

International Policy Overview: Antibiotic Resistance

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This International Policy Overview has been reviewed by an expert.

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This policy overview is linked to the following topic in the National Public Health Compass [in Dutch] ([Nationaal Kompas Volksgezondheid](#)): > [Preventie gericht op antibioticaresistentie](#) (prevention aimed at antibiotic resistance), especially to the sub-topics:

- [Wat zijn de effecten?](#) (What are the effects of the intervention?)
 - [Zijn er verschillen tussen Nederland en andere landen?](#) (Are there differences between the Netherlands and other countries?)
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This policy overview is linked to the following European Community Health Indicators (ECHI):

- [18. Selected communicable diseases](#)
- [74. Medicine use, selected groups](#)
- [82. Surgical wound infections](#)

Currently only for selected communicable diseases data are available in the European Health Indicators database/[data presentation tool](#) on the website of the European Commission.

1a. Summary

Antibiotic resistance policies: evidence for effective policy measures and interventions

Antibiotic policies should aim at prudent use of antibiotics and at the prevention of spread or transmission of resistant bacteria. Therefore antibiotic policies need a mix of several preventive interventions which should be implemented on different levels. National campaigns may help to create awareness of the problem of antibiotic resistance and the need for prudent use among European citizens. The repetition of these awareness campaigns increases effectiveness. Furthermore, educational interventions and restrictive prescribing policies may reduce resistance through a decrease of antibiotic use. Computer-based programs improve prescribing practices among healthcare professionals. In addition, hygienic measures are effective in combating transmission of antibiotic resistance. Therefore the Dutch 'search and destroy' policy can be seen as an effective approach within hospitals. However, little is known about the effectiveness of infection control strategies in nursing homes. Finally, surveillance of antibiotic use and resistance can help shape effective antibiotic policies.

Antibiotic resistance policies in international perspective: EU policies and strategies

In 2001 the European Commission adopted the European Community Strategy against antimicrobial resistance. The Council Recommendation 2002/77/EC on the prudent use of antimicrobial agents in human medicine states that multidisciplinary coordination on the Community-level is needed to lower the burden of antibiotic resistance. This Council Recommendation asks Member States to take action on a national level through:

- The development of national surveillance systems on antibiotic use and resistance;
- The implementation of prevention methods and infection control (support of prudent use and elimination of the transmission of infectious diseases);
- The improvement of education and training of health professionals (such as on the appropriate use of antimicrobials and hygiene standards);
- Informative approaches to raise awareness of prudent use of antibiotics among the general public.

In addition several projects on antibiotic resistance are funded through the EU Public Health Action Programmes or the Seventh Framework Programme. The main European Institution in the field of antibiotic resistance is the European Centre for Disease Prevention and Control (ECDC), which coordinates and funds a European network of national surveillance systems. Another important European institution is the European Food Safety Authority (EFSA), which provides scientific advice on the risks of spread and transfer to humans of antimicrobial resistant micro-organisms via food products.

Antibiotic resistance policies in international perspective: impact of WHO

At European level, the WHO is developing a regional strategy, recognizing the need for an interdisciplinary approach to combat antibiotic resistance. This policy is expected to be finished in September 2011 and will contain seven strategic objectives to promote this integrated approach:

1. Promote national intersectoral coordination;
2. Strengthen surveillance of antimicrobial resistance;
3. Strengthen surveillance and promote stewardship of antimicrobial drug use;
4. Strengthen surveillance of resistance to and use of antimicrobial agents in the animal food industry;
5. Improve infection control and stewardship of antimicrobial resistance in health care settings;
6. Promote research and innovation on new drugs and technology; and
7. ensure patient safety and improve awareness of antimicrobial use and resistance.

National antibiotic resistance policies and strategies

In spite of large differences in the incidence rates of antibiotic resistance, most European countries base their policies to combat antibiotic resistance on the same European approach, which is described in Recommendation [2002/77/EC](#) on the prudent use of antimicrobial agents in human medicine. Therefore, their national policies contain similar elements although there are some striking differences as well. The Commission summarized the main actions taken at Member States and European Union level in the first (2005) and the second report (2009) from the Commission to the Council on the implementation of the Recommendation. The general conclusion from both reports is that even though progress has been made since the implementation of Recommendation 2002/77/EC, still work has to be done in order to combat antimicrobial resistance. Overall, the participation in European projects and partnerships is well established, but the field of raising awareness via campaigns targeting health professionals and the general public needs to be further developed. Also more focus is needed on collaboration between the human and animal health sectors, especially in the countries where no collaboration between the two sectors has been initiated yet. More information on the main conclusions of these reports can be found in chapter 5.

1b. Samenvatting (Summary in Dutch)

Beleid gericht op antibioticaresistentie: bewijs voor doeltreffende maatregelen en interventies

Beleid op het gebied van antibioticaresistentie zou zich moeten richten op het verantwoorde gebruik van antibiotica en op het voorkómen van de verspreiding van resistente bacteriën. Daarom zou het antibioticabeleid moeten bestaan uit een mix van diverse preventieve interventies die moeten worden uitgevoerd op verschillende niveaus. Nationale campagnes kunnen wellicht helpen om Europeanen bewust te maken van het probleem van antibioticaresistentie en de noodzaak van verantwoord gebruik van antibiotica. Herhaling van deze campagnes verhoogt de effectiviteit. Bovendien kunnen educatieve interventies en beleid dat zich richt op het beperkt voorschrijven van antibiotica leiden tot een afname van resistentie door een daling van het antibioticagebruik. Computerprogramma's en richtlijnen kunnen het voorschrijfgedrag van antibiotica door zorgprofessionals verbeteren. Ook hygiënemaatregelen zijn effectief tegen de verspreiding van resistente bacteriën. Daarom kan het Nederlandse 'search and destroy' beleid gezien worden als een effectieve aanpak binnen ziekenhuizen. Er is echter weinig bekend over de effectiviteit van infectiebestrijdingstrategieën in verpleeghuizen. Ten slotte zijn de surveillance van antibioticagebruik en van resistentie belangrijke elementen in effectief antibioticabeleid.

