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DRAFT REPORT

on the Microbial Challenge - Rising threats from Antimicrobial Resistance (2012/2041(INI))

Committee on the Environment, Public Health and Food Safety

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MOTION FOR A EUROPEAN PARLIAMENT RESOLUTION

on the Microbial Challenge - Rising threats from Antimicrobial Resistance

(2012/2041(INI))

The European Parliament,

– having regard to the Council conclusions of 22 June 2012 on 'The impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective',

– having regard to the Commission communication of 15 November 2011 on an action plan against the rising threats from antimicrobial resistance (COM(2011)0748),

– having regard to the Commission recommendation of 27 October 2011 on the research Joint Programming Initiative 'The Microbial Challenge – An Emerging Threat to Human Health' (C(2011)7660),

– having regard to its resolution of 27 October 2011 on the public health threat of antimicrobial resistance,[1]

– having regard to its resolution of 12 May 2011 on antibiotic resistance,[2]

– having regard to the staff working paper of the Commission's services of 18 November 2009 on antimicrobial resistance (SANCO/6876/2009r6),

– having regard to the Joint Technical Report by the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) of 17 September 2009 on 'The bacterial challenge: time to react – A call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents'[3],

– having regard to the second joint report of the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) of 14 March 2012 on antimicrobial resistance in zoonotic bacteria affecting humans, animals and food,[4]

– having regard to the 2876th Council Conclusions of 10 June 2008 concerning Antimicrobial resistance,

– having regard to the 2980th Council Conclusions of 1 December 2009 concerning innovative incentives for effective antibiotics,

– having regard to the Council recommendation of 9 June 2009 on patient safety, including

[1] Texts adopted, P7_TA(2011)0473.
[2] Texts adopted, P7_TA(2011)0238.
[3] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/11/WC500008770.pdf
[4] http://www.efsa.europa.eu/en/efsajournal/pub/2598.htm EFSA Journal 2012;10(3):2598 [233 pp.].

the prevention and control of healthcare-associated infections,[1]

– having regard to the second revision of the WHO list of critically important antimicrobials for human medicine (report of the first meeting of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance [AGISAR], Copenhagen, 2009),

– having regard to the second report from the Commission to the Council of 9 April 2010 on the basis of Member States' reports on the implementation of the Council recommendation (2002/777/EC) on the prudent use of antimicrobial agents in human medicine[2], and to the Commission staff working document accompanying that report[3],

– having regard to Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition prohibiting the use of antibiotic growth promoters[4],

– having regard to the Council recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine[5] (2002/77/EC) and to the European Parliament resolution of 23 October 2001 on the proposal for that recommendation (COM(2001)0333),

– having regard to the Commission communication of 20 June 2001 on a Community strategy against antimicrobial resistance (COM(2001)0333),

– having regard to its resolution of 5 May 2010 on evaluation and assessment of the Animal Welfare Action Plan 2006-2010,[6]

– having regard to the recommendations for future collaboration between the US and EU of the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR),[7]

– having regard to the CODEX Alimentarius Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance,[8]

– having regard to Rule 48 of its Rules of Procedure,

– having regard to the report of the Committee on Environment, Public Health and Food Safety and the opinion of the Committee on Agriculture and Rural Development (A7–0000/2012),

A. whereas the development of drug resistance is a natural and unavoidable consequence of antimicrobial treatment; whereas this process can be accelerated by inordinate and indiscriminate use in human and veterinary medicine, which, combined with insufficient hygiene and infection control, can compromise the effective use of an already limited

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[1] OJ C 151, 3.7.2009, p.1.
[2] http://ec.europa.eu/health/antimicrobial_resistance/docs/amr_report2_en.pdf
[3] http://ec.europa.eu/health/antimicrobial_resistance/docs/cswd_technicalannex_en.pdf
[4] OJ L 268, 18.10.2003, p. 29.
[5] OJ L 34, 5.2.2002, p.13
[6] Texts adopted, P7_TA(2010)0130.
[7] http://ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf
[8] CAC/GL 77- 2011

number of existing antimicrobials;

B. whereas resistance to antibiotics for certain bacteria is as high as 25 % or more in several Member States;

C. whereas in the EU, Iceland and Norway alone antimicrobial resistant bacteria cause some 400 000 infections and 25 000 deaths annually, with at least EUR 1.5 billion spent on extra healthcare costs and productivity losses;

