Clinical Infectious Diseases

VIEWPOINTS

Ensuring Antibiotic Development, Equitable Availability, and Responsible Use of Effective Antibiotics: Recommendations for Multisectoral Action

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Antibiotic resistance is a growing threat to global public health. The World Health Organization's Global Action Plan on Antimicrobial Resistance recommends engaging multisectoral stakeholders to tackle the issue. However, so far, few studies have addressed barriers to antibiotic development, equitable availability, and responsible antibiotic use from the perspective of stakeholders outside healthcare facilities or patient communities: the so-called third-party stakeholders. Third-party stakeholders include, *inter alia*, governments, regulatory agencies, and professionals working in antibiotic research and development and medical ethics. This viewpoint provides an overview of barriers to antibiotic development, equitable availability of effective antibiotics, and the responsible use of antibiotics. The barriers were identified in an exploratory, qualitative interview study with an illustrative sample of 12 third-party stakeholders. Recommendations to lift these barriers are presented, together with examples of recently-made progress. The recommendations should guide future antibiotic policies and multisectoral policy action.

Keywords. multisectoral stakeholders; barriers and facilitators; antimicrobial resistance; antibiotic access; antibiotic discovery; global health.

The world is currently facing an antibiotic crisis with the rapid emergence and spread of antimicrobial resistance (AMR), which endangers antibiotic effectiveness and constitutes a substantial clinical and economic burden [1, 2]. In parallel, drug discovery has been struggling with introducing new classes of antibiotics, as mainly drugs belonging to already-existing antibiotic classes have received regulatory approval over the past several decades [3]. In 2016, the United Nations declared AMR a major global health priority [4]. If efforts to safeguard the effectiveness of antibiotics are to be successful, multisectoral stakeholders' perspectives —as advised by the World Health Organization (WHO) [5]—should be considered.

The first stakeholders that come to mind when acknowledging the burden of clinical failure or costs are the prescribers and the patients. So far, barriers to and facilitators of responsible antibiotic use have been extensively studied among prescribers [6, 7] and, to a lesser extent, among patients [8]. These are, however, not the only stakeholders concerned by AMR. Other stakeholders, the so-called third-party stakeholders involved in the process—from drug development to drug regulation and dispensing—are also expected to work actively to solve the issue. The third-party stakeholders include, *inter alia*, governments, regulatory agencies, and professionals working in antibiotic research and development (R&D) and medical ethics.

There is scarce literature addressing barriers and facilitators from the perspective of a broad range of third-party stakeholders. Previously, the economic trade-offs associated with responsible antibiotic use and antibiotic development have been reviewed [9]. Ethical aspects of the equitable access of antibiotics and their responsible antibiotic use have also been addressed [10, 11]. These reviews, however, describe barriers and facilitators from single-sector perspectives (ie, health economics or ethics). In addition, reports from the United Kingdom provide recommendations to tackle AMR based on expert consultation [12].

This viewpoint provides an overview of barriers to antibiotic development, equitable availability of effective antibiotics, and the responsible use of antibiotics, as defined below (Table 1). The barriers were identified in an exploratory, qualitative interview study with an illustrative sample of third-party

Received 14 June 2018; editorial decision 13 September 2018; accepted 20 September 2018; published online September 26, 2018.

Presented in part: The 28th European Congress of Clinical Microbiology and Infectious Diseases, Madrid, Spain, 21-24th April 2018. Abstract P1713.

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Clinical Infectious Diseases® 2019;68(11):1952–9

