

## The global threat of antimicrobial resistance: science for intervention

I. Roca<sup>1</sup>, M. Akova<sup>2,25</sup>, F. Baquero<sup>3</sup>, J. Carlet<sup>4</sup>, M. Cavaleri<sup>5</sup>, S. Coenen<sup>6</sup>, J. Cohen<sup>7</sup>, D. Findlay<sup>8</sup>, I. Gyssens<sup>9</sup>, O. E. Heur<sup>10</sup>, G. Kahlmeter<sup>11,25,26</sup>, H. Kruse<sup>12</sup>, R. Laxminarayan<sup>13,14</sup>, E. Liébana<sup>15</sup>, L. López-Cerero<sup>16</sup>, A. MacGowan<sup>17,26</sup>, M. Martins<sup>18</sup>, J. Rodríguez-Baño<sup>19,25</sup>, J.-M. Rolain<sup>20</sup>, C. Segovia<sup>21</sup>, B. Sigauque<sup>22</sup>, E. Tacconelli<sup>23,25</sup>, E. Wellington<sup>24</sup> and J. Vila<sup>1,25</sup>

1) ISGlobal, Barcelona Ctr. Int. Health Res. (CRESIB), Hospital Clínic—Universitat de Barcelona, Barcelona, Spain, 2) Department of Medicine, Section of Infectious Diseases, Hacettepe University School of Medicine, Ankara, Turkey, 3) Department of Microbiology at the Ramón y Cajal University Hospital, Ramón y Cajal Institute for Health Research (IRYCIS), Division for Research in Microbial Biology and Evolution, CIBERESP, Madrid, Spain, 4) Fondation Hôpital St. Joseph, Paris, France and World Alliance Against Antibiotic Resistance (WAAAR), Creteil, France, 5) European Medicines Agency (EMA), London, UK, 6) Laboratory of Medical Microbiology, Vaccine and Infectious Disease Institute (VAXINFECTIO), Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium, 7) Brighton and Sussex Medical School, Brighton, 8) Global Commercial Lead, GlaxoSmithKline (GSK), London, UK, 9) Department of Medicine, Radboud University Medical Center and Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands, 10) European Centre for Disease Prevention and Control (ECDC), Stockholm, 11) Clinical Microbiology, Central Hospital, Växjö, Sweden, 12) WHO Regional Office for Europe, UN City, Marmorvej, Copenhagen, Denmark, 13) Center for Disease Dynamics, Economics and Policy, Washington, DC, 14) Princeton University, Princeton, NJ, USA, 15) Scientific Unit on Biological Hazards, European Food Safety Authority (EFSA), Parma, Italy, 16) Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena, Seville, Spain, 17) Department of Medical Microbiology, Southmead Hospital, Bristol, UK, 18) School of Public Health, Physiotherapy and Population Science, UCD Centre for Food and Safety, Molecular Innovation and Drug Discovery, University College Dublin, Dublin, Ireland, 19) Unidad Clínica de Enfermedades Infecciosas y Microbiología, Hospital Universitario Virgen Macarena, and Departamento de Medicina, Universidad de Sevilla, Seville, Spain, 20) Aix-Marseille Université, Unité de Recherche en Maladies Infectieuses et Tropicales Emergentes (URMITE), Inserm, IHU Méditerranée Infection, Faculté de Médecine et de Pharmacie, and APHM, CHU Timone, Pôle Infectieux, Marseille, France, 21) Instituto de Salud Carlos III, ISCIII, Madrid, Spain, 22) Centro de Investigação em Saúde da Manhica and Instituto Nacional de Saúde/Ministério de Saúde, Maputo, Mozambique, 23) Division of Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany, 24) School of Life Sciences, University of Warwick, Coventry, UK, 25) ESCMID Executive Committee, Basel, Switzerland and 26) EUCAST Steering Committee, Växjö, Sweden

### Abstract

In the last decade we have witnessed a dramatic increase in the proportion and absolute number of bacterial pathogens resistant to multiple antibacterial agents. Multidrug-resistant bacteria are currently considered as an emergent global disease and a major public health problem. The B-Debate meeting brought together renowned experts representing the main stakeholders (i.e. policy makers, public health authorities, regulatory agencies, pharmaceutical companies and the scientific community at large) to review the global threat of antibiotic resistance and come up with a coordinated set of strategies to fight antimicrobial resistance in a multifaceted approach. We summarize the views of the B-Debate participants regarding the current situation of antimicrobial resistance in animals and the food chain, within the community and the healthcare setting as well as the role of the environment and the development of novel diagnostic and therapeutic strategies, providing expert recommendations to tackle the global threat of antimicrobial resistance.