Beleid gericht op antibioticaresistentie in internationaal perspectief: EU beleid en strategieën

In 2001 heeft de Europese Commissie de Europese communautaire strategie tegen antimicrobiële resistentie aangenomen. De aanbeveling van de Raad 2002/77 /EC betreffende het zorgvuldige gebruik van antimicrobiële medicijnen stelt dat multidisciplinaire coördinatie op het communautaire niveau nodig is om de last van antibioticaresistentie te verlagen. Deze aanbeveling van de Raad verzoekt de lidstaten om op nationaal niveau actie te ondernemen door:

- De ontwikkeling van nationale surveillance systemen gericht op antibioticagebruik en antibioticaresistentie;
- De uitvoering van preventiemaatregelen en infectiebestrijding (ondersteuning van verantwoord gebruik en tegengaan van de verspreiding van besmettelijke ziekten);
- De verbetering van onderwijs en opleiding van zorgprofessionals (inclusief educatie over het juiste gebruik van antibiotica en hygiënestandaarden);
- Informatieve interventies om het bewustzijn van zorgvuldig antibioticagebruik bij het grote publiek te promoten.

Daarnaast worden er ook verschillende projecten gericht op het verminderen van antibioticaresistentie gefinancierd door de EU Public Health Action programma's en het zevende kaderprogramma. De belangrijkste Europese instelling op het gebied van antibioticaresistentie is het Europese Centrum voor ziektepreventie en -bestrijding (ECDC), dat een Europees netwerk van nationale surveillance systemen coördineert en financiert. Een andere belangrijke Europese instelling is de Europese Autoriteit voor Voedselveiligheid (EFSA), die wetenschappelijk advies geeft over de risico's van verspreiding en overdracht op de mens van resistente micro-organismen via voedselproducten.

Beleid gericht op antibioticaresistentie in internationaal perspectief: impact van de WHO en andere intergouvernementele organisaties

Op Europees niveau is de WHO een regionale strategie aan het ontwikkelen. Hierin wordt de noodzaak van een interdisciplinaire benadering om antibioticaresistentie te bestrijden onderkend. De strategie zal naar verwachting in september 2011 worden gepubliceerd en bevat zeven strategische doelstellingen om deze geïntegreerde aanpak te bevorderen:

1. Het bevorderen van nationale intersectorale coördinatie;
2. Het versterken van de surveillance van antibioticaresistentie;
3. Het versterken van surveillance van antibioticagebruik en het bevorderen van het verantwoorde antibioticagebruik;
4. Het versterken van de surveillance van antibioticaresistentie en -gebruik in de diervoederindustrie;
5. Het verbeteren van infectiebestrijding en het zorgvuldig omgaan met antibioticaresistentie in gezondheidszorginstellingen;
6. Het bevorderen van onderzoek en innovatie met betrekking tot nieuwe antibiotica en technologie;
7. Het garanderen van patiëntveiligheid en stimuleren van het bewustzijn van gebruik van antimicrobiële middelen en resistentie.

Beleid en strategieën gericht op antibioticaresistentie op nationaal niveau

Ondanks grote verschillen in de incidentie van resistentie tegen antibiotica, hebben de meeste Europese landen hun antibioticaresistentiebeleid gebaseerd op dezelfde Europese aanpak. Deze aanpak staat in Aanbeveling [2002/77/EC](#) over het verantwoorde gebruik van antimicrobiële middelen in de menselijke gezondheidssector. Om deze reden bevat het beleid van Europese landen veel dezelfde elementen, maar toch zijn er ook enkele opvallende verschillen. De Commissie heeft de belangrijkste acties van de lidstaten en op het niveau van de Europese Unie in de eerste (2005) en het tweede verslag (2009) over de uitvoering van de aanbeveling van de Europese Raad samengevat. De algemene conclusie van beide rapporten is dat er weliswaar vooruitgang geboekt is sinds de uitvoering van Aanbeveling 2002/77/EC, maar er kan nog veel verbeterd worden in de strijd tegen antibioticaresistentie. Over het algemeen is de deelname aan Europese projecten en samenwerkingsverbanden goed opgebouwd, maar op het gebied van bewustwording via campagnes gericht op zorgprofessionals en het algemene publiek kan nog veel vooruitgang geboekt worden. Ook is er meer aandacht nodig voor de samenwerking tussen de humane en veterinaire gezondheidssector, vooral in de landen waar tot op heden geen samenwerking tussen de twee sectoren was. Meer informatie over de belangrijkste conclusies van deze rapporten is te vinden in hoofdstuk 5.

2. Definition and scope

2.1. Description of problem that needs to be addressed

Antibiotics can be defined as medicines that have the ability to eliminate the growth of or to kill bacteria in order to cure bacterial infections either in human beings, animals or in flora. There are several antibiotics that differ in their chemical structure and therefore they are not all effective against the same bacteria.

According to the [European Centre of Disease Prevention and Control](#) (ECDC), antibiotic resistance is present when specific antibiotics have lost their ability to kill or stop the growth of bacteria. Although some micro-organisms are already resistant to specific antibiotics by their nature, the process of developing resistance to antibiotics can be accelerated by a high consumption frequency and by imprudent use of antibiotics (e.g. premature treatment failure due to a shorter duration, using leftovers of treatment, higher doses, etc). Due to this resistance, antimicrobial agents become less effective or completely lose their effectiveness. For some infectious multi-drug resistant bacteria only a limited number of remaining effective antibiotics are available. This is a serious problem because several surgical operations cannot be performed if no effective antibiotics are available anymore. Furthermore, antibiotic resistance leads to higher mortality and increased health care costs.

The occurrence of resistant micro-organisms in the agricultural sector can lead to public health problems as well. Food may be contaminated with these resistant bacteria, posing a potential health risk to people who eat uncooked food. Besides, direct contact with infected animals also increases the risk of transmission of resistant micro-organisms from animals to humans. Furthermore, resistant bacteria may end in agricultural sewage which may reach humans through drinking water or contaminated irrigation water.

2.2. Which types of policies are described in this overview?

One of the major drivers for the development of antibiotic resistance is imprudent use of medicines:

- In humans: in the community, in hospitals as well as in other health care settings;
- In food producing animals.

Another major driver is the spread and transmission of resistant micro-organisms between humans, between animals, and between humans and animals. Therefore, antibiotic policies should aim at prudent use of antibiotics and at the prevention of spread or transmission of bacteria resistant to antibiotics.

- Strategies to improve prudent use of antibiotics in the community include raising awareness of rational use of antibiotics. In the hospital and in other health care settings this can be done through educating health professionals on rational use and through good prescribing trainings for health professionals. Within the agricultural sector, strategies to improve prudent use include limiting the use of antibiotics in animals.
- Strategies to prevent the spread of resistant bacteria include promoting proper personal hygiene within the community setting. In health care settings such strategies include improvements in hospital hygiene, prescreening of patients before entering hospitals, the isolation of patients infected with resistant bacteria and – in general - effective outbreak management.