DOI: 10.1093/cid/ciy824

Table 1. Definitions and Background

Equitable availability	Equitable availability means ensuring that innovative antibiotics are registered and priced affordably across countries with a public health need for them [13].
Responsible antibiotic use	The DRIVE-AB project developed a consensus-based definition of responsible antibiotic use consisting of 22 elements [14]. Fourteen elements correspond to patient-level elements relating to aspects of responsible use of antibiotics: Antibacterial Activity, Antibacterial Spectrum, Documentation, Dosing-PK/PD*-Interval, Duration Indication, Interactions, Microbiological Diagnostics, Patient Compliance, Patient Outcome, Route, Timing, Toxicity and Unintended Consequences. Eight elements were considered societal-level as they relate to responsible antibiotic use in a broader societal context: Access-Availability, Education, Evidence-based Guidelines, Expertise and Resources, Future Effectiveness, Resistance, Resistance Surveillance, and Waste Disposal.
Platform trial	A platform trial is a clinical trial with a single master protocol in which multiple treatments are evaluated simultaneously [15]. Antibiotic platform trials would allow investigators to focus on the disease rather than any particular experimental therapy, and to investigate multiple experimental and control treatments, as a way to handle patient involvement as effectively as possible [16].
Antibiotic shortages	Defined as the unavailability of a specific antibiotic agent as a result of non-supply by the usual producers and wholesalers. Shortages are known to negatively impact antibacterial prescribing policies and expenses [17, 18].
Regulatory harmonization	Regulatory harmonization is the process by which technical guidelines are developed to be uniform across participating authorities [19].
Regulatory convergence	Regulatory convergence represents a process whereby the regulatory requirements across countries or regions become more similar over time as a result of the gradual adoption of internationally recognized technical guidance documents, standards and scientific principles, common or similar practices and procedures, or adoption of regulatory mechanisms that might be specific to a local legal context but that align with shared principles to achieve a common public health goal [19]. It does not necessarily represent the harmonization of laws and regulations.
Education and awareness of the public	The global impact of AMR contrasts with the levels of awareness of this issue among the general public. Taking Europe as an example, only less than a quarter of surveyed Europeans were able to answer four basic questions about antibiotics in 2016, and no progress in knowledge was measured between 2013 and 2016 [20]. Strikingly, at the same time, the wish to be informed on how to use antibiotics was expressed [20]. Suggestions to boost education of the public at an earlier age have been made previously, in view of several decades of only modestly successful post-graduate educational antibiotic stewardship interventions or national campaigns directed towards the general public [21].
Labeling	Regulatory drug labels contain rich and comprehensive information about drug products, such as disease indications, target populations, drug–drug interactions, and adverse drug reactions [22].
One health	A One Health approach, taking into account the connections between human and animal health and the environment, is of paramount importance in efforts to curb AMR [23]. Release of antibiotic-containing wastewater in effluents of drug manufacturers is driving antibiotic selection pressure in the environment [24]. In addition, reducing antibiotic use in animal health should lead to decreased levels of antibiotic residues in the environment and subsequent emergence and spread of AMR in humans [25].

*Pharmacokinetic/pharmacodynamic.

stakeholders. Next, recommendations to lift these barriers are presented, together with examples of recently-made progress.

Equitable Availability

Equitable availability means ensuring that innovative antibiotics are registered and priced affordably across countries with a public health need for them [13].

Responsible Antibiotic Use

The Driving Reinvestment in Research and Development and Responsible Antibiotic Use (DRIVE-AB) project developed a consensus-based definition of responsible antibiotic use, consisting of 22 elements [14]. There are 14 patient-level elements relating to aspects of responsible use of antibiotics: (1) antibacterial activity, (2) antibacterial spectrum, (3) documentation, (4) dosing pharmacokinetic/pharmacodynamic interval, (5) duration, (6) indication, (7) interactions, (8) microbiological diagnostics, (9) patient compliance, (10) patient outcome, (11) route, (12) timing, (13) toxicity, and (14) unintended consequences. There are 8 elements that were considered societal-level, as they relate to responsible antibiotic use in a broader societal context: (1) access/availability, (2) education, (3) evidence-based guidelines, (4) expertise and resources, (5) future effectiveness, (6) resistance, (7) resistance surveillance, and (8) waste disposal.

Platform Trial

A platform trial is a clinical trial with a single master protocol in which multiple treatments are evaluated simultaneously [15]. Antibiotic platform trials would allow investigators to focus on the disease, rather than any particular experimental therapy, and to investigate multiple experimental and control treatments as a way to handle patient involvement as effectively as possible [16].

Antibiotic Shortages

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Regulatory Harmonization

Regulatory harmonization is the process by which technical guidelines are developed to be uniform across participating authorities [19].

