2.2. Analysis and exploitation of AMR data, with special analysis of expanding AMR.

1.2.3. Crossing of information on AMR and consumption to make a biannual presentation of the results, identifying the pairs of antibiotics and bacteria that are especially representative.

ANIMAL HEALTH

ACTIONS

1.2.4. Analysis and exploitation of bacterial resistance data and their evolution in zoonotic and indicator bacteria, with a special analysis of expanding AMR.

1.2.5. Crossing of information on AMR and consumption to make a biannual presentation of the results, identifying the pairs of antibiotics and bacteria that are especially representative.



MEASURE

I.3

Control of the use of critical antibiotics

Critical antibiotics have been identified by the WHO as those which are indispensable in the treatment of infections caused by multiresistant bacteria in humans. Therefore, they are the object of a specific vigilance in both human and veterinary medicine.

Bearing in mind the inherent peculiarities of our health situation, it is fundamental to identify the areas of specific action to reduce their use and, whenever necessary, develop new recommendations and/or actions.

HUMAN AND ANIMAL HEALTH

ACTIONS

I.3.1. Identify and list the antibiotic classes considered as critical in order to proceed to a specific vigilance of their consumption and the appearance of resistance.

HUMAN HEALTH

ACTIONS

I.3.2. Raise awareness among prescribers in order to limit the use of the listed antibiotics with the help of consumption data.

ANIMAL HEALTH

ACTIONS

I.3.3. Limit the prescription of those antibiotics whose effectiveness has to be particularly conserved.



MEASURE

I.4

Participation in European and international projects for the exchange of information

It is fundamental to know and understand the European and international situation as an essential tool in placing our national plan in context. Moreover, it is necessary to present the actions included in this plan to our European partners for their knowledge, with a view to coordinating the actions in the appropriate EU forums and making them participants and conscious of the need to unite efforts in addressing these problems.

HUMAN AND ANIMAL HEALTH

ACTIONS

I.4.1. A continuous revision of the current European and international situation as regards AMR and the rational use of medicines will be performed, with the aim of distributing information and making it available to the interested parties.

I.4.2. Continue contribution in the different European projects already being developed with regard to antibiotic consumption and use, and the vigilance networks of AMR (ESVAC, monitoring of zoonotic pathogens, ESAC-net and EARS-net) and participate in other European and international activities to exchange information.

5.2
STRATEGIC LINE II
Control of bacterial resistance

This strategic line seeks to strengthen the knowledge, application and use of national and international recommendations for the control of AMR. Improvement in administrative regulations through the signing of prescription protocols together with advice as regards antibiotic treatments and knowledge of the basis for responsible and rational use of antibiotics is fundamental in the prevention and fight against AMR and infections, consequently allowing their use to be limited.

This strategic line consists of four important measures (figure 6) which include control of the dissemination of resistance, design and dissemination of tools for the promotion of good practice in the use of antibiotics, preparation of guidelines for exceptional antibiotic prescriptions within veterinary health programmes and the limiting of prophylactic use of antibiotics to those cases with well-defined clinical needs.

Control of bacterial resistance			
<p>MEASURE</p> <p>II.1</p> <p>Control of the dissemination of resistance</p>	<p>MEASURE</p> <p>II.2</p> <p>Design and dissemination of tools for the promotion of good practice in the use of antibiotics</p>	<p>MEASURE</p> <p>II.3</p> <p>Preparation of guidelines for exceptional antibiotic prescription within veterinary health programmes</p>	<p>MEASURE</p> <p>II.4</p> <p>Limiting prophylactic use of antibiotics to cases with well-defined clinical needs</p>

Figure 6. Strategic line II



MEASURE

II.1

Control of the dissemination of resistance

It is necessary to control the dissemination of resistant bacteria in health settings, the home, among animals and in the environment, especially those with mechanisms of transferable resistance and those emerging or imported in our territory.

A surveillance network of resistance in zoonotic and indicator bacteria exists in animal health. However, a vigilance network of resistance in pathogen bacteria is still not implemented at a national level in veterinary medicine.

HUMAN HEALTH

ACTIONS

- II.1.1.** Identify and strengthen the setting up of a network of laboratories for early detection of resistant bacteria and identification of their mechanisms of resistance.
- II.1.2.** Consolidate and harmonise the vigilance systems and control of infections associated with health care and reinforce these so that the multidisciplinary teams increase their capacity of reaction when facing alerts.
- II.1.3.** Work with the regional governments to reinforce surveillance and notification of outbreaks.

ANIMAL HEALTH

ACTIONS

- II.1. 4.** Develop the surveillance network of pathogen bacteria in animals and establish a plan according to animal species, identifying the route of implementation.
- II.1.5.** Identify collaborator and/or reference laboratories for the isolation and identification of pathogen bacteria resistant to antibiotics.