In the agricultural setting:

- Strategies should address to proper hygiene of farmers and preventing animals infected with resistant micro-organisms from being used for producing food.

Adequate surveillance should assist both in improving prudent use of antibiotics and preventing the spread of resistance micro-organisms, in humans, as well as in animals.

This overview aims to provide information on the range and effectiveness of measures, ranging from national law to local preventive interventions. Obviously the (potential) role of national governments differs, depending on the type of strategy discussed. More generally, national governments and health care systems influence the coordination of surveillance systems. Furthermore, the emergence and development of antibiotic resistance is also determined by legislation and policies related to the development, licensing, distribution and sale of existing and new antimicrobial agents.

In this policy overview information on antibiotic resistance policies is described at a rather general level, as to provide a quick overview of what is known about effectiveness of different types of strategies (see chapter 3), the international (policy) framework (see chapter 4), and what kind of strategies are being applied in other countries (see chapter 5). This means for example that policies and strategies will not be described at the level of specific settings. More details can be found in the literature and resources used for compiling this policy overview.

2.3. Are there relevant subgroups to address?

Several subgroups in the community, hospitals and other health care settings and the agricultural sector are at increased risk of developing and spreading antibiotic resistance, and are therefore a target group for prevention. Relevant subgroups in the community are people with a weak immune system, such as pregnant women, children, persons who have chronic illnesses and elderly people. In the hospital and other health care settings, antibiotics are used frequently and resistance can easily develop and spread. Therefore, both patients and health care professionals have a higher risk of developing resistance or contracting and transmitting resistant bacteria. Another important subgroup in the health care setting is the group of emigrants and travellers who received hospitalized care in another country with high antibiotic resistance rates. Also the elderly population is especially susceptible to the occurrence and consequences of antibiotic resistance. Not only do they have a weaker immune system, they also use antibiotics more frequently and more often stay in health care settings. In the agricultural sector, farmers not only are at increased risk for antibiotic resistance through frequent contact with antibiotics and through transmission of resistance from animals, they also play an important role in prudent use of antibiotics in food producing animals. This IPO therefore, both describes strategies to improve rational use of antibiotics and to prevent the spread of transmission targeted towards the general public, hospital patients, health care professionals, veterinarians and farmers.

2.4. Limitations related to mapping policies

When describing policies, one is usually limited to official documents, e.g. laws or national strategy papers. This implies that it is often not clear to what extent rules and regulations are being enforced in practice, or to what extent plans have actually been put into action. This limitation should be taken into account while reading this policy overview. An additional limitation comes from the fact that only information available in English and/or Dutch has been used for compiling this overview.

2.5. Geographical scope

The focus in this overview is mainly on Europe. This is because a lot of information has been compiled for the broader European region under the antibiotic resistance strategies and recommendations provided by the European Union and WHO (see chapter 4). Although there are common initiatives against antibiotic resistance at European level, large differences in prevalence and incidence rates of resistant bacteria can be found within the European region, especially between the southern and northern part of Europe (see chapter 5).

2.6. Terminology applied in international context

Different terms are used to describe the problem of antibiotic resistance, such as 'antibiotic resistance', 'antimicrobial resistance', 'antimycobacterial drugs resistance' and 'antibacterial drug

resistance'. These terms are not identical. 'Antibacterials', which is the synonym of antibiotics, is a subgroup of antimicrobials. Antibacterials are only effective against bacterial infections, whereas other subgroups of antimicrobials are effective against tuberculosis and other mycobacterial infections (antimycobacterial drugs), viral infections (antivirals), fungal infections (antifungals), malaria and other infections due to parasites (antiparasital drugs). This international policy overview will focus on antibacterial and antimycobacterial resistance only.

3. Antibiotic resistance policies: evidence for effective policy measures and interventions

Antibiotic policies need a mix of several preventive interventions

Antibiotic policies should aim at prudent use of antibiotics and at the prevention of spread or transmission of resistant bacteria. Therefore antibiotic policies need a mix of several preventive interventions, such as;

- Raising awareness on the rational use of antibiotics;
- Educating health professionals in good prescribing practices and using prescription guidelines;
- Limits on the use of antibiotics for animals;
- Improving personal and hospital hygiene and hospital infection control programs.

The most ideal situation exists when all previous mentioned interventions are combined with surveillance of resistance and antibiotic use. This combination may help contain the emergence and spread of resistant organisms (Stein, 2005).

Surveillance of antibiotic use and resistance needed to determine effectiveness of policies

The level of resistance to antibiotics is correlated with the level of consumption (WHO, 2005). The impact of policies, with the aim to tackle antibiotic resistance via the reduction of antibiotic consumption, can be assessed by monitoring antibiotic consumption (expressed in Defined Daily Doses, DDDs) (Coast et al, 1998; Mach et al, 2007) or by monitoring the total amount of antibiotic prescriptions (Wutzke et al, 2006). The ultimate goal is to determine a significant reduction of antibiotic resistance in the community. For this surveillance of antibiotic use and resistance is needed.

The need for a multi-level approach

The control of antibiotic resistance is viewed as effective if implemented on different levels: national programs, hospital infection control programs and prescribing practices programs (Cunha, 2001; DiazGranados et al, 2008). The strengthening or development of international partnerships in multiple sectors should help to combat antimicrobial resistance (DiazGranados et al, 2008). Additionally the development of regulations in this field should be of assistance too. Campaigns targeting different levels and groups, such as the general public and the health professionals may be more effective than those focusing on one of the groups only (McNulty et al, 2010).

National campaigns may reduce consumption through creating awareness among European citizens

Public campaigns are implemented in several European countries and may contribute to a more prudent use of antibiotics in outpatients (Huttner et al, 2010).

The French national campaign from 2002-2007 aimed at both general public and health care professionals and resulted in a reduction in the number of unnecessary antibiotic prescriptions. This campaign stresses the importance of awareness; on the one side creating awareness of the problem of antibiotic resistance, on the other side creating awareness of the need for proper surveillance of

antibiotic use and resistance (Sabunca et al, 2002). The national campaign in the United Kingdom (2008) resulted only in a small reduction in antibiotic use (McNulty et al, 2010).