D. whereas the rise of antimicrobial resistance (AMR) is a complex issue driven by a variety of interconnected factors; whereas individual intervention measures will have minimal effect;

E. whereas there is a growing gap between rising AMR and the development of new antimicrobials; whereas since the 1970s only three new systemically-administered antibiotics for multidrug-resistant Gram-positive bacteria[1] have been developed; whereas two-thirds of antimicrobial resistance-related deaths in the Union are due to Gram-negative bacteria, with no new agents planned to enter the market soon;

F. whereas, given the lack of new antibacterial drug development, it is of paramount importance that the effective exploitation of existing antimicrobials is maintained for as long as possible via infection spread prevention, vaccinations, alternative treatments, prudent use and controlled antimicrobial dosage;

G. whereas there is a link between antimicrobials use in animals and the spread of resistance in humans, which requires further research; whereas there is a need for a coordinated, multisectoral policy approach to AMR targeting both practitioners and users in each sector;

H. whereas there is still a lack of sufficiently detailed and comparable data at European level for purposes of comprehensive cross-country monitoring and analysis linking antimicrobial use and resistance;

1. Considers that, while almost all Member States have developed national AMR strategies, progress with regard to meeting set objectives has been slow and uneven; calls for firm governmental commitment to full and timely implementation at national level;

Prudent use of antimicrobials in human and veterinary medicine

2. Underlines that the key objective of any AMR strategy is to maintain the efficiency of existing antimicrobials by using them responsibly at the correct therapeutic level only when strictly prescribed over a limited time at the appropriate dosage, and reducing the use of antimicrobials in general and especially of Critically-Important Antimicrobials (CIAs)[2] in human and veterinary medicine;

[1] Refers to the retention or rejection of the violet colour of the stain used in Gram's method of staining micro-organisms; the staining property is a common method of classifying bacteria.
[2] Report of the first meeting of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR), Copenhagen, 2009.

3. Stresses that more efforts are needed to control the use of antimicrobials in the veterinary sector; strongly disapproves of the uncontrolled prophylactic use of antimicrobials in animal husbandry;

4. Calls on the Commission to come up with a legislative proposal for the veterinary sector to limit the use of third- and fourth-generation CIAs for humans; stresses that any such proposal must be founded on evidence-based European guidelines on the prudent use of antimicrobials in veterinary medicine;

5. Calls on the Commission to maintain its renewed momentum and publish its progress report on implementation of the AMR Action Plan by the end of 2013;

6. Calls on the Commission to assess and monitor Member States' implementation of the relevant European legislation on antimicrobials, especially with regard to the prescription-only use of antibiotics and the ban on antimicrobials as growth promoters in animal feed;

Prevention

7. With a view to limiting the use and easy availability of antimicrobial agents, welcomes Member States' initiatives to review the legal status of all oral, inhaled and parenteral antibiotics (namely antimalarial, antiviral and antifungal drugs) that remain available to patients without a prescription;

8. Notes the important role of vaccines in limiting the development of AMR by reducing the amounts of antimicrobial agents required to treat infections;

9. Calls on the Commission to devise and promote prudent use guidelines aimed at reducing non-essential and inappropriate exposure to antimicrobials in human and veterinary medicine, livestock farming, agriculture, aquaculture and horticulture;

Development of new antimicrobials or alternatives for treatment

10. Calls on the Commission and the Member States to encourage efforts to develop new and innovative public-private partnership (PPP) business models that delink investment in R&D for new antibiotics and diagnostic tools from sales transactions, in order to promote greater access and affordability and limit the unnecessary use of antimicrobials;

11. Highlights the need to be restrictive with the use of CIAs and newly developed antimicrobial agents and technologies for use in human and veterinary medicine; stresses the importance of appropriately targeting the use of CIAs to specific cases;

12. Calls on the Commission and the Member States to examine new regulatory approaches, including transferable intellectual property rights and patent term extensions, with a view to encouraging private-sector investment in antimicrobial development;

Monitoring and reporting

13. Calls on the Commission and Member States to seek greater cooperation and coordination on the early detection of pathogenic antimicrobial resistant bacteria in humans, animals, fish and foodstuffs in order to continuously monitor the extent and growth of AMR;