MEASURE

II.2

Design and dissemination of tools for the promotion of good practice in the use of antibiotics

The promotion and dissemination of the regulations for good use of antibiotics as well as raising awareness in all the different groups involved are one of the priorities of the Plan. For the implementation of this good practice in use it is fundamental to reach the greatest number of agents involved by using appropriate tools, and in particular, the guidelines of good practice in use.

The development of guidelines of good practice in antibiotic prescription in all the sectors and reaching a consensus in "protocols of treatment and metaphylaxis of bacterial diseases" are fundamental tools for the optimal use of antibiotics.

Given the tremendous density of antibiotic use in hospitals (prescriptions per number of patients) with the subsequent selection of AMR, the possibility of nosocomial transmission of multiresistant bacteria and the clinical impact of AMR, have meant that the majority of programmes on rational use of antibiotics have been developed in this setting. However, the phenomenon of the development of AMR and its real impact is less known and studied in primary care even though this does not mean it is a less important area. Although the density of antibiotic use is less than in hospitals, the total number of prescriptions is much greater and the possibility of inappropriate use and self-medication is high. It is therefore necessary to act in health centres through programmes promoting prudent use [e.g. in hospitals by means of programmes of optimal use of antibiotics (PROA) and the programme resistance zero (PRZ); in primary care through education, guidance and raising awareness in professionals and patients, and perhaps, in the future other programmes adapted to primary care].

→

MEASURE

II.2

Design and dissemination of tools for the promotion of good practice in the use of antibiotics

→ In these actions the different degree of development between human and veterinary medicine and between primary and hospital care should be taken into account. This justifies that although following parallel paths, the redaction of the actions should therefore be more specific in those areas that are currently less developed and more extensive in those with greater development.

HUMAN HEALTH

ACTIONS

II.2.1. PLaunching of programmes promoting prudent use of antibiotics.

II.2.2. Implementation of guidelines for specific use in the community.

ANIMAL HEALTH

ACTIONS

II.2.3. Develop more extensively a specific section on the good use of antibiotics for each animal species in the guidelines on responsible use.

II.2.4. Identify if it is necessary to develop other specific guidelines (Fish, birds bred for hunting purposes, other ornamental birds, etc).

II.2.5. Promote that antibiotic treatments are based on microbiological diagnosis and susceptibility testing.

II.2.6. Develop guidelines in which specific recommendations are given for the use of certain antibiotics such as "first line", "second line" or "final line" in relation to specific infections.



MEASURE

II.3

Preparation of guidelines for exceptional antibiotic prescriptions within veterinary health programmes

Provide help to the prescriber on infectious bacterial diseases and antibiotic use, either to prevent or cure, using information and communication technologies (ICTs) and develop guidelines on the exceptional prescription of antibiotics when there are no other existing alternatives within the health programmes of livestock exploitation.

ANIMAL HEALTH

ACTIONS

II.3.1. Develop guidelines pertaining to the exceptional prescription of antibiotics.



MEASURE

II.4

Limiting prophylactic use of antibiotics to cases with well-defined clinical needs

The use of antibiotics to prevent diseases in animals must be limited. The identification by animal species of the diseases in which prophylactic use of antibiotics is indispensable will establish guidelines that will help to improve the prudent use of these. Likewise, in human health, the identification of all the situations in which prophylactic use of antibiotics is required is a key to establishing guidelines of use.

HUMAN HEALTH

ACTIONS

II.4.1. Identify the clinical situations in which prophylactic use of antibiotics is required and write guidelines on the administration of prophylaxis in primary and hospital care. This will be carried out under the programmes of prudent use in the hospital setting.

ANIMAL HEALTH

ACTIONS

II.4.2. The diseases in which the prophylactic use of antibiotics is indispensable shall be identified by animal species and included in the plan.

II.4.3. Antibiotic use in conditions different from those specified in the authorisation conditions will be controlled.

5.3 STRATEGIC LINE III

Identification and spearheading of alternative and/or complementary measures of prevention and treatment

The optimisation of antibiotic use and the promotion of good practice cannot be completely achieved without the development of necessary alternatives for human and animal health.

Moreover, investigation actions are required to develop solutions in the fight against infectious diseases and ensure a better knowledge of pathogenic agents and their mechanisms of resistance.

This strategic line consists of four important measures (Figure 7), which include promotion of improved measures in animal hygiene, handling and wellbeing, promotion of the development and use of susceptibility tests and rapid methods of diagnosis, development of regulations in order to reduce the risk of infection and transmission of resistant organisms in the hospital and community setting and promotion of measures to improve the administration conditions of old products that contain non-critical antibiotics.

