



COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 20.06.2001  
COM(2001) 333 final

VOLUME II

Proposal for a

**COUNCIL RECOMMENDATION**

**on the prudent use of antimicrobial agents in human medicine**

(presented by the Commission)

## EXPLANATORY MEMORANDUM

The use of antimicrobial agents has greatly contributed to improvements in health. Such “antimicrobial agents” (which for the purposes of this Recommendation encompass substances produced either synthetically or naturally by bacteria, fungus or plants, used to kill or inhibit the growth of micro-organisms, including bacteria, viruses and fungus, and parasites, in particular protozoa, exhibiting the phenomenon of resistance) have been introduced for decades to treat communicable diseases and prevent infections. However, in addition to their benefits, their use has also resulted in certain selected micro-organisms previously sensitive to these agents to develop resistance so-called “antimicrobial resistance”. Antimicrobial resistance leads to prolonged suffering of the individual and enhanced costs for health care and society. It has developed into a wide spread public health problem, particularly for antibacterial agents (the term antibiotic is used in a generic way in common parlance to cover substances that kill or inhibit micro-organisms but is not specific enough for the purposes of this Recommendation).

The purpose of this proposal is to recommend a number of specific measures aimed at containing the spread of antimicrobial resistance by prudent use of antimicrobial agents in humans within the Community. Of major concern is the overuse and inappropriate use of antibiotics, especially in children with respiratory infections. Studies in Iceland, Finland and Sweden have shown the impact of intervention measures which reduced consumption of certain antibiotics, and consequently reduced the rate at which pathogens acquire resistance.

In 1998 a European Union Conference on “The Microbial Threat” resulted in “The Copenhagen Recommendations”<sup>1</sup>, calling for action to preserve the effectiveness of antimicrobial agents by restricting their use to treatment and prevention of infectious diseases. Similar conclusions were drawn by the EC Economic and Social Committee<sup>2</sup>, the WHO 51<sup>st</sup> World Health Assembly<sup>3</sup>, and further supported by national evaluations of the situation such as the report of the Standing Medical Advisory Committee (SMAC) report in the United Kingdom<sup>4</sup>.

The Committees for Proprietary Medicinal Products (CPMP<sup>5</sup>) and Veterinary Products (CVMP<sup>6</sup>) of the European Agency for the Evaluation of Medicinal Products (EMEA) identified areas where regulatory actions are relevant for antimicrobial resistance.

On 24 September 1998 the European Parliament and Council adopted Decision 2119/98/EC setting up a Community Network for the Epidemiological Surveillance and Control of Communicable Diseases<sup>7</sup>. Antimicrobial treatment is one of the major tools employed in the control of communicable diseases. On the basis of that Decision the Commission in its Decision 2000/96/EC of 22 December 1999 on the communicable diseases to be

---

<sup>1</sup> Report from the Invitational European Union Conference on “The Microbial Threat” hosted by the Danish Government in Copenhagen, Denmark, 9-10 September 1998

<sup>2</sup> Economic and Social Committee opinion on the “Resistance to antibiotics as a threat to public health”, OJ C 407, 28.12.1998, p. 7

<sup>3</sup> World Health Organisation: Emerging and other Communicable Diseases: Antimicrobial Resistance, May 1998

<sup>4</sup> “The Path of Least Resistance”, Standing Medical Advisory Committee Sub-group on Antimicrobial Resistance, Department of Health, United Kingdom, 1998

<sup>5</sup> see table

<sup>6</sup> see table

<sup>7</sup> OJ L 268, 3.10.1998, p. 1

progressively covered by the Community Network under Decision 2119/98/EC<sup>8</sup> listed antimicrobial resistance as a priority health issue to be addressed by this Community Network.

Since then the Commission has developed a comprehensive strategy to tackle antimicrobial resistance in areas such as human and veterinary medicine, animal production and plant protection. This initiative fulfils requests made by the Scientific Steering Committee of the Commission in its opinion of May 1999, the Council in its Resolution of June 1999<sup>9</sup> and the Council Conclusions of December 1999<sup>10</sup>. This strategy is outlined in the recent Commission Communication<sup>11</sup>.