14. Stresses the importance of establishing an effective European network of national surveillance systems in the human health and veterinary sectors in order to facilitate the compilation of clear, comparable, transparent and timely reference data on antimicrobial drug usage; believes this should be based on the existing monitoring networks operated by EFSA, the ECDC European Surveillance of Antimicrobial Consumption Network (ESAC-net), the ECDC European Antimicrobial Resistance Surveillance Network (EARS-net), and the EMA European Surveillance of Veterinary Antimicrobial Consumption (ESVAC);

Communication, education and training

15. Notes that the encouragement of appropriate antimicrobial use depends on a change of attitude and practice among patients, farmers and practitioners in the spheres of veterinary and human medicine; considers that more effective and continuous educational and training measures should be taken at both national and European level;

16. Welcomes the annual European Antibiotic Awareness Day (18 November) instituted to promote the responsible use of antimicrobials; considers, however, that its visibility and potential could be more effectively maximised through coordinated, innovative and high-impact campaigns based on the experience derived from successful European and international initiatives;

17. Calls on the Commission to compile a best practice list with regard to the implementation of effective communication campaigns and professional training courses aimed at raising AMR awareness;

International cooperation

18. Highlights that burgeoning international travel and, more significantly, global food and feed trade could increase the crossborder spread of AMR; believes that concerted and timely international action that avoids overlap and builds critical mass is the only way forward in minimising the threat to public health that AMR poses globally;

19. Acknowledges the importance of adopted international initiatives by the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), the Food and Agriculture Organization (FAO), and other relevant global organisations; stresses, however, the importance of global adherence to adopted international standards and guidelines; calls on the Commission, in its evaluation of the implementation of the current AMR Action Plan, to report on Member States' progress on key international AMR commitments;

20. Welcomes the establishment of the TATFAR and the set of recommendations, adopted in September 2011, for future EU-US cooperation; stresses, in particular, the importance of specific actions for:

- comparable data collection and data sharing for veterinary antimicrobials;

- the development of common blueprints based on best practice for the management of healthcare-associated infections;

- enhanced cooperation between the US Food and Drug Administration and EMA on coordinated approaches facilitating antibacterial drug development and regulation, specifically with regard to the clinical trials stage;

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21. Instructs its President to forward this resolution to the Council, the Commission and the Member States.

EXPLANATORY STATEMENT

Since the discovery of penicillin, in the 1930s, antimicrobials have revolutionised medical and veterinary practice, leading to significant reductions in the mortality rate from a wide range of serious and often fatal bacterial infections while paving the way for innovative invasive surgeries to enter widespread use. The extraordinary medicinal progress of the antibiotic era, however, risks being undermined by the growing threat of antimicrobial resistance (AMR).

AMR is the ability of a microbial organism to flourish and survive in the presence of an antimicrobial at a usually sufficient dosage to inhibit or kill microorganisms of the same species. As a result, antimicrobial organisms may develop a profound resistance to certain antimicrobial agents to which they are ordinarily sensitive[1].

After eighty years of widespread use, the evolution and adaptation of disease-causing microbes has resulted in many antimicrobials losing their effectiveness. This nascent crisis is a consequence of two fundamental and related issues: the inappropriate use of antimicrobials in human and veterinary medicine, and a forty-year innovation gap in the development of novel antimicrobials due to low returns on R&D investments.

The issue of AMR has been further exacerbated by the emergence of multi-drug resistance in some bacterial organisms, which can counteract the effectiveness of a variety of unrelated antimicrobials and compromise treatment choices for both humans and animals, prolong recovery, or lead to treatment failure.

While many are familiar with very difficult- to-treat MRSA (Methicillin-resistant Staphylococcus aureus) bacterium, which is commonly spread by patients moving between hospitals, the list of multi-drug resistant infections is long and includes among others, urinary tract infections, pneumonia, and tuberculosis. According to the World Health Organization (WHO), there are at least 440,000 individual cases of multi-drug resistant tuberculosis across the globe, resulting in more than 150, 000 deaths annually[2].

Unsurprisingly, European healthcare systems are already shouldering increased expenditures resulting from antimicrobial resistant infections. Not only are the costs of the drugs needed to treat these cases often high, but also treatment plans are longer and more complex. According to the WHO and the European Centre for Disease Control (ECDC), in 2007 drug-resistant infections resulted in more than 2.5 million additional days of hospitalisation in the EU, Norway, and Iceland[3], and 25,000 extra fatalities in the same region[4]. Without concerted efforts to address the growing problem of antimicrobial resistance, these figures are expected to increase significantly in the coming years.

