

Only through rational use of medicines will we keep life-saving antibiotics for future generations ...

... ReAct Now!

We need a strong Resolution on the Rational Use of Medicines at the World Health Assembly in May.

Antibiotics have saved millions of lives, but are losing their effectiveness because of the increase of antibiotic resistant bacteria.

- the use of antibiotics has contributed to the dramatic decline in global mortality and morbidity from infectious diseases over the last 50 years.¹ But the use of these drugs is also the key driver of resistance.^{2,3} An important reason for antibiotics losing their effectiveness is due to their widespread irrational use, either wrongly selected, not needed at all, or taken in courses cut short by the expense of these drugs. We are witnessing the emergence of diseases such as extremely drug resistance tuberculosis and multiply-resistant blood stream infections caused by Gram negative bacteria for which health systems are ill-prepared and our drug armamentarium inadequate.

Rational use of medicines is essential to responding to this public health challenge. Health care providers, pharmacists, consumers, and communities all over the world need to be supported to be more independent and knowledgeable about prescribing, recommending or matching medicines to people's needs.

People are dying from infections because of the lack of effective therapy. The appropriate treatment may be delayed when second-line antibiotics are not used initially or in time for a resistant infection.

Significant numbers of people globally are at risk from antibiotic resistant bacteria NOW. The most vulnerable are malnourished children, the immunocompromised, and the elderly.

- in South Asia alone, estimates show that one newborn baby dies every second minute due to treatment failure caused by antibiotic resistance causing over 300,000 excess deaths from neonatal sepsis in this region,^{4,5}
- about 3 million women are at risk of impaired fertility following failure in treatment of gonorrhoea,⁶
- mortality due to blood infections with methicillin resistant Staphylococci (MRSA) can be almost double that compared with non-resistant strains,⁷
- in Israel, 3% of all hospital mortality has been estimated to be caused by multiresistant Gram negative bacteria.⁸

Antibiotic resistance imposes significant costs on the health care system due to increased reliance on more expensive second-line therapy and delay of appropriate treatment.

- the use of antibiotics other than first-line treatment may increase costs 100-folds, making them unaffordable for many governments and patients,
- outpatient costs stemming from antimicrobial resistance in the United States are estimated to lie between US\$400 million and US\$18.6 billion, and inpatient costs are likely to be several times higher,⁹
- a full course to treat multidrug-resistant tuberculosis in the northwest province of South Africa would cost Rand 26,354 (approximately US\$4300) in contrast to the treatment for susceptible TB for Rand 215 (approximately US\$35),¹⁰
- to treat drug-resistant neonatal sepsis in South Asia with second-line antibiotic therapy would cost an additional US\$120 million per year.⁴

Globalization carries antibiotic resistance across the world. Effective surveillance and monitoring systems are key to protecting the public's health.

The global widespread use and misuse of antibiotics are making these drugs ineffective at a worrying pace. In addition, bacteria that have become resistant are rapidly spreading, facilitated through poor hygiene and infections control, and human mobility. Regular monitoring of drug use and resistance are vital for producing treatment guidelines for bacterial diseases to minimize the risk for treatment failure

Rational use will require better diagnostics and new drugs to treat resistant infections

- only two new classes of antibiotics have been brought to the market in the past 30 years. It is already clear that new treatments are needed for hospital-acquired Gram-negative bacterial infections, for community-acquired resistant infections, and for infections common in developing countries such as tuberculosis and typhoid fever,
- rapid diagnostics would help rational use and prolong the lifespan of available drugs.

ReAct believes that rational use of medicines is a key intervention in combating antimicrobial resistance and supports the WHO Executive Board to forward a strong resolution on the rational use of medicines to the 60th World Health Assembly that:

