

To the Members of the EU-US Transatlantic Task Force:

It is with great hope and expectations that we, *ReAct--Action on Antibiotic Resistance* (www.reactgroup.org), welcome the efforts of the EU-US Taskforce on antimicrobial resistance announced during the Swedish EU Presidency in the fall of 2009. *ReAct* links a wide range of individuals, organizations and networks committed to respond to antibiotic resistance. Our vision is that current and future generations of people around the globe will have access to effective treatment of bacterial infections. This urgent challenge, particularly of bacterial resistance, requires concerted action and strong leadership. We are convinced that the EU and the US together with the WHO can provide this leadership and initiate the global action necessary to respond to this urgent problem.

Supported by Sida (the Swedish International Development Cooperation Agency), ReAct has:

- Worked to raise the policy profile of antibiotic resistance among developing countries by holding regional dialogues on this issue in Africa, Asia and Latin America and launching a web portal on antibiotic resistance on SciDev.Net, a science and development gateway mostly reaching those in the developing world;
- Provided leadership on both the Antimicrobial R&D and Rational Use working groups of the WHO / World Alliance for Patient Safety's process to develop a strategy for tackling antimicrobial resistance;
- Partnered with the Ecumenical Pharmaceutical Network (EPN) in launching the "Fight AMR: Save Medicines for Our Children" campaign at the 2009 World Health Assembly, efforts building on the USAID-ReAct-EPN co-sponsored workshop on antibiotic resistance in Moshi, Tanzania in 2008;
- Seeded a vibrant grassroots Latin American network centered at the University of Cuenca Medical School in Ecuador, whose partnership with the Pan-American Health Organization is developing a graduate-level curriculum for healthcare providers on antibiotic resistance; and
- Supported the Swedish EU Presidency in organizing the September 2009 Stockholm conference on "Innovative Incentives for Effective Antibacterials."

As the Transatlantic Task Force begins to undertake its important charge, we at ReAct would like to propose potential directions for the Task Force's work.

Connecting the burden of antibiotic resistance to priority setting and action

Antibiotic resistance is a threat to health security that transcends national boundaries. It is a challenge with broad political, social and economic implications. However, no global picture captures the magnitude or trends of antibiotic resistance. The fact that antibiotic resistance spans many diseases makes its consequences less visible in health statistics from any one disease. Building upon the regional work of the European Antimicrobial Resistance Surveillance System and country-level efforts like the CDC's NARMS (National Antimicrobial Resistance Monitoring System) and Strama (The Swedish Strategic Programme Against Antibiotic Resistance), the architecture for a global surveillance and alert system for antibiotic resistance might take shape.

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The Task Force might consider:

- Developing approaches to incorporating surveillance data globally from sentinel sites that allow for timely and locally actionable feedback;
- Providing a framework for assessing the clinical and economic impact of antibiotic resistance in community and hospital-based delivery systems;
- Tap into the signaling potential of monitoring news and activity on the Internet, but go further in tracking trends rather than just outbreaks and identifying prospectively findings that merit true rather than false alarm; and
- Translating surveillance data on antibiotic resistance into metrics for priority setting (e.g., the value of investing in a new diagnostic technology might be measured in terms of numbers of treatments averted).

Appropriate therapeutic use in medical communities

Rational therapeutic use for antibiotics is a cornerstone to conserving the effectiveness of existing antibiotics. Through regional dialogues in Asia, Africa and Latin America, we have come to realize the difficulties of suggesting a one size fits all tool kit of best practices for policy makers and healthcare providers to encourage rational use of antibiotics. We have to move beyond inventories of best practices and checklists. In putting forward such guidance, the Task Force might consider:

- Moving beyond checklist approaches to a more context-sensitive strategy where potential best practices recognize differences in local health systems, cultures and resource levels;
- Aligning economic incentives for rational use of antibiotics, both for providers and patients, through prescription, pricing, and reimbursement practices, again in a manner sensitive to the local context of health care delivery systems; and
- Enabling effective feedback mechanisms that promote rational use of antibiotics and risk management strategies that minimize liability for watchful waiting by healthcare providers; and
- Curbing marketing activities of antibiotics that mispromote the irrational use of antibiotics.

Appropriate therapeutic use in veterinary communities

The transmission of bacterial resistance from animals to humans has prompted concerns over appropriate therapeutic use of these drugs in animal husbandry and efforts to halt the non-therapeutic use of these drugs, particularly for growth promotion. Purchasers and consumers can influence upstream suppliers over their use of antibiotics by conditioning what inputs enter the supply chain. Further approaches to hold accountable the use of antibiotics for rational, therapeutic purposes deserve attention.