As a follow up to the Council Resolution of June 1999 and the Council Conclusions of December 1999, this Recommendation proposes a number of specific measures to be implemented by the Member States to contain the spread of antimicrobial resistance by prudent use of antimicrobial agents in human medicine:

- Collection and analysis of data on antimicrobial resistant micro-organisms and on consumption of antimicrobial agents available to prescribers, pharmacies, industry, health insurance providers etc. to detect potential links for intervention measures;
- Enforcing the principle that antibacterial agents should be available by prescription only, and evaluating whether this rule should be applied to all antimicrobial agents as a precaution;
- Developing guidelines and principles on the prudent use of antimicrobial agents, including principles for evaluation of applications for marketing authorisation;
- Improving prevention of infections to reduce the need for antimicrobial agents by reinforcing immunisation programmes and developing infection control standards in hospitals and the community;
- Enhancing knowledge on the problem by specialised education programmes for health professionals;
- Raising awareness of the problem of antimicrobial resistance by informing the general public;
- Encouraging research on the development of antimicrobial resistance and the development of rapid diagnostics to enable efficient early treatment of communicable diseases;
- Identify or establish, for these purposes, national organisations with effective co-ordination between the Member States and the Commission to achieve Community results.

---

<sup>8</sup> OJ L 28, 3.2.2000, p. 50

<sup>9</sup> Council Resolution on Antibiotic Resistance “A Strategy Against the Microbial Threat” (OJ C 195, 13.7.1999, p.1)

<sup>10</sup> Council Conclusions on Future Actions in the Framework of the Strategy against Antimicrobial Resistance, DG B II 13920/99

<sup>11</sup> Commission Communication ...

The Commission will establish an advisory group through the Community network on the epidemiological surveillance and control of communicable diseases (Dec. 2119/98/EC) to support Member States' efforts and ensure a co-ordinated Community approach in addressing this action plan. The Commission will also ensure close co-operation with EEA/EFTA countries, applicant countries and international organisations such as WHO to increase synergy and avoid duplication of effort in the fight for a prudent use of antimicrobial agents.

The enclosed table lists epidemiological surveillance networks concerned with antimicrobial resistance and their recommendations on the containment of antimicrobial resistance in Member States, the Commission, the European Agency for the Evaluation of Medicinal Products (EMA), the U.S. and the WHO.

## Table

### **Epidemiological surveillance networks on antimicrobial resistance and reports with recommendations to contain antimicrobial resistance**

Denmark	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP): Consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark, July 1999. <a href="http://www.svs.dk">http://www.svs.dk</a>
Finland	A national committee was nominated consisting of members from the Ministry of Health and Ministry of Agriculture to enhance development of national policy. In the human health care, the Finnish Study Group for Antimicrobial Resistance (FiRe) network collects on antibiotic resistance in Finland. The FINRES report is published annually. <a href="http://www.mmm.fi/publications/">www.mmm.fi/publications/</a>
France	Proposals for a national action plan to control antibiotics resistance in France ("Propositions pour un plan national d'actions pour la maîtrise de la résistance aux antibiotiques": InVS, Janvier 1999, Engl. Version July 1999)
Ireland	A draft strategy document has been drawn up and the Ministry of Health will consider the final report during 2000. <a href="http://www.ndsc.ie/">http://www.ndsc.ie/</a> A Strategy for control of Antimicrobial Resistance in Ireland (SARI)
The Netherlands	<p>Dutch Working Party on Infection Prevention (WIP): In 1981 the WIP was found to stimulate infection prevention in the Netherlands. Professionals from four Dutch societies are participating in this working party:</p> <ul style="list-style-type: none"> <li>The Infectious Diseases Society of the Netherlands and Flanders</li> <li>The Dutch Society of Medical Microbiology</li> <li>The Dutch Society of Microbiology</li> <li>The Society for Hygiene and Infection Prevention in Health Care</li> </ul> <p>The aim is to develop and publish up-to-date, scientifically based guidelines for infection prevention in hospitals, nursing homes, institutions for the mentally handicapped, dental care and home care.</p>
Sweden	<p>An expert group on the national level was formed : Swedish Strategic Program for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA). 1994. <a href="http://www.strama.org/eng.html">http://www.strama.org/eng.html</a></p> <p>A "National plan against antibiotic resistance" has been proposed for the government by the National Board of Health and Welfare in collaboration with 17 government boards, institutions and other interested parties. 2000. <a href="http://www.sos.se">http://www.sos.se</a> (In Swedish)</p>
UK	<p>UK Department of Health. Standing Medical Advisory Committee, Sub-Group on Antimicrobial Resistance. Main Report: The path of least resistance, London, UK. Dept. of Health September 1998. <a href="http://www.doh.gov.uk/smacsyn.htm">http://www.doh.gov.uk/smacsyn.htm</a></p> <p>UK Antimicrobial Resistance Strategy and Action Plan: <a href="http://www.doh.gov.uk/arbstrat.htm">http://www.doh.gov.uk/arbstrat.htm</a></p>