Mass media campaigns have the potential to change the antimicrobial prescribing practices (Lambert et al, 2007). In the United States this kind of campaign, focusing mainly on the general public and healthcare providers, has led to a significant reduction in antibiotic consumption (Gonzales et al, 2008), even though some antibiotics in the United States are available as over-the-counter drugs.

Repetition of awareness campaigns increases effectiveness

Repetition of awareness campaigns increases effectiveness and especially simple repeated messages increase a campaign's effectiveness. In Belgium this has led to a decreased sale of antibiotics (Bauraind et al, 2001). The repetition of campaigns over several years may contribute to the reduction of antibiotic resistance prevalence rates (McNulty et al, 2010).

Restrictive prescribing policies can reduce antibiotic use

In Spain restrictive antibiotic prescription policies have led to positive outcomes, including reduced antibiotic use and reduced costs (Jover et al, 2007). These restrictive policies promote restrictive prescribing through the use of guidelines. A reduction of antibiotic use and the reduction of costs due to restrictive prescribing have been found in other European countries as well, such as the Czech Republic (Mach et al, 2007) and Greece (Ntagiopoulus et al, 2007). In France guidelines for rational prescribing and prudent use of antibiotics have only led to reduced health care costs (Blanc et al, 1999). Also guidelines in Norway have shown to be effective in altering prescribing practices which resulted in reduced antibiotic consumption (Berild et al, 2002).

Educational interventions may reduce resistance through decrease of antibiotic use

Educational interventions on prescribing practices for physicians can potentially reduce the incidence of antibiotic resistant bacteria. Multi-faceted interventions combining education of physicians, patients and general public in a variety of venues and formats were the most successful in reducing antibiotic prescribing and reducing antibiotic resistance. More research is needed to conclude which elements of these educational interventions are most effective (Arnold et al, 2005).

According to a review of Davey et al (2005) both restrictive and persuasive interventions to improve antibiotic prescribing to hospital inpatients are successful in improving drug treatment and can reduce antimicrobial resistance or hospital acquired infections. However, restrictive methods (e.g. putting a limit on the amount of prescriptions) appeared to have a larger effect than persuasive methods (e.g. education, advice and feedback) (Davey et al., 2005).

Computer-based programs improve prescribing practices

Other effective interventions are computer programs restricting prescription of antibiotics and computer-based order forms for health providers (Weinstein et al, 2001; Grayson, 2004). These programs include electronic guidelines, protocols and other ways to support prescribing practices for health care professionals (Sintchenko, 2008). Computerized advice on drug use can also be effective in reducing the length of hospital stay (Weinstein et al, 2001; Durieux et al, 2010). Also computer advices on drug dosages have improved prescribing practices (Weinstein et al, 2001). Prudent use of antibiotics increases the effectiveness of antibiotic therapy.

Hygienic measures effective in combating transmission of antibiotic resistance

Effective hygienic measures include:

- Hand hygiene of health professionals. Hand hygiene measures include washing hands with soap, hygienic hand disinfection or the use of gloves (Kampf et al, 2009; Trick, 2007). Long-lasting improvement of compliance with hand hygiene protocols can be successful in decreasing the spread of hospital infections, if an effective and accessible alcohol-based hand rub with a proven dermal tolerance and excellent user acceptability is supplied, accompanied by education of

- Disinfection of hospital rooms where patients spend the whole day in bed in order to contain personal hygiene of patients (Caron, 2010).

Proper hygiene contributes to the prevention of contamination and may break the chain of infection (Kampf et al, 2009). Therefore, these kinds of hygienic measures result in decreased hospital length of stay, health care costs and mortality as a result of decreased number of transmissions of antibiotic resistant bacteria (Weinstein et al, 2001; Essack et al, 2006; Caron et al, 2010).

The Dutch 'search and destroy' policy effective in reducing antibiotic resistance in hospitals

Especially in hospitals the emergence and spread of resistant bacteria needs to be controlled (Anderson et al, 2009). Several studies have shown that when infection-control measures are strictly enforced, the numbers of infections can be reduced. An example of this is the so-called 'search and destroy' policy in Dutch hospitals. The principles of this policy are:

- Prescreening of patients before entering the hospital (by testing blood samples);
- Isolating patients expected to be infected with resistant bacteria;
- Keeping patients infected with resistant bacteria in quarantine;
- Screening of the staff members;
- Closing the whole department in case of large outbreaks.

This policy is effective, especially in case of MRSA-infections (Wannet et al, 2005). According to the review of Cooper, isolation policies have the potential to reduce MRSA infections within the hospital sector (Cooper et al, 2003). Furthermore, the Dutch policy has shown to be effective in other countries as well, including Ireland and Denmark, where it also led to a decreased prevalence of antibiotic resistance (Hunter, 2009). A hospital administration could help enhance the outcomes by educating health professionals (Ward et al, 2005). Although some people suggest that infection control measures are time-consuming and expensive, others state that these measures can help reduce the costs related to the consequences of resistance (Murray, 1994).

Little known about effectiveness of infection control strategies in nursing homes

There is not much information about the effectiveness of infection-control strategies for preventing the transmission of MRSA in nursing homes for older people (Hughes et al, 2008). More is known about the effectiveness of infection-control measures in acute care settings. Isolation processes, for example, have mostly shown to be effective in hospital environments, but this information is not compiled for nursing homes (Hughes et al, 2008).

Surveillance of antibiotic use and resistance can help shape effective antibiotic policies

Surveillance of both antibiotic use and antibiotic resistance is needed to describe the relation between use of antibiotics and resistance to antibiotics (Livermore et al, 1998). This can help shape prescription guidelines and help choose a treatment with more potential to be effective. Therefore, they contribute to prudent use and infection control. More generally, effective surveillance systems report microbial data from laboratory tests which are needed to shape antibiotic policies (Cornaglia et al, 2004; Masterton, 2008). International collaboration in surveillance can help to control outbreaks (Livermore, 1998).

4. Antibiotic resistance policies in an international perspective

EU countries work on their antibiotic resistance policies within different supra- and international settings. They are member states of the supranational European Union (EU) and have to work under EU rules, regulations and agreements. Furthermore, they collaborate under the umbrella of

intergovernmental organizations such as the World Health Organization (WHO). Both perspectives will be addressed here.