Identification and spearheading of alternative and/or complementary measures of prevention and treatment

MEASURE	MEASURE	MEASURE	MEASURE
III.1 Promotion of improved measures in animal hygiene, handling and wellbeing	III.2 Promotion of the development and use of antimicrobial susceptibility testing and rapid diagnostic methods	III.3 Development of regulations in order to reduce the risk of infection and transmission of resistant organisms in the hospital and community setting	III.4 Foster the adoption of measures to improve the administration conditions of old products that contain non-critical antibiotics

Figure 7. Strategic Line III



MEASURE

III.1

Promotion of improved measures in animal hygiene, handling and wellbeing

The application of biosecurity measures as well as good livestock and animal wellbeing practices are effective means of prevention and fighting against microorganisms and infections, permitting a subsequent limiting of antibiotic use.

The dissemination of these good practices and raising awareness in all the agents involved are one of the priorities of this Plan.

ANIMAL HEALTH

ACTIONS

- III.1.1. Promote the dissemination and use of the existing guidelines of good livestock practice and identify and develop those which are necessary but not yet prepared.
- III.1.2. Modify the existing guidelines to include recommendations solely intended for livestock farmers, giving a clear and comprehensible explanation of how antibiotics should be administered and/or prepared (in the case of medicinal products administered orally) and/or applied, so as to guarantee their appropriate use.
- III.1.3. Establish effective mechanisms which ensure that livestock farmers receive and use the guidelines.



MEASURE

III.2

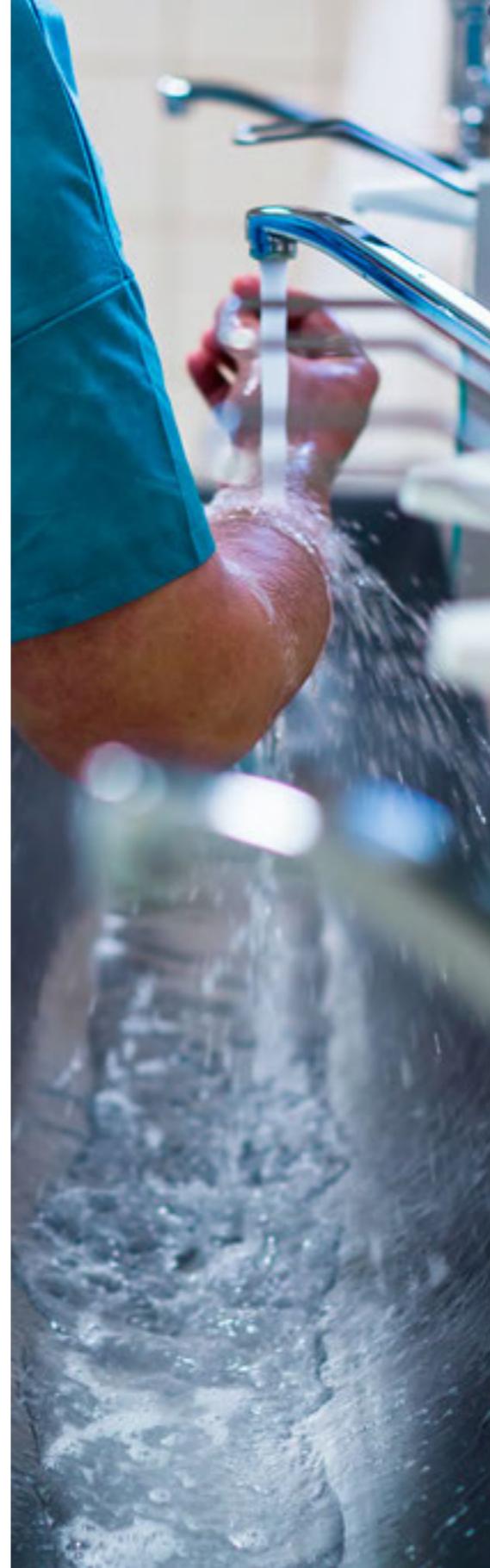
Promotion of the development and use of antimicrobial susceptibility testing and rapid diagnostic methods

The promotion of the development and use of rapid microbiological diagnostic methods and antimicrobial susceptibility testing using EUCAST criteria that permit early guidance in the diagnosis and, where appropriate, correct identification of the elected antibiotics in the treatment of bacterial diseases, guiding prescription appropriately and avoiding ineffective treatments.