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**Keywords:** Antibiotic consumption, antibiotic resistance, antibiotic stewardship, antibiotics as growth promoters, drug discovery, infection control measures, multidrug resistant bacteria, self-medication, surveillance, wastewater treatment plants

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**Corresponding author:** J. Vila, Department of Clinical Microbiology, Hospital Clinic, Villarroel 170, 08036, Barcelona, Spain  
**E-mail:** [jvila@ub.edu](mailto:jvila@ub.edu)

## Facing the problem

In the last decade we have witnessed a dramatic increase both in the proportion and absolute number of bacterial pathogens presenting multidrug resistance to antibacterial agents. Organizations such as the US Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) are considering infections caused by multidrug-resistant (MDR) bacteria as an emergent global disease and a major public health problem.

The emergence of resistant microorganisms, either by mutations or the acquisition of mobile genetic elements carrying resistance genes, may take place irrespective of the presence of antibacterial agents. It is the exposure to these drugs what provides the necessary selective pressure for the rise and spread of resistant pathogens. Therefore, the driving force behind the increasing rates of resistance can ultimately be found in the abuse and misuse of antibacterial agents, whether used in patients and livestock or released into the environment. This is no longer a medical issue. Antimicrobial resistance has become a global health threat that will require the coordinated action of many different stakeholders to tackle antibiotic resistance at its very root.

The aim of the meeting organized jointly by B-Debate (Bio-Cat) and the Barcelona Institute for Global Health (ISGlobal) in partnership with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Spanish Network for Research in Infectious Diseases (REIPI) was to generate debate among the main stakeholders (i.e. policy makers, public health authorities, regulatory agencies, pharmaceutical companies and the scientific community at large) and come up with a coordinated set of strategies to fight antimicrobial resistance in a multifaceted approach. The meeting focused on three major areas: antimicrobial resistance in animals and the food chain; in the environment and the community; and within the healthcare setting. Also discussed was the lack of new therapeutic options.

## Antimicrobial resistance in animals and the food chain

The widespread use of antimicrobial agents in animals and the food chain constitutes an important source of antimicrobial

resistance, although the impact of such use on human health remains controversial [1]. Massive amounts of antibiotics have been used as growth promoters as well as for prophylaxis and the treatment of infections among farm animals and in aquaculture, increasing the selective pressure on both commensal and pathogenic microorganisms that can spread to humans through direct contact and via the food chain or indirectly from the environmental pollution of farm effluents [2].

Interventions to limit the emergence and spread of resistant bacteria in the animal setting may include the following: (a) banning antibiotic use as growth promoters and limiting its use for other nontherapeutic applications, (b) reducing the dissemination of MDR bacteria through the food chain by improving farm biosecurity and developing alternative treatment strategies and increasing hygienic conditions and practices along the food chain, (c) developing education programs, mainly directed at veterinarians, farmers, and food handlers and (d) linking surveillance systems on antibiotic resistance established for humans and animals.

The European Food Safety Authority (EFSA) is playing an essential role in detecting emerging risks in the area of MDR bacteria within the food industry. Several proposals have been made by EFSA for the harmonization of monitoring and reporting of resistant bacteria, such as: (a) agreeing a comprehensive set of antibacterial agents to be included in the monitoring plans, (b) reinforcing antimicrobial resistance monitoring in sentinel bacteria, (c) conducting active monitoring programs in healthy animals based on randomized sampling plans and (d) harmonizing of epidemiological values [3].

Antibiotics that have become critical for human health should be clearly identified and their use restricted to humans only in order to avoid cross-resistance. In this respect, the WHO has established a list of essential antimicrobial agents for human use to be avoided in nonhuman interventions [4]. Compliance with the WHO recommendations, however, is neither mandatory nor regulated. WHO has also initiated different collaborative programs to tackle foodborne antimicrobial resistance through the promotion of national coordination and integrated surveillance, prevention and control of antibiotic resistance in the food chain and the improvement of awareness on antibiotic use and risk of resistance among veterinarians and the food industry.

## Antimicrobial resistance within the community

Antimicrobial resistance in the community has steadily been increasing during the last decades, especially regarding resistance to quinolones, carbapenems and third-generation

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