4.1 EU policies and strategies

Historic overview of policies

Antibiotic resistance recognized as a European health problem

In 1999 the European Council launched a [Resolution](#) on antibiotic resistance, called “A strategy against the microbial threat”. This Resolution is a result of the [Copenhagen Recommendations](#). These Recommendations are the conclusions of the European Union Conference on “The Microbial Threat”, which was held in Copenhagen in 1998. The representatives of all sectors have acknowledged that the inappropriate use of antimicrobial agents is related to the increasing problem of resistance to antibiotics. Furthermore, it has been recognized that antibiotic resistance is no longer a national problem, but has become a European problem. Therefore it requires a common strategy and coordinated action.

The Council Resolution recommends the establishments of risk assessment systems to control and prevent infectious diseases. Also investment in research activities is seen as important in order to improve quality of life and decrease health care costs.

The European Community Strategy against antimicrobial resistance

In 2001 the European Commission adopted the [European Community Strategy against antimicrobial resistance](#), which proposes to take action in four main areas:

- Surveillance;
- Prevention of communicable diseases and infection control (mainly through the prudent use of antimicrobial agents);
- Research and development of alternative products;
- International cooperation.

Council Recommendation 2002/77/EC on the prudent use of antimicrobial agents in human medicine

Additionally, the European Commission presented the [proposal](#) for a Recommendation on the prudent use of antimicrobial agents in human medicine. This [Council Recommendation \(2002/77/EC\)](#) came into force in 2001, stating that multidisciplinary coordination on the Community-level is needed to lower the burden of antibiotic resistance. This Council Recommendation asks Member States to take action on a national level through:

- The development of national surveillance systems on antibiotic use and resistance;
- The implementation of prevention methods and infection control (support of prudent use and elimination of the transmission of infectious diseases);
- The improvement of education and training of health professionals (such as on the appropriate use of antimicrobials and hygiene standards);
- Informative approaches to raise awareness of prudent use of antibiotics among the general public.

Countries should draw up a general strategy plan for the implementation of these measures

In 2005 [the first Report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Recommendation \(2002/77/EC\)](#) had been published and already in 2009 the [2nd report of the Commission to the Council on the basis of Member States' reports on the implementation of the Council Recommendation](#) was published. The main purpose of the latter was to illustrate to what extent the national actions, requested by the Council Recommendation, had been implemented in the Member States. Most Member States have taken action, but there are still numerous areas of the Recommendation where only limited improvement

has been achieved, such as the implementation of national strategies and the closer cooperation between the countries. The report was accompanied by a so-called [Staff Working Document](#) to provide even more detailed information on the progress made by individual countries (see also chapter 5: national antibiotic policies and strategies). Furthermore, in 2008 the [Council Conclusions on Antimicrobial Resistance](#) also addressed the importance of international cooperation to reduce the burden of antibiotic resistance. Additionally, the countries should work in close cooperation and learn from each other.

EU directive forbids over the counter sale of antibiotics

In 2001 the [Directive 2001/83/EC of the European Parliament and the Council on the Community code relating to medicinal products for human use](#) got into force. This Directive stated that it is not possible to sale prescription medicines without prescription in pharmacies. Since then in the whole EU these medicines, including antibiotics, are legally only available after prescription by a doctor. However, in some EU countries antibiotics are still illegally available as over-the-counter drugs.

Council Recommendation on patient safety addresses the importance of prudent use

In 2009 also the [Council Recommendation on patient safety, including the prevention and control of healthcare associated infections](#) was launched, which also addresses the importance of prudent use of antimicrobials. This Recommendation includes also other relevant issues related to patient safety, e.g. e-health.

Importance of coordination between public and animal health sector recognized

Since the [Copenhagen Recommendations](#) it has become clear that more attention had to be paid to the agricultural sector. Because the rise of antimicrobial resistance has been traced to the use of antibiotics in both human and veterinary medicine, [DG SANCO](#) has been working towards the development of initiatives which would be relevant for both human and veterinary medicine, such as a technical intraservice platform to exchange information and enhance the coordination of activities between public health and animal health. Also cooperation has been established with the [European Food Safety Authority](#) (EFSA). Since 2006 [EU legislation on additives for use in animal nutrition](#) prohibits the use of antibiotics as growth promoters in animal food.

Staff Working Paper on antimicrobial resistance informs on progress made

In November 2009 the Commission published a [Staff Working Paper](#) on antimicrobial resistance to inform the Parliament and the Council on the progress made in monitoring and controlling antimicrobial resistance in human and veterinary medicine and to start an exchange of views. This document differs from the other Staff Working Paper published in 2009, since it uses data from European institutions rather than national reports.

EU projects and institutions

Several projects funded through EU Public Health Action Programmes

Both the [first](#) (2003-2008) and second (2008-2013) Programme of Community action in the field of Public Health pay attention to antibiotic resistance. In the [Second Programme](#) antibiotic resistance is still seen as an emerging health threat. Therefore the collection and analysis of relevant data in this field is still needed in order to combat antibiotic resistance.

The Action Programmes have led to the development of several projects, among which the former European Antimicrobial Resistance Surveillance System (EARSS) is one of the most important ones. In 2010 the coordination of EARSS was transferred from the [National Institute for Public Health and the Environment](#) (RIVM) to the ECDC and it was renamed the [European Antimicrobial Resistance Surveillance Network](#) (EARS-NET).

Other projects funded through EU Public Health Action Programmes are (chronologically ordered):

- [European Surveillance of Antimicrobial Consumption](#) (ESAC) from 2001-2011. In 2011 the ESAC project will be transferred to the ECDC;
- [European Committee on Antimicrobial Susceptibility Testing](#) (EUCAST) from 2004-2007 (and since then ongoing);
- [Improving Patient Safety in Europe](#) (IPSE) from 2005-2008;
- [E Bug Pack](#) from 2006-2009;
- [ABS International](#) from 2006-2009;
- [Burden of Disease and Resistance in European Nations](#) (Burden) from 2007-2009.

An overview of all EU Public Health Action Programme projects on antimicrobial resistance can be found [here](#).

In the Seventh Framework Programme (DG Research and Innovation), running from 2007 till 2013, antibiotic resistance constitutes one of the four areas in infectious diseases research. An overview of EU research projects (2007-2010) on antimicrobial resistance is given [here](#). The different research programmes to explore the development of antibiotic resistance and its relation to genomics are collected in the report [Antimicrobial Resistance](#). Furthermore, the project Appropriateness of PREscribing antibiotics in primary health care in Europe with respect to antibiotic resistance ([APRES](#)), is funded throughout the Seventh Framework Programme. The aim of this project is to understand and contribute knowledge to the appropriateness of prescribing antibiotics in Europe.