HUMAN AND ANIMAL HEALTH

ACTIONS

- III.2.1. Promote the use of microbiological diagnostic tests.
- III.2.2. Standardisation of the antimicrobial susceptibility testing and their interpretation.
- III.2.3. Promote use of rapid diagnostic tests.



MEASURE

III.3

Development of recommendations in order to reduce the risk of infection and transmission of resistant organisms in primary and hospital care environments

The availability at a national level of recommendations on standard precautions, specific isolation precautions, environmental precautions, measures for the prevention of infections associated with medical devices and measures for hygiene and disinfection based on already existing national and International documents would permit the risk of infections to be reduced and help prevent their transmission.

HUMAN HEALTH

ACTIONS

- III.3.1. Develop recommendations and/or guidelines on the prevention of infection in the hospital setting at a national level.
- III.3.2. Develop recommendations and/or guidelines on the prevention of infection in primary care at a national level.
- III.3.3. Promote the prevention of transmission of resistant bacteria during health care by means of already existing programmes.



MEASURE

III.4

Foster the adoption of measures to improve the administration conditions of old products that contain non-critical antibiotics

With our current knowledge and particularly in view of the variation in AMR patterns and their influence on used doses, the administration conditions of antibiotics that have been in the market for many years need to be updated. This procedure should be carried out by the marketing authorisation holders voluntarily but they are products that would never recoup the investment needed. Finding strategies to facilitate laboratories to improve the administration conditions of these groups of antibiotic molecules so as to optimise their efficacy, especially the improvement of treatment regimes, would permit critical antibiotics to be reserved for those cases in which their use is indispensable.

ANIMAL HEALTH

ACTIONS

III.4.1. Find strategies to facilitate laboratories to improve the administration conditions of these groups of antibiotic molecules so as to optimise their efficacy, especially the improvement of treatment regimes.

5.4 STRATEGIC LINE IV Defining of priorities in research

How the appearance of bacterial resistance to antibiotics, the mechanisms of resistance development and the transmission of resistant bacteria are determined is still relatively unknown. Therefore, it is necessary to improve our knowledge of the mechanisms of action against bacteria, the causes and the consequences of the appearance and propagation of resistance and specific alternatives for antibiotic treatment.

On the other hand, the development of new active substances is complex and will perhaps require in the future similar initiatives to those followed with orphan and/or paediatric medicinal products. For a number of years pharmaceutical companies have invested very little in the search for new antibiotics. Paradoxically, new classes of antibiotics effective in resistant bacteria are needed but their use will be restricted. The result is a decrease in the therapeutic alternatives available.

Defining of priorities in research

MEASURE

IV.1

Develop and promote a common strategy in research

MEASURE

IV.2

Development of epidemiological and socioeconomic research

Figure 8. Strategic Line IV



MEASURE

IV.1

Develop and promote a common strategy in research

Transfer the importance of financing projects linked to this plan and give priority to their funding. Promote and support the search for new molecules so as to increase the therapeutic arsenal and provide new alternatives. This search and its application in veterinary medicine will be developed bearing in mind the importance and impact of said molecules in human medicine.

HUMAN AND ANIMAL HEALTH

ACTIONS

- IV.1.1. Promote research to improve knowledge of the mechanisms of AMR.
- IV.1.2. Encourage research to improve knowledge of the causes and consequences of the appearance and dissemination of AMR as well as the measures for its control and improvement in antibiotic use.
- IV.1.3. Promote the development of value added antibiotics against those already on the market.
- IV.1.4. Promote research of alternatives to antibiotics in the field of immunity.
- IV.1.5. Support research of new antibiotics that are restricted for use in veterinary medicine but not critical for human medicine.
- IV.1.6. Promote the development of new methods of detection and characterisation of AMR.
- IV.1.7. Study incentive mechanisms for research projects based on the identified needs.
- IV.1.8. Encourage research of new indications and ways of using known antibiotics.



MEASURE

IV.2

Development of epidemiological and socioeconomic research

A better understanding is required of the socioeconomic and medical context of antibiotic consumption and the development of AMR and its consequences. Not only is it a medical problem but also one that is social and the election of actions may depend on the comparative assessment of the principal strategies for prevention of the appearance or propagation of AMR.

HUMAN HEALTH

ACTIONS

- IV.2.1. Improve knowledge of the critical aspects that lead to inappropriate use of antibiotics in outpatients and obtain conclusions to propose interventions aimed at the rational use of antibiotics.
- IV.2.2. Evaluate the consequences of antibiotic resistance (mortality/morbidity, years of healthy life lost), as well as the associated costs (from the point of view of the community, social protection bodies and healthcare centres) and the effects of the strategies of prevention and care of infections due to resistant bacteria.
- IV.2.3. Improve knowledge of the quality of therapeutic care in primary and hospital care (quality factors, propagation factors and application of recommendations, assessment of the impact of public decisions on the control of bacterial resistance).