- *ensures national coordination and monitoring of the use of medicines.* It is important to restore the language lost in the draft resolution between EB118/6 (11 May 2006) and EB120/7 (7 December 2006). Specifically, the resolution should call for the establishment of national programmes for monitoring the use of medicines and coordinating implementation of strategies to promote rational use of medicines. WHO, especially by strengthening regional expert staff, should assume the responsibility for providing the necessary technical support to Member States and to these national coordinating bodies, along with non-governmental organization partners, to accomplish these ends,
- *draws on a full range of potential strategies for implementation.* Of note, WHO found in three separate, independent prioritization exercises (Eastern Mediterranean Regional Office, South East Asia Regional Office, and health officials in Nepal) that five highly feasible interventions were consistently given priority for antimicrobial resistance: “(1) conducting educational interventions, e.g., training prescribers and dispensers and preparing guidelines and formularies; (2) training undergraduates and postgraduates on antimicrobial resistance; (3) establishing infection control committees and guidelines for antimicrobial use; (4) developing national drug policies, essential drug lists, and standard treatment guidelines; and (5) ensuring drug quality”.¹¹ In the broader context of rational use of medicines, we support not only these measures, but also drug and therapeutic committees, promoting systems of supervision, audit and feedback, making continuing medical education a requirement of licensure, and avoiding perverse financial incentives. The range of interventions should recognize the importance of financing drugs and the impact of methods of provider payment on rational use. Such measures would create an enabling environment for combating antimicrobial resistance,
- *supports research, piloting and implementation of various approaches to national monitoring systems for rational use of medicines.* The emphasis of such monitoring systems should be on actionable data, and might be developed in collaboration with existing monitoring efforts at national level, where local data help to determine the selection of optimal first-line therapy (e.g. the HIV ResNet), or international level such as the Health Action International/WHO Medicine Prices Project,
- *calls for improved and novel approaches to stimulate innovation for diagnostics, new antibacterials, and their combinations as well as other drugs and vaccines that address public health priorities, so that rational use of medicines remains possible.* Effective antibacterial drugs must be available. The R&D pipeline for new antibacterials is troublingly inadequate. Complementary technologies, diagnostics and vaccines, will also improve the rational use of medicines. Health care workers require at their disposal effective diagnostics for determining pharmacotherapy,
- *provides a floor budget of no less than USD 30 million over six years to implement effectively this resolution.* The figure of USD 30 million over six years is minimum commitment and based on the WHO’s own estimate last May of the resources required for carrying out the original draft resolution (EB118/6 Add.1, 11 May 2006). Considering the economic costs of antimicrobial resistance alone and the potential gains from improved rational use of antibiotics, this would be a very cost-effective investment.

ReAct also calls upon the WHO to report back to the 60th World Health Assembly on its resolution, “Improving the containment of antimicrobial resistance” (WHA58.27, Agenda item 13.10) and regular reporting thereafter.

Importantly, this report back should emphasize what has or has not been accomplished in the last two years in the area of **antibacterial drug resistance**, not just HIV/AIDS, TB and malaria. The role of antimicrobial resistance in the larger context of WHO activities planned to support rational use of medicines should also receive specific attention. Plans for improved coordination of these activities within WHO and a “State of Antimicrobial Resistance Report” would be welcomed.

References:

1. WHO Report on Infectious Diseases. Geneva: World Health Organization, 2000. Available from: www.who.int
2. Rubin MA, Samore MH. Antimicrobial Use and Resistance. *Curr Infect Dis Rep.* 2002 Dec; 4(6): 491-497.
3. Bronzwaer SL, Cars O, Buchholz U, Molstad S, Goettsch W, Veldhuijzen IK, Kool JL, Sprenger MJ, Degener JE. European Antimicrobial Resistance Surveillance System. A European study on the relationship between antimicrobial use and antimicrobial resistance. *Emerg Infect Dis.* 2002 Mar; 8(3): 278-82.
4. Bhutta Z, 2006, Personal communication/manuscript in process
5. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. *Lancet.* 2005 Mar 26-Apr 1; 365(9465): 1175-88.
6. Tapsall, J.W. What is the economic burden imposed by antimicrobial resistance in *Neisseria gonorrhoeae*? Draft paper presented for discussion at the React seminar in September 2005
7. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis.* 2003 Jan 1; 36(1): 53-9.
8. Carmeli Y. Estimating nationwide Mortality Attributable to bacteremia by Multidrug (MDR) Gram Negative Pathogens (GMR) in Israel. in 46th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). 2006. San Francisco: American Society of Medicine; Abstract no. L-1538
9. Okeke IN, Laxminarayan R, Bhutta ZA, et al. Antimicrobial resistance in developing countries. Part I: recent trends and current status. *Lancet Infect Dis* 2005; 5: 481-93.
10. Hensher M. Budget planning assistance for north west province. TB and HIV/AIDS/STD programmes. Final report, 1999 as cited in Okeke IN, Laxminarayan R, Bhutta ZA, et al. Antimicrobial resistance in developing countries. Part I: recent trends and current status. *Lancet Infect Dis* 2005; 5: 481-93.
11. Okeke IN, Klugman KP, Bhutta ZA, et al., Antimicrobial resistance in developing countries. Part II: Strategies for containment. *Lancet Infect Dis* 2005; 5: 568-80.