EMEA	<ol style="list-style-type: none"> <li>1. Discussion Paper on Antimicrobial Resistance (EMEA 9880/99.Rev 1). <a href="http://www.eudra.org/humandocs/humans/general.htm">http://www.eudra.org/humandocs/humans/general.htm</a></li> <li>2. <a href="#">EMEA/CVMP/818/99</a> A Risk Management Strategic Plan for controlling Antimicrobial Resistance through the Authorisation of Veterinary Medicines: Recommendations consequent to the Report and Qualitative Risk Assessment of the CVMP of July 1999</li> </ol>
European Commission	<p><u>Scientific Steering Committee: Opinion of the Scientific Steering Committee on Antimicrobial Resistance.</u> <a href="http://europa.eu.int/comm/dg24/index.html">http://europa.eu.int/comm/dg24/index.html</a></p> <p><u>Network for the epidemiological surveillance and control of communicable diseases in the Community (Council Decision 2119/98/EC).</u> One of the priorities to be covered by that network is antimicrobial resistance (Commission Decision 2000/96/EC). Technical backbone is the Health Surveillance System on Communicable Diseases within the European Public Health Information Network (HSSCD-EUPHIN), comprising two areas of information: A restricted one for exchange of information between public health authorities and specific surveillance structures, and a website on information for the general public: <a href="http://hsscd.euphin.org">http://hsscd.euphin.org</a> It links to home pages of the following specific networks supported by the European Commission and dealing with antimicrobial resistance:</p> <ol style="list-style-type: none"> <li>1. European Antimicrobial Resistance Surveillance System (EARSS), a laboratory based network of national surveillance systems which aims to aggregate comparable and reliable data on resistant pathogens for public health purposes, having started on staphylococcus aureus and streptococcus pneumoniae in 1998. <a href="http://www.earss.rivm.nl">http://www.earss.rivm.nl</a></li> <li>2. Enter-Net, established in 1994 for the surveillance of salmonella and verotoxin-producing <i>E.coli</i> (VTEC) infections, is also concerned with the surveillance of antibiotic resistance in enteric pathogens: <a href="http://www2.phls.co.uk">http://www2.phls.co.uk</a></li> <li>3. EuroTB, a specific network for the Surveillance of Tuberculosis in Europe to provide epidemiological information on tuberculosis (TB) for improving TB control, has included surveillance on drug resistance a key component of tuberculosis surveillance since 1999: <a href="http://www.ceses.org/eurotb.htm">http://www.ceses.org/eurotb.htm</a></li> </ol>
USA	Draft public health action plan to combat antimicrobial resistance, part I: Domestic issues. <a href="http://www.cdc.gov/drugresistance/actionplan/">http://www.cdc.gov/drugresistance/actionplan/</a>
WHO	Containing Antimicrobial Resistance: Review of the Literature and Report of a WHO Workshop on the Development of a Global Strategy for the Containment of Antimicrobial Resistance. Geneva, Switzerland, 4-5 February 1999. <a href="http://www.who.int/emc-documents">http://www.who.int/emc-documents</a>

Proposal for a

## **COUNCIL RECOMMENDATION**

### **on the prudent use of antimicrobial agents in human medicine**

**(Text with EEA relevance)**

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 152(4) thereof,

Having regard to the proposal from the Commission<sup>12</sup>,

Having regard to the opinion of the European Parliament<sup>13</sup>,

Whereas:

- (1) The use of antimicrobial agents has greatly contributed to improvements in health. Such “antimicrobial agents” have been introduced for decades to treat communicable diseases and prevent infections. For the purposes of this Recommendation, antimicrobial agent means substance produced either synthetically or naturally by bacteria, fungi or plants, used to kill or inhibit the growth of micro-organisms including bacteria, viruses and fungi, and of parasites, in particular protozoa, exhibiting the phenomenon of resistance. However, their use has also resulted in certain selected microbes previously sensitive to these agents developing resistance, so-called “antimicrobial resistance”. This leads to increased danger, to prolonged suffering of the individual, and to enhanced costs for health care and society. Therefore concerted action is necessary at Community level to contain this problem by encouraging the prudent use of antimicrobial agents in human medicine and better hygiene and infection control;
- (2) The Council of the European Union on 8 June 1999 adopted a Resolution on antibiotic resistance "A strategy against the microbial threat"<sup>14</sup>. The Resolution highlights that antimicrobial resistance increases morbidity and mortality due to communicable diseases leading not only to a diminution of quality of life but also to additional health and medical care costs, and that actions need to be taken at Community level;
- (3) The own-initiative opinion of the Economic and Social Committee on the “Resistance to antibiotics as a threat to public health”<sup>15</sup> identified possible initiatives and actions that should be taken at Member States’ and Community level to address the problem of antimicrobial resistance;

---

<sup>12</sup> OJ ...