ANIMAL HEALTH

ACTIONS

- IV.2.4. Improve understanding of the critical factors that lead to a high consumption of antibiotics on farms.

5.5
STRATEGIC LINE V
 Training and information
 for healthcare professionals

Healthcare professionals are the primary actors in the launching of the strategy of prudent use of antibiotics. Therefore, through training and information we will achieve their adherence to the public health strategy initiated.

The training of healthcare professionals must cover all the stages of their professional life and said training should include all aspects of the prudent use of antibiotics, including misuse and the appearance of AMR. The development of self-evaluation tools completes this strategic line.

Training and information for healthcare professionals

<p>MEASURE</p> <p>V.1</p> <p>Mobilise healthcare professionals</p>	<p>MEASURE</p> <p>V.2</p> <p>Encourage training of healthcare professionals</p>	<p>MEASURE</p> <p>V.3</p> <p>Develop ongoing training programmes for healthcare professionals according to uniformity criteria in those issues related to AMR</p>	<p>MEASURE</p> <p>V.4</p> <p>Develop the self-evaluation of prescribers</p>
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Figure 9. Strategic Line V



MEASURE

V.1

Mobilise healthcare professionals

The adherence of healthcare professionals to the Plan is critical for its success. Said healthcare professionals are the principal actors in the implementation of a policy of rational use of antibiotics. Therefore, it is essential that they are well informed about the challenges of this rational use policy and their role in this respect.

HUMAN AND ANIMAL HEALTH

ACTIONS

- V.1.1.** Inform professionals about the risks of the development of antimicrobial resistance.
- V.1.2.** Make known the individual and collective benefits of the rational use of antibiotics to professionals.
- V.1.3.** Foster communications on the control of antibiotic resistance and prudent use of antibiotics in scientific forums.



MEASURE

V.2

Encourage training of healthcare professionals

Given that the position of healthcare professionals is central in any Plan which attempts to improve the rational use of antibiotics, training of said professionals should encompass their first contacts with the teaching of the elected profession, ongoing training and postgraduate courses or masters. Since we are dealing with different professions on many occasions, it is necessary that all of these have segments included in their training programmes and curricula that guarantee a close approximation to the problem.

HUMAN AND ANIMAL HEALTH

ACTIONS

- V.2.1.** Promote the training of healthcare professionals in all periods of their education: university, specialisation and ongoing training. Complete their training in all its cycles (pre-graduate, graduate, postgraduate, specialisation).
- V.2.2.** Ensure that the acquisition of necessary competences to improve the rational use of antibiotics and reduce microbial resistance is guaranteed in the official specialisation programmes in Health Sciences.



MEASURE

V.3

Develop ongoing training programmes of healthcare professionals with uniform criteria in those matters relating to AMR

In order to guarantee long-term maintenance of the actions foreseen in this Plan, it is necessary to incorporate ongoing training actions that share the highest quality criteria and that reach the maximum possible number of healthcare professionals.

HUMAN AND ANIMAL HEALTH

ACTIONS

- V.3.1.** Include the rational use of antibiotics in the continuous training modules.
- V.3.2.** Encourage already existing initiatives so that they reach the maximum number of healthcare professionals.
- V.3.3.** Complete ongoing training in Health Sciences and related disciplines (Medicine, Dentistry, Pharmacy, Nursing and Veterinary Science).



MEASURE

V.4

Develop the self-evaluation of prescribers

It is considered necessary to launch a coordinated feedback mechanism with prescribers both in the community and in hospital care that permits them to know their antibiotic prescriptions grouped together (personalised prescription profile). This feedback, together with the respective local and regional comparison, should make the professional aware of what his practice is compared to other professionals.

HUMAN AND ANIMAL HEALTH

ACTIONS

- V.4.1.** Define the assessment modalities of antibiotic prescription practice and actions for their improvement and propose a prepared and validated method for health authorities.
- V.4.2.** Develop the criteria to audit prescription practice in healthcare centres.
- V.4.3.** Have a common and updated system of information of prescribed antibiotics available (personal profile).
- V.4.4.** Integrate into the prescription programmes the list of antibiotics that need a special reserve with a specific control.
- V.4.5.** Develop guidelines of good prescription practice of antibiotics in veterinary medicine, with specific measures adapted to each species and a treatment and metaphylaxis protocol of bacterial diseases.

5.6

STRATEGIC LINE VI

Communication and raising awareness in the population as a whole and in population subgroups

The actions to raise awareness in the population are of two types. On one hand, campaigns aimed at the general public, and on the other, specific communication intended for population groups at risk.