Role of European institutions

The main European Institution in the field of antibiotic resistance is the [ECDC](#), which coordinates and funds the [EARS-NET](#). This European network of national surveillance systems collects and provides all the necessary data on the occurrence and spread of antimicrobial resistance in Europe and publishes this in an [annual report](#). The results of EARS-NET are also available from a continuously updated interactive [database](#).

The main task of the ECDC is the surveillance of infectious diseases in Europe which is in agreement with the [Decision No 2119/98/EC](#) of the European Parliament and of the Council of 24 September 1998 and [Regulation \(EC\) no 851/2004](#) of the European Parliament and of the Council of 21 April 2004, both aimed at the establishment of the ECDC.

Other activities organized by the ECDC:

- [Programme on antimicrobial resistance \(AMR\) and healthcare-associated infections \(HAI\)](#) with the [European Antibiotic Awareness Days](#) in close cooperation with the WHO;
- [Trans Atlantic Task Force on Antimicrobial Resistance](#) (TATFAR), which aims to enhance cooperation between the USA and Europe in the field of antibiotic resistance.

Another important European institution is the [European Food Safety Authority](#) (EFSA), which also contributes to the reduction of antimicrobial resistance in Europe, mainly through the provision of scientific advice on the risks of spread and transfer to humans of antimicrobial resistant micro-organisms via food products. This advice includes recommendations on the monitoring of antimicrobial resistance in the food chain.

Other initiatives include the development of the [European Platform RUMA](#) by different stakeholders, to promote the responsible use of medicines, including antimicrobials, in animals.

Finally, the [European Medicine Agency](#) (EMA) is an important European Institution. It works in close cooperation with other European institutions and international partners (e.g. TATFAR). Their main task is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use. This institution monitors the risk to human health when using antibiotics. Furthermore, the EMA addresses the development of new medicinal

products. The [European Committee on Antimicrobial Susceptibility Testing](#) (EUCAST) is a committee initiated by the EMA, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and national breakpoint committees. This project standardizes the breakpoints and other technical aspects of antimicrobial susceptibility testing and functions as the breakpoint committee of EMA and ECDC.

Following a [joint request](#) by the Commission departments, the [ECDC](#), [EFSA](#), [EMA](#) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) work together to provide a common state of play on antimicrobial resistance.

4.2 Impact of WHO and other intergovernmental organizations

Due to the global nature of the problem of antibiotic resistance, the European Commission works in close cooperation with international institutions, such as the WHO. Antibiotic resistance was the theme of the [World Health Day](#) organized by the WHO on 7 April 2011. This stresses the urgency of the problem.

At European level, the WHO is developing [a regional strategy](#), recognizing the need for an interdisciplinary approach to combat antibiotic resistance. This policy is expected to be finished in September 2011 and will contain seven strategic objectives to promote this integrated approach:

1. promote national intersectoral coordination;
2. strengthen surveillance of antimicrobial resistance;
3. strengthen surveillance and promote stewardship of antimicrobial drug use;
4. strengthen surveillance of resistance to and use of antimicrobial agents in the animal food industry;
5. improve infection control and stewardship of antimicrobial resistance in health care settings;
6. promote research and innovation on new drugs and technology; and
7. ensure patient safety and improve awareness of antimicrobial use and resistance.

Other WHO documents on the topic of antibiotic resistance in Europe can be found [here](#).

At global level, the [WHO](#) has published the [WHO Global Strategy for Containment of Antibiotic Resistance](#) in 2001. In 2004 the WHO investigated which diseases are considered a health threat with a pharmaceutical gap, meaning that new innovations or medicines have the potential to reduce the burden of disease. The results have been reported in the [Priority Medicines for Europe and the World- document](#). In 2005 the World Health Assembly approved the [WHA 58.27 Resolution Improving the containment of antimicrobial resistance](#). This Resolution addresses the strengthened role of the WHO in containing antimicrobial resistance.

The WHO has published several reports on antibiotic resistance. See the [WHO Antimicrobial Resistance Document Centre](#) for an overview of global documents.

The WHO works in close cooperation with several organizations, including the [ECDC](#) (EARS-NET), [EFSA](#), [ESAC](#) and many others, such as the [Antibiotic Resistance Surveillance & Control in the Mediterranean Region, Improving Patient Safety in Europe](#) (IPSE), the [European Union Invasive Bacterial Infections Surveillance Network](#) (EU-IBD) and the project responsible for [Antibiotic Resistance and Prescribing in European Children](#) (ARPEC).

5. National antibiotic resistance policies and strategies

Antibiotic consumption and resistance differs among European countries

Antibiotics are used throughout Europe, but the frequency of using and prescribing them is different. Countries that have lower human related antibiotic consumption rates include Finland, Sweden and Norway (Grave et al, 2010). Especially in the south of Europe antibiotic consumption and prescription is high compared to other parts of Europe (ESAC, 2010). Cultural factors may partly explain this high prescription rate, since doctors in southern European countries prescribe antibiotics more frequently. Furthermore, there is a great diversity in the incidence rates of antibiotic resistance among European countries. In the northern European countries (including the Netherlands) rates of antibiotic resistance in humans are low, whereas the southern countries have higher rates (EARSS, 2009; ECDC, 2010). This is due to more restrictive prescribing policies in the northern countries (ECDC, 2010). However, compared to the rest of Europe, the Netherlands has the highest antibiotic consumption and antibiotic resistance rates in the agricultural sector (Grave et al, 2010) also posing risks to human health.

High prevalence rates of MRSA in holdings with breeding pigs are found in several European countries, such as Germany, Spain, Italy and the Netherlands (EFSA, 2009). Nowadays, more initiatives are taken to reduce the consumption of antibiotics in the agricultural setting. Other differences in resistance are related to tuberculosis; although the overall numbers of people detected with tuberculosis (TB) and multi-drug resistant tuberculosis (MDR-TB) are decreasing, the numbers of people with extensive drug-resistant TB (XDR-TB) almost tripled in 2009 compared to 2008 in the EU (ECDC, 2009). This trend is most common in the eastern part of Europe, especially in Estonia, Latvia, Lithuania, Romania and Poland (WHO TB profile, 2009; ECDC, 2009; Eurotbccentre, 2007). Finally, increased migration rates will have a significant impact on antibiotic resistance incidence rates in all European countries, since infectious diseases have been crossing borders and are no longer limited to national borders only.

