6  INTRODUCTION
What Will It Take to Address the Global Threat of Antibiotic Resistance?
Steven J. Hoffman and Kevin Outterson

1. A CROSS-BORDER PROBLEM

12  Antibiotic Resistance Spreads Across Borders
Tamar F. Barlam and Kalpana Gupta
Antibiotic-resistant (ABR) bacteria develop when bacteria are exposed to antibiotics either during treatments in humans or animals or through environmental sources contaminated with antibiotic residues. Resistant bacteria selected by medical, agricultural, and industrial use spread globally through international travel, the export of animals and retail products, and the environment. It is essential that nations work together to identify how to reduce emergence and amplification of resistant bacteria through sensible antibiotic treatment guidelines and restrictions, concerted efforts for surveillance, and infection control.

2. ACCESS TO ANTIBIOTICS

17  Universal Access to Effective Antimicrobials: An Essential Feature of Global Collective Action against Antimicrobial Resistance
Nils Daulaire, Abhay Bang, Göran Tomson, Joan N. Kalyango, and Otto Cars
Universal access to effective antimicrobials is essential to the realization of the right to health. At present, 5.7 million people die from treatable infections each year because they lack this access. Yet, community-based diagnosis and appropriate treatment for many of the leading causes of avoidable infectious deaths has been shown to be feasible and effective, demonstrating that strategies to reach the under-served need to receive high priority. This is a necessary part of a broad strategy to assure the long-term benefits of antimicrobials and to combat antimicrobial resistance, both because the lack of systematic and rigorous efforts to assure effective coverage increases the likelihood of antimicrobial resistance, and because global efforts aimed at antimicrobial stewardship and innovation cannot succeed without explicitly addressing the needs of the under-served. Elements of this strategy will include clear evidence-based treatment protocols, a robust international framework and locally tailored regulations, active engagement with communities and local health providers, strong attention to program management and cost considerations, a focus on the end user, and robust surveillance and response to emerging resistance patterns. Only by balancing the needs of universal access with stewardship and innovation, and assuring that they are mutually reinforcing can a global strategy hope to effectively address antimicrobial resistance.

3. INNOVATION FOR ANTIBIOTICS

22  A Pathway towards an Alternative Business Model for Antibiotic Innovation: A Framework, Fund and Institutional Mechanism
Manica Balasegaram, Charles Clift, and John-Arne Røttingen
The dangers presented by antibiotic resistance (ABR) have now established themselves as a global health security issue. From an international policy perspective, three key pillars have been established — responsible access, conservation, and innovation. These pillars are intrinsically linked, meaning that any attempt to address one, must take into account the implications for the other two. This article attempts to address all three of these pillars.
4. HISTORICAL PERSPECTIVE

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History Teaches Us That Confronting Antibiotic Resistance Requires Stronger Global Collective Action
Scott H. Podolsky, Robert Bud, Christoph Gradmann, Bård Hobaek, Claas Kirchhelle, Tore Mitvedt, María Jesús Santesmases, Ulrike Thoms, Dag Berild, and Anne Kveim Lie

Antibiotic development and usage, and antibiotic resistance in particular, are today considered global concerns, simultaneously mandating local and global perspectives and actions. Yet such global considerations have not always been part of antibiotic policy formation, and those who attempt to formulate a globally coordinated response to antibiotic resistance will need to confront a history of heterogeneous, often uncoordinated, and at times conflicting reform efforts, whose legacies remain apparent today. Historical analysis permits us to highlight such entrenched trends and processes, helping to frame contemporary efforts to improve access, conservation and innovation.

5. ECONOMIC PERSPECTIVE

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Antibiotic Resistance Is a Tragedy of the Commons That Necessitates Global Cooperation
Aidan Hollis and Peter Maybarduk

Antibiotics may be thought of as a common pool resource that can be depleted over time; the economics of this problem are relatively well known. The importance of antibiotics to human health means that limiting access through privatization is undesirable. Therefore, other solutions to prevent overuse are essential — stewardship programs, and for non-human use, taxation, all within the context of an international agreement. To solve problems of access while offering adequate rewards for innovation, a key tool is delinking prices from payment to innovators.