Regulatory Convergence

Regulatory convergence represents a process whereby the regulatory requirements across countries or regions become more similar over time as a result of the gradual adoption of internationally-recognized technical guidance documents; standards and scientific principles; common or similar practices and procedures; or regulatory mechanisms that might be specific to a local legal context but that align with shared principles to achieve a common public health goal [19]. It does not necessarily represent the harmonization of laws and regulations.

Education and Awareness of the Public

The global impact of AMR contrasts with the levels of awareness of this issue among the general public. Taking Europe as an example, only less than a quarter of surveyed Europeans were able to answer 4 basic questions about antibiotics in 2016, and no progress in knowledge was measured between 2013 and 2016 [20]. Strikingly, at the same time, the wish to be informed on how to use antibiotics was expressed [20]. Suggestions to provide the public with educational information at an earlier age have been made previously, in view of several decades of only modestly successful, post-graduate, educational antibiotic stewardship interventions or national campaigns directed towards the general public [21].

Labeling

Regulatory drug labels contain rich and comprehensive information about drug products, such as disease indications, target populations, drug–drug interactions, and adverse drug reactions [22].

One Health

A One Health approach, taking into account the connections between human and animal health and the environment, is of paramount importance in efforts to curb AMR [23]. The release of antibiotic-containing wastewater in effluents of drug manufacturers is driving antibiotic selection pressure in the environment [24]. In addition, reducing antibiotic use in animal health should lead to decreased levels of antibiotic residues in the environment and a resulting decrease in the subsequent emergence and spread of AMR in humans [25].

BARRIERS AND FACILITATORS IDENTIFIED THROUGH INTERVIEWS

Barriers were explored using qualitative, individual interviews with third-party stakeholders. A detailed description of the applied methodology is provided in the Supplementary Materials. This study built on the consensus-based definition of responsible human antibiotic use (Supplementary Table 1) developed by the Driving Reinvestment in Research and Development and Responsible Antibiotic Use (DRIVE-AB) project [14]. We conducted 12 interviews with stakeholders representing the following perspectives: antibiotic R&D, health economics, medical ethics, government, health law and bioethics, public health, and regulatory agencies. All participating stakeholders had senior positions at relevant organizations or institutes and experience in the field of antibiotic use and/or stewardship; a short affiliation for each stakeholder is provided in the Acknowledgment section. The interviews were conducted in 2016 and 2017. The barriers and facilitators mentioned in the interviews are explained below and, for each of them, illustrative quotes from the stakeholders are shown in Supplementary Table 2. This study reports opinions and perceptions of an illustrative sample of stakeholders, but these may not be representative of the entire community they portray.

Antibiotic Development

Several scientific barriers were identified during stakeholder interviews. An urgent need for new antibiotics and a robust and sustainable antibiotic pipeline was highlighted. An additional barrier reported by the stakeholders was the uncertainty of future medical needs. Moreover, the need for better drugs (eg, single-dose oral regimens with fewer side effects) was emphasized.

Among economic barriers, many stakeholders reported the lack of sufficient financial incentives for companies to develop new antibiotics. It was stated that the right financial incentives are crucial for innovation. This barrier was also reported to be relevant for the development of new diagnostic tools. New economic models that would partially or fully delink antibiotic sales revenues from their consumption were proposed as a facilitator. The example of a model in which only partial rights of the drug are owned by the company was suggested.

In addition, regulatory barriers were addressed by the stakeholders, including the designs and outcomes of clinical trials. Currently, a new antibiotic is approved for commercialization if it is demonstrated to be at least as effective as an already-commercialized comparator using a non-inferiority trial design. Also, it was pointed out that often, data on older antibiotics and data on real-world situations are lacking, making it hard to establish which treatment is actually the most effective. Moreover, stakeholders reported that this design does not allow for testing additional patient outcomes relevant to physicians and society (eg, clinical response and time to return to work/school). It was also suggested that the patient's perspective should be included as an outcome (eg, patient questionnaires). Stakeholders advocated for the consideration of longer-term patient outcomes and more patient follow-up data (eg, hospital readmissions). The difficulties of designing a trial to test a drug against resistant organisms were highlighted, from identifying patients with the target-resistant bacteria to setting up a trial that is both ethical (patients with severe infection) and feasible (acceptable comparator for that setting). Nonetheless, it was reported that encouraging progress was noticed with recent registration trials.