Communication and raising awareness in the population as a whole and in population subgroups

MEASURE

VI.1

Campaigns for the general population

MEASURE

VI.2

Specific information for population subgroups

Figure 10. Strategic Line VI



MEASURE

VI.1

Campaigns for the general population

The objective is to raise awareness in consumers about the individual and collective benefits of the rational use of antibiotics and provide information on the risks of AMR so as to encourage adherence to the policy of prudent use of antibiotics.

HUMAN AND ANIMAL HEALTH

ACTIONS

- VI.1.1.** Identify the communication campaigns already carried out and explore the continuity of communication campaigns for the rational use of antibiotics that have demonstrated a positive impact on the reduction of AMR.
- VI.1.2.** Use the European awareness conference on November 18 to strengthen the rational use of antibiotics through actions aimed at professionals and the general public.
- VI.1.3.** Publish press articles signed by opinion leaders that reinforce the campaign issues on a regular basis.
- VI.1.4.** Establish and disseminate an information platform for consumers.



MEASURE

VI.2

Specific information for population subgroups

Reach out to the population groups that present a greater risk of bacterial infection due to their work or health circumstances.

HUMAN AND ANIMAL HEALTH

ACTIONS

- VI.2.1.** Livestock farmers.
- VI.2.2.** Household pet owners.
- VI.2.3.** Primary care and hospital patients, with specific actions through the network of schools of NHS patients.
- VI.2.4.** Children of school age.
- VI.2.5.** The elderly.
- VI.2.6.** Caregivers of patients, children and the elderly.

5.7 SUMMARY OF THE STRATEGIC LINES

I. Surveillance of antibiotic consumption and antimicrobial resistance			
MEASURE	MEASURE	MEASURE	MEASURE
I.1 Monitoring of antibiotic consumption	I.2 Improvement of the surveillance of antibiotic resistance	I.3 Control of the use of critical antibiotics	I.4 Participation in European and international projects to exchange information
HUMAN HEALTH ACTIONS I.1.1. Improve the data collection of antibiotic consumption in the community and hospitals. I.1.2. Ensure the exploitation and analysis of data at a local, regional and national level and information feedback.	HUMAN HEALTH ACTIONS I.2.1. Strengthen AMR data collection, with a special analysis of expanding AMR. I.2.2. Analysis and exploitation of AMR data, with special analysis of expanding AMR. I.2.3. Crossing of information on AMR and consumption to make a biannual presentation of the results, identifying the pairs of antibiotics and bacteria that are especially representative.	HUMAN AND ANIMAL HEALTH ACTIONS I.3.1. Identify and list the antibiotic classes considered as critical so as to proceed to a specific vigilance of their consumption and the appearance of resistance. HUMAN HEALTH ACTIONS I.3.2. Raise awareness among prescribers in order to limit the use of the listed antibiotics with the help of the consumption data.	HUMAN AND ANIMAL HEALTH ACTIONS I.4.1. A continuous revision of the current European and international situation as regards AMR and the rational use of medicines will be performed, with the aim of distributing information and making it available to the interested parties. I.4.2. Continue contribution in the different European projects already being developed with regard to antibiotic consumption and use, and the AMR (ESVAC, monitoring of zoonotic pathogens, ESAC-net and EARS-net) and participate in other European and international activities to exchange information
ANIMAL HEALTH ACTIONS I.1.3. Improve the vigilance systems of antibiotic sales, including data at a distribution level. I.1.4. Development and implementation of the electronic prescription and telematic control systems of treatments linked to exploitation. I.1.5. Ensure the exploitation and analysis of data at a local, regional and national level and information feedback	ANIMAL HEALTH ACTIONS I.2.4. Analysis and exploitation of bacterial resistance data and their evolution in zoonotic and indicator bacteria, with a special analysis of expanding AMR. I.2.5. Crossing of information on AMR and consumption to make a biannual presentation of the results, identifying the pairs of antibiotics and bacteria that are especially representative.	ANIMAL HEALTH ACTIONS I.3.3. Limit the prescription of those antibiotics whose effectiveness has to be particularly conserved.	