European countries have similar policy approaches

In spite of large differences in the incidence rates of antibiotic resistance, most European countries base their policies to combat antibiotic resistance on the same European approach, which is described in [Recommendation 2002/77/EC on the prudent use of antimicrobial agents in human medicine](#). Therefore, their national policies contain similar elements although there are some striking differences as well (see table 1). Member States and EEA countries were asked to report to the Commission on the implementation of the Recommendation within two years of its adoption and the Commission summarized the main actions taken at Member States and European Union level in the [first](#) (2005) and the [second](#) report (2009) from the Commission to the Council on the implementation of the Recommendation. The general conclusion from both reports is that even though progress has been made since the implementation of Recommendation 2002/77/EC, still work has to be done in order to combat antimicrobial resistance. More information on the main conclusions of these reports is presented in the paragraph below.

More attention needed on raising awareness targeting health professionals and the general public

According to the second report, by the end of 2008 15 of the 27 EU countries had a national strategy, which is the same as in 2005 (see table 1). Overall, the participation in European projects and partnerships is well established, but the field of raising awareness via campaigns targeting health professionals and the general public needs to be further developed. Especially the campaigns targeting the different health professionals are under-implemented with only a little bit more than half of the countries having implemented awareness raising campaigns on antimicrobial resistance for healthcare professionals in 2006/2007. In most countries, the campaigns targeted medical

doctors (in all countries except Denmark, the Netherlands and Wales), pharmacists, nurses and/or veterinarians. Only Denmark and the Netherlands report having campaigns targeting veterinarians only. Since the Netherlands has the highest level of antibiotic use in the agricultural sector, it is important to create awareness of the consequences of antibiotic use in the agricultural sector. National awareness campaigns on the prudent use of antibiotics targeting the general public also require more attention, because they have shown to be effective (McNulty, 2010). Although all Member States are partner of the European Antibiotics Awareness Day (EADD), not all countries have implemented an ongoing awareness campaign (see table 1). On the ECDC [website](#) the different national awareness campaign websites are listed.

Use of indicators helpful when evaluating the implementation process of Recommendation 2002/77/EC

Besides reporting the progress with regard to the implementation of Recommendation 2002/77/EC based on national reports, the second report of the Commission also emphasizes the use of indicators to evaluate the implementation. These indicators should be used to monitor the impact of the national action plans, guidelines and measures, and will help to indicate which sectors need further attention.

More focus needed on collaboration between the human and animal health sectors

Based on the findings identified in the second report of the Commission, the areas on which future work could focus include the collaboration between the human and animal health sectors on antibiotic resistance and antibiotic use. This should be done at both national and European level and especially in the countries where no collaboration between the two sectors has been initiated yet.

Only half of the EU countries implemented guidelines on prudent use in hospitals

By the end of 2008 most countries had implemented national guidelines on the prudent use of antimicrobials within the community. However, only half of the EU countries had implemented hospital guidelines. Additionally, both assessment of compliance with national guidelines and evaluation of the impact of the guidelines on prescription practices are not very common in practice, but compared to the first report (2005) progress had been made.

Evaluation of the implementation of Directive 2001/83/EC

According to the findings of the second report of the Commission, positive action regarding Directive 2001/83/EC on the Community code relating to medicinal products for human use has taken place. By the end of 2008 sixteen EU countries had reported that sales without prescription were not considered a significant source of misuse of antibiotics. However, from those eleven countries in which the estimated percentage of antibiotics sold without prescription was higher than 1%, three countries did not take measures to enforce the European legislation limiting the availability of antibiotics to prescription only.

Although most policy approaches are based upon Recommendation 2002/77/EC national policy approaches of the EU countries can differ on specific elements. Textbox 1 shows some noticeable examples.

Table 1: Implementation of Recommendation 2002/77/EC on national level, based on Commission Staff Working Document and awareness campaigns listed on the ECDC website.

Country	National strategy	Development of national surveillance systems					Implementation of prevention methods and infection control			Informative approaches to raise awareness of prudent use of antibiotics	
		Antimicrobial resistance (AR)			Prescription and use of antimicrobial agents		No (or <1%) antibiotics sold without prescription	National guidelines on appropriate use of AR	National programme for hospital hygiene + infection control	National awareness campaigns	Partnership in EAAD
	Strategy and national action plan	Partnership in EARS-NET	National surveillance in community	National surveillance in hospitals	Partnership in ESAC	Additional system antimicrobial use					
Austria		+	+			+		+	+	+	+
Belgium	+	+	+	+		+		+	+	+	+
Bulgaria	+	+	+	+		+		+	+		+
Cyprus		+				+			+		+
Czech Republic		+	+			+		+		+	+
Denmark		+	+	+		+		+	+	+	+
Estonia		+		+		+				+	+
Finland	+	+	+	+		+		+	+	+	+
France	+	+	+	+		+		+	+	+	+
Germany	+	+	+	+		+		+	+		+
Greece	+	+				+		+	+	+	+
Hungary		+	+	+		+		+		+	+
Ireland	+	+	+	+		+		+	+		+
Italy		+		+		+		+	+	+	+
Latvia		+	+	+		+			+	+	+
Lithuania	+	+	+	+		+		+	+	+	+
Luxembourg	+	+				+		+	+	+	+
Malta	+	+		+		+		+			+
Netherlands	+	+	+	+		+		+	+	+	+
Poland		+	+	+		+		+		+	+
Portugal		+				+		+	+		+
Romania		+	+	+		+		+	+	+	+
Slovakia	+		+	+		+		+	+	+	+
Slovenia	+	+		+		+		+	+	+	+
Spain		+	+	+		+			+	+	+
Sweden	+	+	+	+		+		+	+	+	+
United Kingdom	+	+	+	+		+		+	+	+	+
Total (27 MS)	15	26	20	22	27	17	16	23	22	21	27

Source: http://ec.europa.eu/health/antimicrobial_resistance/docs/cswd_technicalannex_en.pdf

Textbox 1: Examples of (elements of) national policies/strategies implemented in EU countries.