6. ONE HEALTH PERSPECTIVE

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International Agreement to Address the Contribution of Animal Agriculture to Antibiotic Resistance: A One Health Approach
Anthony D. So, Tejen A. Shah, Steven Roach, Yoke Ling Chee, and Keeve E. Nachman

The growing demand for animal products and the widespread use of antibiotics in bringing food animals to market have heightened concerns over cross-species transmission of drug resistance. Both the biology and emerging epidemiology strongly support the need for global coordination in stemming the generation and propagation of resistance, and the patchwork of global and country-level regulations still leaves significant gaps. More importantly, discussing such a framework opens the door to taking modular steps towards solving these challenges — for example, beginning among targeted parties rather than all countries, tying accountability to financial and technical support, or taxing antibiotic use in animals to deter low-value usage of these drugs. An international agreement would allow integrating surveillance data collection, monitoring and enforcement, research into antibiotic alternatives and more sustainable approaches to agriculture, technical assistance and capacity building, and financing under the umbrella of a One Health approach.

7. ENVIRONMENTAL PERSPECTIVE

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Much Can Be Learned about Addressing Antibiotic Resistance from Multilateral Environmental Agreements
Steinar Andresen and Steven J. Hoffman

Antibiotic resistance (ABR) is a common-pool resource challenge. This means that efforts to address ABR can learn from similar collective action problems faced within the environmental sector. Multilateral environmental agreements are the backbone of global environmental governance. Their ability to effectively solve environmental problems depends on the problem structure and the regime's problem-solving capacity. The success or failure of environmental agreements is mainly determined by the problem structure, including the degree of political consensus and scientific certainty. But agreements' institutional design also matter because they can change the problem structure and problem-solving capacity. Based on experiences with environmental agreements, an international ABR agreement should contain robust reporting/verification procedures, sanctions for non-compliance, assistance for implementation, majority vote decision-making rules, a strong secretariat, an independent scientific panel, and specific commitments. More research on global strategies for achieving collective action is needed to help inform future institutional designs that are both effective and politically feasible.
8. ACCOUNTABILITY

53 Addressing Antibiotic Resistance Requires Robust International Accountability Mechanisms
Steven J. Hoffman and Trygve Ottersen
A proposed international agreement on antibiotic resistance will depend on robust accountability mechanisms for real-world impact. This article examines the central aspects of accountability relationships in international agreements and lays out ways to strengthen them. We provide a menu of accountability mechanisms that facilitate transparency, oversight, complaint, and enforcement, describe how these mechanisms can promote compliance, and identify key considerations for a proposed international agreement on antibiotic resistance. These insights can be useful for bringing about the revolutionary changes that new international agreements aspire to achieve.

9. INTERNATIONAL LAW

65 International Law Has a Role to Play in Addressing Antibiotic Resistance
Steven J. Hoffman, John-Arne Røttingen, and Julio Frenk
If an international legal agreement is needed for any of today’s global health challenges, it would be antibiotic resistance (ABR). This challenge is transnational, its solution justifies coercion, tangible benefits are likely to be achieved, and other commitment mechanisms have thus far not been successful. Since addressing ABR depends on near-universal and interdependent collective action across sectors, states should utilize an international legal agreement — which formally represents the strongest commitment mechanism available to them.

10. LEGALIZING COMMITMENTS

68 Some Global Policies for Antibiotic Resistance Depend on Legally Binding and Enforceable Commitments
Asha Behdinan, Steven J. Hoffman, and Mark Pearcey
To address the challenge of antibiotic resistance (ABR), the international community must ensure access, conservation and innovation of antibiotics. These goals can be significantly advanced through ten global policies that have been recommended to form part of an international legal agreement. Policies that could be central to this agreement include the establishment of standards, responsible antibiotic use regulations, and strengthening global surveillance systems. Funding for access, mobilizing resources for infrastructure, strengthening infection control practices, and regulating antibiotic marketing could also be helpful if included in a legal agreement. Incentives for innovation could also be included to mobilize support for its implementation. The inclusion of these policies in an international legal agreement could effectively support global collective action towards several ABR policy goals, some of which may depend on it for their achievement.

11. CONVENING FORUM

74 Effective Global Action on Antibiotic Resistance Requires Careful Consideration of Convening Forums
Zain Rizvi and Steven J. Hoffman
Global collective action is needed to address the growing transnational threat of antibiotic resistance (ABR). Some commentators have recommended an international legal agreement as the most promising mechanism for coordinating such action. While much has been said about what must be done to address ABR, far less work has analyzed how or where such collective action should be facilitated — even though the success of any international agreement depends greatly on where it is negotiated and implemented. This article evaluates four different forums that states may use to develop an international legal agreement for antibiotic resistance: (1) a self-organized venue; (2) the World Health Organization; (3) the World Trade Organization; and (4) the United Nations General Assembly. The need for a multisectoral approach and the diverse institutional landscape suggest that an effective response may best be coordinated through linked action pursued through multiple forums.