Equitable Availability of Effective Antibiotics

A reported barrier is antibiotic shortages of off-patent drugs as a direct consequence of high manufacturing costs. High manufacturing costs were also reported as discouraging the production of older antibiotics, which are now back in use due to increasing resistance. Among the most frequently-mentioned barriers to access and availability of antibiotics, especially in lower-income countries, was the affordability and pricing of the antibiotics. The relatively short life-cycle of antibiotics was identified as a barrier to the long-term conservation of antibiotics, which can affect pricing. Examples of suggested facilitators for the affordability of antibiotics, especially in low-income settings, included tiered pricing, a global purchaser, and a global stewardship and access framework. In contrast, the low pricing of generic antibiotics was considered to encourage overuse. Regulatory harmonization was proposed by several stakeholders as a facilitator to improve availability in low-income settings and thereby ensure equal availability across the world. Some of the stakeholders expect this regulatory reform to also stimulate antibiotic R&D.

Responsible Antibiotic Use

Regarding responsible antibiotic usage, stakeholders mentioned the invisibility of antibiotic resistance in the eyes of both the general public and the medical community. Also, the lack of awareness of increasing resistance and the tendency to focus on the benefits of antibiotic treatments rather than on their negative consequences were cited. Other barriers were the lack of recognition of the true societal value of effective antibiotics and the lack of understanding of the high unmet need they represent. Education of both patients and the public was believed to facilitate responsible use. However, reservations on the effectiveness of education were expressed by stakeholders for both target groups. Finally, the difficulties of changing behavior and achieving cultural change were addressed as barriers.

Restricting the overall amount of antibiotic use was reported as a way of facilitating limits to the selection and spread of resistance and of conserving effectiveness, and was reported as the best policy for the future. Preventing the distribution of antibiotics without a prescription, improving the availability of rapid point-of-care diagnostics, considering alternatives for antibiotics (eg, vaccination) and ensuring that antibiotic stewardship (ABS) and infection prevention measures are in place in healthcare facilities were also reported as facilitators.

In addition, labeling by regulatory agencies according to ABS principles (eg, limiting to indications when no alternatives are available) was reported as another facilitator of responsible antibiotic use. It was expressed that no financial incentive for prescribing antibiotics should be in place at the healthcare facility. Finally, controlling veterinary use and controlling the release of antibiotic waste in the environment were proposed to facilitate responsible use.

When discussing responsibility and key players in the endeavor towards responsible antibiotic use, the answers of stakeholders diverged. Some agreed there is world-level responsibility as AMR spreads across the globe, while others highlighted the importance of national action plans to address AMR. In addition to the role of the medical community in prescribing antibiotics appropriately, the need for responsible citizenship was highlighted. The importance of governments was stressed, in the same way politics is involved with environmental problems. Another participant expressed a preference for a body strictly independent from politics and industry. AMR was

Table 2. Recommendations for Lifting the Barriers to Antibiotic Development, Equitable Availability of Effective Antibiotics, and Responsible Antibiotic Use

Recommendations	Main Sectors Accountable for Action
Antibiotic development	
1. Evaluate and implement new economic models for antibiotic R&D	Antibiotic R&D/pharmaceutical industry, scientific community, governments
2. Continue to refine and implement refined clinical trial designs for antibiotics	Regulatory agencies, scientific community, Antibiotic R&D/pharmaceutical industry
Equitable availability of antibiotics	
3. Structurally solve antibiotic shortages	Antibiotic R&D/pharmaceutical industry, regulatory agencies, governments
4. Put in place a global antibiotic stewardship and access framework	Governments, public health organizations, antibiotic R&D/pharmaceutical industry
5. Pursue efforts towards regulatory convergence and harmonization	Regulatory agencies, governments
Responsible antibiotic use	
6. Increase awareness of AMR as a societal problem	Governments (ministries of education and other relevant bodies), public health organizations
7. Ensure regulatory labeling according to antibiotic stewardship principles	Regulatory agencies, governments
8. Ensure implementation of antibiotic stewardship and infection prevention and control programs in every healthcare facility	Governments, healthcare community
9. Remove all financial incentives for prescribing antibiotic drugs	Antibiotic R&D/pharmaceutical industry, healthcare community, public health organizations, regulatory agencies, governments
10. Restrict release of antibiotics in the environment	Antibiotic R&D/Pharmaceutical industry, Governments, public health organizations, scientific community, farmers and veterinarians