Community-based programs
The Swedish strategic programme against antibiotic resistance (Program Strategigruppen for Rationell Antibiotikaanvandning och Minskad Antibiotickaresistens, STRAMA) was effective in reducing antibiotic resistance prevalence rates without any components of public health campaigns. STRAMA consists of a national executive working group funded by the government and a network of independent local multidisciplinary groups in each county that provide prescribers with feedback on antibiotic use on an individual basis
In Portugal the awareness campaigns on appropriate use of antimicrobial agents are completely funded by the pharmaceutical sector
In Belgium awareness campaigns for the general public as part of national policy were effectively implemented. These campaigns include also hand hygiene campaigns and are all designed by the Belgian Antibiotic Policy Coordination Committee (BAPCOC). BAPCOC is the main responsible organization for the promotion of prudent antibiotic use in Belgium. Other initiatives of BAPCOC are antibiotic management teams in hospitals, guidelines on appropriate use of antibiotics for healthcare professionals, surveillance programmes on antibiotic use and resistance in humans and animals and several research projects which are funded by BAPCOC
In England a similar group, the Antimicrobial Resistance Action Plan (AMRAP) is working on the elimination of antibiotic resistance. This group is focusing on the six common key areas: 1) prudent human use of antimicrobials in the community, 2) prudent human use of antimicrobials in hospitals, 3) prudent use of antimicrobial in animals, 4) infection control, 5) education, information dissemination and research and 6) surveillance of resistant antimicrobial agents.
In The Netherlands, a working party of professional experts on antibiotic policies has been established in the late nineties. The aim of the Dutch Working Party on Antibiotic Policy (SWAB) is the containment of antimicrobial resistance and expanding costs. Recommendations based on scientific evidence are used for national guidelines on prudent use of antimicrobial agents
In 2002, the French Ministry of Health launched a program to educate physicians and consumers about the dangers of antibiotic overuse, namely, the fast development of antibiotic resistance. This campaign, called ‘Les antibiotiques, c’est pas automatiques’ (“antibiotics are not automatic”) aimed to reduce antibiotic prescriptions. It was very successful. The program actually exceeded expectations, reducing prescriptions by 26.5% in the first five years. However, France still remains one of the European countries with the highest antibiotic consumption in Europe, and prescriptions of antibiotics appear to rise again, which is happening in the whole of Europe
In Poland high prevalence rates of tuberculosis are present. Therefore, policy approaches have another focus. More attention is paid to the reduction of resistance to antimicrobial agents used against tuberculosis infections
Hospital sector
The Dutch ‘search and destroy’ policy in hospitals is well-known because of low antibiotic resistance prevalence rates in hospitals in The Netherlands. The principles of this policy are as follows; prescreening of patients before entering the hospital (by testing cultures), isolating patients expected to be infected with resistant bacteria, keeping patients infected with resistant bacteria in quarantine, screening of the staff members, and in case of large outbreaks closing the whole department. This policy is effective, especially in case of the MRSA-infections (Warrant, 2005). Furthermore, this Dutch policy has worked out in other countries as well including Ireland and Denmark, where it also led to a decreased prevalence of antibiotic resistance (Hunter, 2009)
Agricultural sector
Sweden was the first country prohibiting the use of antibiotics as growth promoters in the agricultural sector, based on voluntary initiative. The Danish ban on use of antibiotics as growth promoters in the veterinary sector followed immediately, also based on voluntary proposals from agricultural companies. Denmark can be seen as best practice example for the rest of Europe (WHO, 2003).
In the Netherlands not many policies have been implemented in the agricultural sector. Only one awareness campaign has been implemented so far. Last year a proposal from the Ministry of Economics, Agriculture and Innovation to reduce the use of antibiotics in the agricultural sector was developed. This proposal aims at a reduction of antibiotic consumption of 20% by the end of 2011 and a reduction of 50% by the end of 2013

6. References and resources

International/supranational bodies:

- European Union
 - European Commission, antibiotic resistance policy: http://ec.europa.eu/health/antimicrobial_resistance/policy/index_en.htm
 - DG SANCO: http://ec.europa.eu/dgs/health_consumer/index_en.htm
 - ECDC: http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/Pages/index.aspx
 - EFSA: <http://www.efsa.europa.eu/en/topics/topic/amr.htm>
 - EMA: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000439.jsp&murl=menus/special_topics/special_topics.jsp&mid=WC0b01ac058002d4e9&jenabled=true
- WHO
 - WHO Headquarters: <http://www.who.int/drugresistance/en/>
 - WHO, Regional office for Europe: <http://www.euro.who.int/en/what-we-do/health-topics/disease-prevention/antimicrobial-resistance>
 - WHO, Publications: <http://www.euro.who.int/en/what-we-do/health-topics/disease-prevention/antimicrobial-resistance/publications>

Projects

- European Antibiotic Awareness Day: <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>
- World Health Day: <http://www.who.int/world-health-day/2011/en/index.html>
- ABS International: <http://www.abs-international.eu/index.php?id=1171>
- E-bug: <http://www.e-bug.eu/>
- EPRUMA: <http://www.epruma.eu/publications/other-sources.html>
- ESAC: <http://app.esac.ua.ac.be/public/>
- EU-Burden: <http://www.eu-burden.info/>
- EUCAST <http://www.eucast.org/>
- IPSE: <http://www.ecdc.europa.eu/IPSE/>

Databases

- EARS-NET database: <http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/database.aspx>

Policy Documents

European Union

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European Commission

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- [Commission Staff Working Document Accompanying document to the 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. Detailed analysis of countries' reports on the implementation of the Council Recommendation \(2002/77/EC\) on the prudent use of antimicrobial agents in human medicine.](#)

Retrieved from:

http://ec.europa.eu/health/antimicrobial_resistance/docs/cswd_technicalannex_en.pdf

- [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.](#) Retrieved from: http://ec.europa.eu/health/antimicrobial_resistance/docs/amr_report2_en.pdf
- [Staff working paper of the services of the Commission on antimicrobial resistance SANCO/6876/2009r6.](#) Retrieved from: http://ec.europa.eu/food/food/biosafety/salmonella/antimicrobial_resistance.pdf

European Parliament

- [Directive 2001/83/EC of the European Parliament and of the Council of 6 november 2001 on the community code relating to medicinal products for human use.](#) Retrieved from: <http://apps.who.int/medicinedocs/documents/s17096e/s17096e.pdf>
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- [Decisions adopted jointly by the European Parliament and the Council Decision no 1350/2007/EC of the European Parliament and of the Council of 23 October 2007 establishing a second Programme of Community action in the field of health \(2008-13\).](#) Retrieved from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:301:0003:0013:en:PDF>
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Council of Ministers

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WHO

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WHA

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