<sup>13</sup> OJ ...

<sup>14</sup> OJ C 195, 13.7.1999, p. 1

<sup>15</sup> OJ C 407, 28.12.98, p. 7

- (4) There is an association between growing consumption of antimicrobial agents and an increase in the prevalence of micro-organisms resistant to those agents, which can not be overcome by the lengthy process of continuously developing new antimicrobial compounds;
- (5) To develop strategies for prevention of infections and containment of resistant pathogens, accurate surveillance systems generating valid, reliable and comparable data on incidence, prevalence and modes of spread must be established throughout the Community;
- (6) Surveillance on prescription and consumption of antimicrobial agents should form an essential component for an overall surveillance strategy to address the problem of antimicrobial resistance;
- (7) An important step to avoid or even reverse further increases in resistant micro-organisms would be to reduce unnecessary and inappropriate use of antimicrobial agents. General principles and methods for the prudent use of these agents in humans must be identified, and defined and implemented;
- (8) Improved strategies for hygiene and infection control in hospitals and the community will help to avoid the spread of resistant micro-organisms and will be an important step to reduce the quantities of antimicrobial agents used;
- (9) To bring about the necessary changes in prescribers' and patients' behaviour, health professionals and the general public need to be informed on the problem of antimicrobial resistance and associated factors by
  - Improved product information (Summary of Product Characteristics (SPC) and Patient Information Leaflet (PIL)),
  - Awareness-raising by adequate information and training during professional education and in-post training,
  - Information campaigns to the general public and specifically to the patient;
- (10) Support of research will be essential for tackling the problem of modes of spread of antimicrobial resistance;
- (11) There is also a relationship between the occurrence of antimicrobial resistant pathogens in humans and their occurrence in animals and the environment. This Recommendation does not preclude further initiatives in other areas;
- (12) Measures taken by the Member States in this area, and the way they have taken into account this Recommendation, should be the object of reports at national and Community level;
- (13) In accordance with the principle of subsidiarity, any new measure taken in an area which does not fall within the exclusive competence of the Community, such as protection of the public against the increase of infectious agents resistant to antimicrobial agents, may be taken up by the Community only if, by reason of the scale or effects of the proposed action, the objectives proposed can be better achieved by the Community than by Member States; antimicrobial resistance, as with



communicable diseases cannot be confined to a geographical region or Member State therefore any necessary action requires concerted action at Community level.

HEREBY RECOMMENDS THAT MEMBER STATES:

- I. set up specific strategies targeted towards the prudent use of anti-microbial agents in the aim of containing the increase of pathogens resistant to these agents. These strategies should be based on the best available scientific data and advice, and should comprise measures in relation to surveillance, education, information, prevention and control, and research. To implement these strategies Member States should establish or designate, according to national use and practice, a multi-disciplinary and cross-sectoral national organisation representing health authorities at all levels, surveillance and research institutions, relevant professionals and consumers. This organisation will be responsible for developing information exchange and co-operation between organisations representing veterinary medicine, animal production and plant protection. Its nature and composition should be communicated to the Commission and the other Member States within the framework of Decision 2119/98/EC within six months of the adoption of this Recommendation.

This national organisation should:

1. Establish or strengthen surveillance systems on antimicrobial resistance and the consumption of antimicrobial agents in order to
  - (1) gather reliable, comparable data by means of a laboratory based system of the susceptibility of pathogens to antimicrobial agents. The data should be amenable to time trend analysis and early warnings and to monitor spread of resistance at national, regional and community level;
  - (2) collect data on prescription and consumption of antimicrobial agents on national, regional, hospital and community level, involving prescribers, pharmacists and other parties collecting such data, in order to be able to potentially link prescription and consumption of antimicrobial agents to the development of pathogens resistant to those agents.

These surveillance systems should be maintainable with clear regulation of data access and ownership. They should comply with the data protection regulations and guarantee the confidentiality and security of data. These systems should build upon existing national and international surveillance systems, using, wherever possible, internationally recognised classification systems and comparable methods

2. Enforce control and preventative measures on the prudent use of antimicrobial agents by
  - (1) developing evidence-based principles and guidelines on good practice for the management of communicable diseases, to maintain the effectiveness of antimicrobial agents. These practices should include
    - Restriction of antibacterial agents to prescription-only use, and promoting and monitoring of optimal prescription practices;