II. Control of bacterial resistance			
MEASURE	MEASURE	MEASURE	MEASURE
II.1 Control of the dissemination of resistance	II.2 Design and dissemination of tools for the promotion of good practice in antibiotic use	II.3 Preparation of guidelines for exceptional antibiotic prescription within the veterinary health programmes	II.4 Limiting of prophylactic use of antibiotics to those cases with defined clinical needs
HUMAN HEALTH ACTIONS II.1.1. Identify and strengthen the setting up of a network of laboratories for early detection of resistant bacteria and identification of their mechanisms of resistance. II.1.2. Consolidate and harmonise the vigilance systems and control of infections associated with health care and reinforce these so that the multidisciplinary teams increase their capacity of reaction when facing alerts. II.1.3. Work with the regional governments to reinforce vigilance and notification of outbreaks.	HUMAN HEALTH ACTIONS II.2.1. Launching of programmes promoting prudent use of antibiotics. II.2.2. Implementation of guidelines for specific use in the community.	ANIMAL HEALTH ACTIONS II.3.1. Develop guidelines pertaining to the exceptional prescription of antibiotics when there are no other existing alternatives, within the health programmes of livestock exploitation.	HUMAN HEALTH ACTIONS II.4.1. Identify the clinical situations in which prophylactic use of antibiotics is required and write guidelines on the administration of prophylaxis in primary and hospital care. This will be carried out under the programmes of prudent use in the hospital setting.
ANIMAL HEALTH ACTIONS II.1.4. Develop the vigilance network of pathogen bacteria in animals and establish a plan according to animal species, identifying the route of implementation. II.1.5. Identify collaborator and/or reference laboratories for the isolation and identification of pathogen bacteria resistant to antibiotics.	ANIMAL HEALTH ACTIONS II.2.3. Develop more extensively a specific section on the good use of antibiotics for each animal species in the guidelines on responsible use. II.2.4. Identify if it is necessary to develop other specific guidelines (Fish, birds bred for hunting purposes, other ornamental birds, etc). II.2.5. Promote that antibiotic treatments are based on microbiological diagnosis and susceptibility testing. II.2.6. Develop guidelines in which specific recommendations are given for the use of determined antibiotics such as "first line", "second line" or "final line" in relation to specific infections.		ANIMAL HEALTH ACTIONS II.4.2. The diseases in which the prophylactic use of antibiotics is indispensable shall be identified by animal species and included in the Plan. II.4.3. Antibiotic use in conditions different from those specified in the authorisation conditions will be controlled.

III.

Identification and spearheading of alternative and/or complementary measures of prevention and treatment

MEASURE	MEASURE	MEASURE	MEASURE
<p>III.1</p> <p>Promotion of improved measures in animal hygiene, handling and wellbeing</p>	<p>III.2</p> <p>Promotion of the development and use of antimicrobial susceptibility testing and rapid diagnostic methods</p>	<p>III.3</p> <p>Development of regulations in order to reduce the risk of infection and transmission of resistant organisms in the hospital and community setting</p>	<p>III.4</p> <p>Foster the adoption of measures to improve the administration conditions of old products that contain non-critical antibiotics.</p>
<p>ANIMAL HEALTH ACTIONS</p> <p>III.1.1. Promote the dissemination use of the existing guidelines of good livestock practice and identify and develop those which are necessary but not yet prepared.</p> <p>III.1.2. Modify the existing guidelines to include recommendations solely intended for livestock farmers, living a clear and comprehensible explanation of how antibiotics should be administered and/or prepared (in the case of medicinal products administered orally) and/or applied, so as to guarantee their appropriate use.</p> <p>III.1.3. Establish effective mechanisms which ensure that livestock farmers receive and use the guidelines.</p>	<p>HUMAN AND ANIMAL HEALTH ACTIONS</p> <p>III.2.1. Promote the use of microbiological diagnostic tests</p> <p>III.2.2. Standardisation of the antimicrobial susceptibility testing and their interpretation.</p> <p>III.2.3. Promote use of rapid diagnostic tests.</p>	<p>HUMAN HEALTH ACTIONS</p> <p>III.3.1. Develop recommendations and/or guidelines on the prevention of infection in the hospital setting at a national level.</p> <p>III.3.2. Develop recommendations and/or guidelines on the prevention of infection in primary care at a national level.</p> <p>III.3.3. Promote the prevention of transmission of resistant bacteria during health care by means of already existing programmes.</p>	<p>ANIMAL HEALTH ACTIONS</p> <p>III.4.1. Find strategies to facilitate laboratories to improve the administration conditions of these groups of antibiotic molecules so as to optimise their efficacy, especially the improvement of treatment regimes.</p>

IV.