ReAct urges the Task Force to consider:

- Identifying effective strategies to control, without jeopardizing the effectiveness of antibiotics for human use, both zoonotic infections and animal diseases endemic in many systems of food animal production;
- Sharing and emulating successful efforts to both phase out certain antibiotic use in livestock, and restrict and track through prescriptions the veterinary use of antibiotics for appropriate therapeutic use;

Examining the supply chain from farm to food outlet for potential intervention points to encourage better antibiotic use (e.g., rapid point-of-use diagnostics to detect food contaminated with pathogenic bacteria and resistant strains); Developing the range of incentives and disincentives, including financial, that might be part of the broader set of measures to encourage better antibiotic use practices in animal husbandry.

Prevention of healthcare drug-resistant infections

Drug-resistant infections worsen health outcomes in both community and hospital settings. From the Institute for Healthcare Improvement's Five Million Lives Campaign to the World Alliance for Patient Safety's Hand Hygiene and Safe Surgery campaigns, various efforts can inform a potential strategy going forward. To mitigate the toll of resistant infections, the Task Force might consider:

- Using a campaign-style approach with measurable goals to mobilize health care institutions and providers to target specific practices that might have the greatest return for infection control;
- Developing continuous quality improvement techniques, alongside guidelines, educational interventions and reporting and learning systems, that could be adapted to a range of community and hospital-based settings, including in resource-limited countries, to improve infection control and appropriate antibiotic use;
- Examining the potential for development and wider adoption of innovative health technologies that might minimize the emergence of antibiotic-resistant infections in the healthcare setting (e.g., medical instrumentation surfaces resistant to bacterial colonization);
- Aligning reimbursement incentives to encourage best practices for infection control; and
- Applying supply chain analysis to studying where and how to overcome information blindspots, stockout problems, and other system-level failures that compound problems of antibiotic resistance.

Strategies to promote innovation for new antimicrobials

While conserving existing antibiotics is key, the dearth of novel antibiotics presents direct consequences. The EMEA-ECDC-ReAct analysis of the pipeline for antibiotics reveals not a single antibiotic with a new mechanism of action in development, and just two with possibly new targets that are active against Gram-negative infections. Reinvigorating this R&D pipeline is essential, but given the potential costs and trade-offs in financing this over other strategies to address antibiotic resistance, the public investment must be made responsibly. This is not a call for throwing every financial incentive at the problem, but one of targeting strategically. Nor is the problem solely financial. There are significant scientific challenges to address.

The preparatory work and productive discussions at the Swedish EU Presidency meeting on "Innovative Incentives for Effective Antibacterials" in Stockholm in September 2009 provides a useful starting point. Responding to this faltering pipeline for health technologies to combat antibiotic resistance, we urge the Task Force to consider:

- In allocating finite public resources for this challenge, that opportunities to develop diagnostics and/or vaccines where appropriate ought not be overshadowed or supplanted by a focus solely on antibacterial drug development. In fact, encouraging co-development of drugs and diagnostics also warrants attention.
- In defining target product profiles for antibacterial drug development, that the focus of R&D incentives be on antibacterial drugs with novel mechanisms of action, not "me too" additions.
- In rethinking the business model for bringing new health technologies to market, that approaches that delink price from R&D costs, thereby making products more affordable in low- and middle-income countries, be developed. Product development partnerships—existing or new—may be required to pilot or test out these approaches.
- In considering fair returns on public investment, that a global perspective taking into account the importance of affordability and access in ensuring rational use, particularly in countries outside Europe and the US.

Next Steps: ReAct/Uppsala University follow-up conference: "The Global Need for Effective Antibiotics: Moving Towards Concerted Action," September 6-8, 2010, in Uppsala, Sweden

Convened under the auspices of the Swedish EU Presidency, the September 2009 conference on "Innovative Incentives for Effective Antibiotics" laid important foundation for these deliberations. The conference and its conclusions now need to be taken further. Moreover, there is an urgent need to expand on the issue and take a global approach in order to stimulate collaborations required for the development of innovations that can supplement current antibiotics and benefit people globally. The Swedish Minister of Health and Social Affairs, Mr Göran Hägglund, and the Swedish Government, consider the AMR issue to be of top priority and support ReAct/Uppsala University in organizing a follow-up conference in order not to lose momentum on this very important issue. The conference is being organized to deepen the discussions from the EU expert conference in 2009 and will address the issue from a global perspective. The conference is set to focus on goals overlapping with the Task Force's charge and could provide input for an innovation strategy targeting both scientific and economic obstacles. The conference will be held in Uppsala, Sweden from September 6-8, 2010. We welcome the participation of all members of the EU-US Task Force to this event.

Our work in ReAct has taught us that antibiotic resistance is a global concern that knows no borders and must be addressed as such. We stand prepared to support the Task Force's efforts in developing concerted action to tackle this threat.

Sincerely,



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