Abbreviations: AMR, antimicrobial resistance; R&D, research and development.

reported as a multi-stakeholder issue and stimulating collaboration (eg, through multisectoral initiatives) was seen as a way towards a solution. It was stated that the responsibility for availability of antibiotics should not lie at the individual pharmaceutical-company level.

RECOMMENDATIONS FOR LIFTING BARRIERS

Recommendations were formulated to lift the main barriers identified during stakeholder interviews. Table 2 shows the recommendations and accountable sectors urged for actions. The recommendations are further explained and illustrated by examples of recent initiatives that emerged during and shortly after the running period of the DRIVE-AB project (2014 till 2017). The recommendations below do not reflect all barriers and facilitators that emerged in stakeholder interviews. The list of recommendations is non-limited and reflects the authors' opinions. While recommendations for antibiotic development, equitable availability of effective antibiotics, and responsible antibiotic use are addressed separately, it should be acknowledged that they are closely intertwined.

Antibiotic Development

Evaluate and Implement New Economic Models

The current business model for antibiotic drugs largely depends on the volume of sales, which contrasts with the need to minimize the use of antibiotics to prevent further selection and spread of antibiotic resistance. This model is a driver of excessive antibiotic use. Therefore, implementing new economic models that create incentives for the discovery of new antibiotics and microbiologic diagnostics, while at the same time safeguarding responsible antibiotic use, is key. There are 4 incentives to boost antibiotic R&D that have recently been advocated for by the DRIVE-AB research project in their report, *Revitalizing the Antibiotic Pipeline* [13]:

1. Grants: non-repayable funds for R&D given to academic institutions, companies, and others;
2. Pipeline coordinators: governmental or non-profit organizations that closely track the antibiotic pipeline, identify gaps, and actively support R&D projects both financially and technically to fill these gaps;
3. Market entry reward: a series of financial payments to an antibiotic developer for successfully achieving regulatory approval for an antibiotic that meets specific, pre-defined criteria to address a defined public health need, with obligations for sustainable use, equitable availability, and supply; and
4. Long-term supply continuity model: a delinked payment to create a predictable supply of important generic antibiotics.

The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator [26] and the Global Antibiotic Research and Development Partnership [27] are promising examples of pipeline coordinators focusing on priority pathogens. Evaluation and wider implementation of the aforementioned incentives should be a priority on a global level.

Continue to Refine and Implement Refined Clinical Trial Designs

The requirements for and the design of clinical trials should be improved to speed up the registration of new drugs. Recently, progress was observed in this field. The designs of non-inferiority trials have been refined for 6 well-characterized, acute, severe bacterial infections [28]. In addition, the STAT-Net group, part of Combatting Bacterial Resistance in Europe (COMBACTE), is currently working on providing guidance to optimize the designs and analyses of clinical trials for antibacterials against multidrug-resistant infections [16]. Furthermore, initiatives are currently being undertaken towards the creation of an antibacterial platform trial (Table 1) in both the European Union with COMBACTE-Net [29] and in the United States with the Antibiotics Resistance Leadership Group [30]. Altogether, these efforts are expected to benefit the global picture of the antibiotic pipeline.

Equitable Availability of Effective Antibiotics

Structurally Solve Antibiotic Shortages

Shortages (Table 1) are known to negatively impact antibacterial prescribing policies and expenses. Recent initiatives to solve shortages include the Access to Medicines Foundation's 6 steps for implementation by pharmaceutical companies (eg, holding local inventory in regional buffer stocks) [31]. In addition, solving shortages would ensure the availability of first-choice therapies, thereby reinforcing responsible antibiotic use. Implementing policies for monitoring antibiotic shortages, mitigating their impact on patient outcomes, and structurally solving them should be a multisectoral policy priority to guarantee equitable availability of antibiotics, as well as their responsible use.