- Setting rules for the use of other antimicrobial agents that are not subject to requirements for prescription-only use and an assessment of the need for changes;
  - Establishment of clinical and microbiological criteria for rapid on-the-spot diagnosis of infections, and
  - Optimising choice of drug, dosage and duration for the treatment and prevention of infections.
- (2) Implementing hygiene and infection control standards in Institutions (hospitals, child care facilities, nursing homes etc.) and in the community, and assessing their impact in the prevention of communicable diseases and the need for antimicrobial agents;
  - (3) Encouraging national immunisation programmes to progressively eliminate vaccine preventable diseases,
3. Promote education and training of health professionals on the problem of antimicrobial resistance by
    - (1) teaching principles and guidelines on the appropriate use of antimicrobial agents by incorporation into undergraduate and postgraduate training and and in regular continuous training for physicians, dentists, pharmacists and nurses and others in the medical profession, using effective good practice methods with continuous feedback;
    - (2) stressing training on hygiene and infection control standards to eventually reduce the need for antimicrobial agents;
    - (3) training on immunisation programmes and their role in preventing infections, thereby reducing outbreaks of diseases and thus the demand for antimicrobial agents.
  4. Inform the general public of the importance of prudent use of antimicrobial agents by
    - (1) raising awareness of the problem of antimicrobial resistance and encouraging realistic public expectations for prescribing of antimicrobial agents;
    - (2) launching national, regional and local campaigns on the importance of interventions to reduce the unnecessary use of antimicrobial agents, and the principles and guidelines on good practice to motivate patients' adherence;
    - (3) highlighting the impact of basic hygiene and vaccination programmes on reducing the need for antimicrobial agents.
  5. Inform and communicate with other Member States and the Commission, through the Network on epidemiological surveillance and control of communicable diseases, on national research initiatives relating to the containment of antimicrobial resistance, with emphasis on

- the mechanisms of emergence and spread of antimicrobial resistance among humans and from animals to man;
  - the quality of diagnostic tools and the development of rapid and reliable diagnostic and susceptibility testing;
  - developing new modalities for prevention and treatment of infections;
  - developing alternatives to antimicrobial agents to contain the spread of infections, and
  - developing new surveillance methods to contain antimicrobial resistance;
6. within one year of the adoption of this Recommendation, provide a strategy plan for the development and implementation of these actions. The plan should be progressively put in place over a period of time not exceeding four years from the adoption of this Recommendation;
- II. co-operate with the Commission in the development of indicators for monitoring prescribing practices of antimicrobial agents on the basis of the evidence-based principles and guidelines on good practice for the management of communicable diseases within two years of the adoption of this Recommendation, and evaluate these indicators once developed with regard to potential improvements of prescribing practices and feedback to prescribers;
- III. establish and implement control systems on good practice of marketing of antimicrobial agents to ensure compliance with the evidence-based principles and guidelines on good practice for the management of communicable diseases within two years of the adoption of this Recommendation;
- IV. initiate with other Member States and the Commission activities aimed at harmonising and updating the product information (SPC) for antibacterial medicinal products particularly related to indications, dose and dose regimen and prevalence of acquired resistance;
- V. inform the Commission within one year of the adoption of this Recommendation, and annually subsequently, of how the provisions of this Recommendation have been implemented.

**HEREBY INVITES THE COMMISSION:**

1. to facilitate mutual information, consultation, co-operation, and action through the procedures and mechanisms available in the Community Network for the epidemiological surveillance and control of communicable diseases (Decision 2119/98/EC) in the field covered by this Recommendation;
2. to establish texts on principles and guidelines of best practice on the prudent use of antimicrobial agents in human medicine having regard to national policies and activities of the European Agency for the Evaluation of Medicinal Products (EMEA) focussing on requirements for market authorisation and on the quality and content of the Summary of Product Characteristics (SPC), which lays the basis for all promotional activities of an antimicrobial agent;

3. to propose, where appropriate, common methodology, case definitions and nature and type of data to be collected for the surveillance on pathogens resistant to antimicrobial agents and the use of these agents;
4. to develop under the auspices of the above mentioned Community Network an information system linking prescribers, pharmacists, other interested parties and the public to the respective surveillance systems on pathogens resistant to antimicrobial agents and the volumes of those agents used at national, regional, hospital and community level for timely feed back regarding the development of antimicrobial resistance;
5. to keep matters covered by this Recommendation under review, with a view to its revision and updating, and submit an annual report to the Council on the basis of Member States' annual reports;
6. to strengthen participation of applicant countries within the framework of the Network on epidemiological surveillance and control of communicable diseases in the Community, to ensure that the problems of antimicrobial resistance are properly taken into account by these States.

Done at Brussels,

*For the Council  
The President*