Defining of priorities in research

MEASURE	MEASURE
<p>IV.1</p> <p>Develop and promote a common strategy in research</p>	<p>IV.2</p> <p>Development of epidemiological and socioeconomic research</p>
<p>HUMAN AND ANIMAL HEALTH ACTIONS</p> <p>IV.1.1. Promote research to improve knowledge of the mechanisms of AMR.</p> <p>IV.1.2. Encourage research to improve knowledge of the causes and consequences of the appearance and dissemination of AMR as well as the measures for its control and improvement in antibiotic use.</p> <p>IV.1.3. Promote the development of value added antibiotics against those already on the market.</p> <p>IV.1.4. Promote research of alternatives to antibiotics in the field of immunity.</p> <p>IV.1.5. Support research of new antibiotics that are restricted for use in veterinary medicine but not critical for human medicine.</p> <p>IV.1.6. Promote the development of new methods of detection and characterisation of AMR.</p> <p>IV.1.7. Study incentive mechanisms for research projects based on the identified needs.</p> <p>IV.1.8. Encourage research of new indications and ways of using known antibiotics.</p>	<p>HUMAN HEALTH ACTIONS</p> <p>IV.2.1. Improve knowledge of the critical factors that lead to inappropriate use of antibiotics in outpatients and arrive at conclusions in order to propose interventions aimed at the rational use of antibiotics.</p> <p>IV.2.2. Evaluate the consequences of resistance to antibiotics (mortality/morbidity, years of healthy life lost), as well as the associated costs (from the point of view of the community, social protection bodies and healthcare centres) and the effects of the strategies of prevention and care of infections caused by resistant bacteria.</p> <p>IV.2.3. Improve knowledge of the quality of therapeutic care in primary and hospital care (quality factors, factors of propagation and application of recommendations, assessment of the impact of public decisions in control of bacterial resistance).</p> <p>ANIMAL HEALTH ACTIONS</p> <p>IV.2.4. Improve understanding of the critical factors that lead to a high consumption of antibiotics on farms</p>

V.

Training and information for healthcare professionals

MEASURE	MEASURE	MEASURE	MEASURE
V.1 Mobilise healthcare professionals	V.2 Encourage training of healthcare professionals	V.3 Develop ongoing training programme for healthcare professionals according to uniformity criteria in those issues related to AMR	V.4 Develop the self-evaluation of prescribers
HUMAN AND ANIMAL HEALTH ACTIONS V.1.1. Inform professionals about the risks of the development of antimicrobial resistance. V.1.2. Make known the individual and collective benefits of the rational use of antibiotics to professionals. V.1.3. Foster communications on the control of antibiotic resistance and prudent use of antibiotics in scientific forums.	HUMAN AND ANIMAL HEALTH ACTIONS V.2.1. Promote the training of healthcare professionals in all periods of their education: university, specialisation and ongoing training. Complete their training in all its cycles (pre-graduate, graduate, postgraduate, specialisation). V.2.2. Ensure that the acquisition of necessary competences to improve the rational use of antibiotics and reduce microbial resistance is guaranteed in the official specialisation programmes in Health Sciences.	HUMAN AND ANIMAL HEALTH ACTIONS V.3.1. Include the rational use of antibiotics in the continuous training modules. V.3.2. Encourage already existing initiatives so that they reach the maximum number of healthcare professionals. V.3.3. Complete ongoing training in Health Sciences and related disciplines (Medicine, Dentistry, Pharmacy, Nursing and Veterinary Science).	HUMAN AND ANIMAL HEALTH ACTIONS V.4.1. Define the assessment modalities of antibiotic prescription practice and of actions for their improvement and propose a prepared and validated method for health authorities. V.4.2. Develop the criteria to audit prescription practice in healthcare centres. V.4.3. Have a common and updated system of information of prescribed antibiotics available (personal profile). V.4.4. Integrate into the prescription programmes the list of antibiotics that need a special reserve with a specific control. V.4.5. Develop guidelines of good prescription practice of antibiotics in veterinary medicine, with specific measures adapted to each species and a treatment and metaphylaxis protocol of bacterial diseases.

VI.

Communication and raising awareness in the population as a whole and in population subgroups

MEASURE	MEASURE
VI.1 Campaigns for the general public	VI.2 Specific information for population subgroups
HUMAN AND ANIMAL HEALTH ACTIONS VI.1.1. Identify the communication campaigns already carried out and explore the continuity of communication campaigns for the rational use of antibiotics that have demonstrated a positive impact on the reduction of AMR. VI.1.2. Use the European awareness conference on November 18 to strengthen the rational use of antibiotics through actions aimed at professionals and the general public. VI.1.3. Publish press articles signed by opinion leaders that reinforce the campaign issues on a regular basis. VI.1.4. Establish and disseminate an information platform for consumers.	HUMAN AND ANIMAL HEALTH Y ANIMAL ACTIONS VI.2.1. Livestock farmers. VI.2.2. Household pet owners. VI.2.3. Primary care and hospital patients, with specific actions through the network of schools of NHS patients. VI.2.4. Children of school age. VI.2.5. The elderly. VI.2.6. Caregivers of patients, children and the elderly.

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