Put in Place a Global Access Framework

Up to this date, access to quality antibiotics to all in need of them remains unrealized. Therefore, sustained global coordination is urgently needed to strengthen equitable availability and access of antibiotics across all geographic regions. In 2016, the WHO launched the Medicines and Health Products Programme Strategic Framework 2016–2030 to focus on and reinforce universal access to safe and quality-assured health products and universal health coverage, including antibiotics [32]. Efforts to ensure availability, especially to those antibiotics included on the WHO's Essential Medicines List, should focus on the registration of products, affordability (ie, pricing), and the consolidation of supply chains [33]. This strategy towards equitable antibiotic availability should involve all concerned sectors, ranging from pharmaceutical industries to governments and public health organizations.

Pursue Efforts Towards Regulatory Convergence and Harmonization

Regulatory convergence and/or harmonization (Table 1) should imply increased efficiency by avoiding duplication of similar work performed by regulatory authorities in different countries or regions. Consequently, convergence and/or harmonization should be paired with important resource savings (eg, human and financial). The US Food and Drug Administration, the European Medicines Agency, and the Japanese Pharmaceutical and Medical Devices Agency reached an agreement in 2017 to align data requirements for the clinical development of new antibiotics [34]. This tripartite collaboration is expected to facilitate a common development program for new antibiotics that satisfies the regulatory requirements of the 3 agencies. Efforts towards streamlining and harmonizing regulatory requirements to expedite antibiotic development, in line with the aforementioned example, should be pursued and expanded further by governments and regulatory agencies.

Responsible Antibiotic Use

Increase Awareness of Antimicrobial Resistance as a Societal Problem

Education of the public (Table 1) should improve awareness of AMR as an important societal problem. To be more successful, education on antibiotic use and resistance should be included in school curricula to shape awareness at a young age. Program materials aimed at educating children on antibiotic use should be implemented by ministries of education. Furthermore, structural funding from governments is needed to ensure continuous updates of available materials, keep the content attractive for children, and develop new materials.

In parallel, the effects of public campaigns on the awareness of adults should be regularly evaluated to identify which key messages and communications are the best suited for any setting and to provide guidance for future actions. Such an analysis was recently carried out by the WHO and informed the endorsement of more communication activities on antibiotics [35].

Ensure Implementation of Programs in Every Healthcare Facility

The importance of infection prevention and control in parallel to ABS activities to limit the emergence and spread of resistant bacteria, as well as reduce the use of antibiotics, is largely recognized. The DRIVE-AB project developed quantity metrics and quality indicators to assess antibiotic use for both inpatient and outpatient care settings, which should guide ABS activities [36–39]. In the Netherlands, since 2014, all hospitals are required by the Health Care Inspectorate and the Minister of Health to establish an antimicrobial stewardship team [40]. Since early 2017, the US Joint Commission requires all (critical access) hospitals, as well as all nursing care centers, to have an evidence-based ABS program in place [41]. A recent initiative by the Study Group for Antimicrobial Stewardship of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) calls for global funding for dedicated human resources to boost the implementation of ABS and infection prevention and control programs [42]. Similar national and international actions should be undertaken to further expand the successful implementation of ABS and infection prevention and control programs to all healthcare facilities worldwide.

Ensure Regulatory Labeling According to Antibiotic Stewardship Principles

Providing regulatory labeling (Table 1) in accordance with evidence-based stewardship guidelines should stimulate responsible antibiotic use. Such regulatory labels should highlight options for the restriction of particular antibiotics in view of specific resistance patterns. Furthermore, labels should also restrict the use of the antibiotic to when no alternative antibiotic treatments are available. A recent initiative includes the WHO Essential Medicines List's Access, Watch, and Reserve (AWaRe) classification [43]. Such a classification could constitute a valuable guidance for a first(-time) stewardship message added to the drug labels of antibiotics. This approach implies a cross-sectoral collaboration between regulatory agencies, scientific communities, and producers, with frequent updates.