Moreover, modern-day medical practices are accelerating the emergence of drug-resistant organisms, namely through the improper use of antimicrobials; including excessive and

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1 http://www.vmd.defra.gov.uk/pdf/leaflet_antimicrobials.pdf
2 http://www.who.int/mediacentre/factsheets/fs194/en/
3 http://whqlibdoc.who.int/publications/2012/9789241503181_eng.pdf
4 http://www.ecdc.europa.eu/en/aboutus/organisation/Director%20Speeches/20120314_AMR_presentation_Copenhagen_EUpresidency.pdf

irresponsible dosages, intake of poor-quality antibiotics, and failure to complete a full treatment cycle as prescribed by a qualified physician. This wasteful consumption of antimicrobial agents is compounded by the link between their use in animal husbandry and the spread of resistance in humans.

All bacteria possess an innate flexibility that enables them to evolve genes that render them resistant to any antimicrobial, and by eradicating susceptible bacteria, antimicrobials provide selective pressures that favour overgrowth of bacteria carrying a resistance gene. The prolonged use of antimicrobial agents therefore serves to encourage the wide-spread dissemination of resistant strains.

The problem is amplified by a notable decline in the development of new antimicrobials. While the list of drug-resistant microbes continues to increase, there are relatively few - and for some evolving drug-resistant organisms no - new antimicrobials being developed. As a result, the trend of infections becoming increasingly difficult to treat is set to become more severe without coordinated prevention and control measures to counter antimicrobial resistance.

The implications are highly alarming; antimicrobials that cost tens of millions of euros in R&D, and take close to a decade to reach the market, tend to have an ever-decreasing life span in which they are effective. As resistance spreads, an antimicrobial's lifespan diminishes, and as fewer new antimicrobials become available, the gulf between infection and control grows ever wider. According to the WHO, AMR threatens a return to 'the pre-antibiotic era'.[1]

The borderless nature of infectious diseases makes the rise of drug-resistant microbes a global problem, and it must be dealt with as such. It remains crucial, however, that the EU takes concerted action to address this issue. Over the past decade, European Council conclusions and European Parliament resolutions have all repeatedly called for the prudent use of existing antimicrobials, and to foster initiatives aimed at the development of new ones. It is the rapporteur's belief that these conclusions and resolutions must finally, and urgently, be acted upon, both by Member States and by the EU as a whole.

It is important to stress that AMR cannot be resolved by one simple solution. Rather, a multifaceted approach is required:

Prudent use of antimicrobials in human and veterinary medicine
First and foremost, it is imperative to ensure the prudent use of antimicrobials. This includes the prescription-only use of antibiotics by a physician and refraining from using antibiotics unnecessarily, such as for the treatment of common human viral-infections; similar prudent use must be applied throughout the veterinary sector. To this end, both the Commission and Member States whole must work together to develop compatible strategic action plans to promote prudent use.

Prevention
It is essential that better measures be taken to prevent both the emergence and the spread of drug-resistance. This includes improved monitoring and reporting of drug-resistance

[1] http://www.who.int/mediacentre/factsheets/fs194/en/

organisms, as well as more effective infection control measures, including the use of vaccinations.

Development of new antimicrobials or alternatives for treatment
While it is essential to limit the emergence of resistant drugs, it is also necessary to foster the development of new antimicrobial agents. One way forward can be through public-private partnerships; however, it is also important to examine new regulatory approaches that can stimulate industry research and the development of novel antimicrobials while at the same time ensuring patient safety.

Monitoring and reporting
Effective action requires accurate and timely data from all Member States. It is therefore important to have Europe-wide surveillance in both the human health and the veterinary sectors. One problem requiring particular attention is the need for clear, comparable, transparent and timely reference data on antimicrobial drug usage across all Member States.

Communication, education and training
The exchange of best practices, together with better communication, education, and training among practitioners in both the veterinary and human health sectors is needed to combat the rise in antimicrobial resistance. In addition, improved communication of information on this issue to the public is essential to ensure prudent use by patients.

International cooperation
Given the borderless nature of the spread of infectious it is imperative that the issue be dealt with on the international level. The work undertaken by the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) presents an excellent model for international cooperation on AMR, and similar multilateral and bilateral commitments should be encouraged.