Remove All Financial Incentives for Antibiotic Prescribing

Financial incentives for antibiotic prescribing lead to over-prescribing and thereby increase antibiotic resistance. Therefore, all financial incentives associated with an increase in unnecessary or inappropriate use of antibiotics should be removed from clinical practice. In parallel, the promotion of antibiotics by the drug industry should be abolished. A handful of companies have already reported actions (eg, decoupling sales volumes from sales agents' revenues) [33]; however, such reforms should be expanded to all antibiotic manufacturing companies.

Restrict Release of Antibiotics in the Environment

A One Health approach (Table 1), taking into account the connections between human and animal health and the environment, is of paramount importance in efforts to curb AMR. A first step towards restricting the release of antibiotic-polluted wastes in the environment is making it mandatory for manufacturers to disclose the amounts being discharged in nature. Recent commitments from producers to set limits on antibiotic wastewater discharges has been reported to the Access to Medicines Foundation [33]. Furthermore, researchers from the Joint Programming Initiative on Antimicrobial Resistance recently highlighted the need for the development of environmental quality standards to guide sustainable antibiotic waste discharge by manufacturers [25]. Increased transparency and quality standards for waste management should, subsequently, be expanded to all sources of antibiotic pollution. Voluntary commitment and goodwill from the industry, as well as the

involvement of many additional stakeholders, including governments, farmers and veterinarians, and the scientific community, are prerequisites to this endeavor.

CONCLUSION: A CALL FOR SHARED RESPONSIBILITY

Today's antibiotic pipeline is not as dynamic as it once was and, in the meantime, antibiotic resistance keeps developing. Identifying the barriers to and facilitators of antibiotic development, equitable availability of antibiotics, and responsible antibiotic use is key to informing solutions. The large scope of challenges, identified in interviews with an illustrative sample of stakeholders, highlights the multifaceted aspects and complexity of the situation. The recommendations presented here should be further developed into cross-sectoral, international policies to address these challenges. Indeed, no single sector can possibly curb AMR on its own. We argue that all involved sectors should take responsibility and contribute their share. Progress can only be made when the priorities of all involved sectors are aligned.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors thank all stakeholders that participated in the study for sharing their knowledge and insights on the subject: Helen Boucher (Tufts Medical Center, US Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria), Claudie Charbonneau (Pfizer), Barry Eisenstein (The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator [CARB-X], Merck Sharpe, and Dohme, Inc.), John Farley (US Food and Drug Administration), David Findlay (GlaxoSmithKline), Cees Hertogh (VU Medical Center), Leonard Leibovici (Rabin Medical Center), Kevin Outterson (CARB-X, Boston University), Diamantis Plachouras (European Centre for Disease Prevention and Control), John H. Rex (AstraZeneca, CARB-X, and F2G, Ltd.), Babette Rump (Dutch National Institute for Public Health and the Environment), and Anna Zorzet (ReAct).

The authors thank Nathalie Baillon-Plot (Pfizer) and Arjun Srinivasan (US Centers for Disease Control and Prevention) for piloting the interview and providing valuable feedback on the interview guide and illustrative examples.

The authors thank the The Driving Reinvestment in Research and Development and Responsible Antibiotic Use steering committee for their critical review of the manuscript.

Disclaimer. The recommendations of this manuscript broadly reflect the results of the research carried out. The recommendations reflect the authors' opinions. No unanimity agreement among participating stakeholders was sought.

Financial support. This work was supported by the Innovative Medicines Initiative Joint Undertaking (grant number 115618 to The Driving Reinvestment in Research and Development and Responsible Antibiotic Use project); the European Union's Seventh Framework Programme (grant number FP7/2007–2013); and the European Federation of Pharmaceutical Industries and Associations (in-kind contribution).

Potential conflicts of interest. C. A. reports a grant from the Research Council of Norway (through the Global Health and Vaccination Programme, project number 234608), during the conduct of the study. S. H. reports personal fees from Sandoz, Bayer, and DNA Electronics, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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