

Anti-microbial resistance: addressing a significant public health challenge

Overview

- The rate of innovation in antibiotics has not kept pace with the rate at which existing medicines have been rendered obsolete by bacterial resistance. A variety of commentators warn that this trend, if not reversed, threatens to undo many of the medical advances of the past 70 years. Yet, previous efforts to build a stronger consensus on the need to manage resistance have failed to address the full range of action needed.
- Leaders from government agencies and civil society have acknowledged that progress on this issue requires focused collaboration among all stakeholders involved in the development, approval, reimbursement and use of these important medicines.
- Tapestry Networks believes that a successful policy approach will require these stakeholders to co-design a new model for the assessment, appropriate use and reward for innovation in antibiotic R&D.

The urgent need for new antibiotics

- In a joint report, the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) characterised the spectre of antimicrobial resistance:

The introduction of antibacterial agents (commonly referred to as antibiotics) led to a revolution in the management of bacterial infections. Today, emerging and increasing resistance to antibiotics has become a threat to public health in Europe and globally. Only 70 years after their introduction, we are now facing the possibility of a future without effective antibiotics for several types of bacteria that cause infections in humans.ⁱ
- The ECDC-EMA report estimates that antimicrobial-resistant (AMR) infections cause 25,000 deaths per year in the EU, as well as annual societal costs exceeding €1.5 billion.ⁱⁱ
- This threat represents an urgent – and unmet – need for new drugs and vaccines.ⁱⁱⁱ The ECDC-EMA report noted a “particular lack” of new agents for the most difficult-to-treat infections.^{iv} The Council of the European Union (the Council) similarly warned that “research into and development of new effective antibiotics has significantly declined and probably will not provide sufficient new therapeutic alternatives to meet medical needs within the next 5-10 years.”^v
- The Council warned that, “[w]ithout access to effective antibiotics, common infectious diseases may again become lethal threats.”^{vi} These and other institutions have called for an urgent European and global strategy to close this gap.

The challenge of ensuring investment in new antibiotics

- In addition to scientific and technical challenges, the development of new antibiotics also faces substantial economic barriers. Estimates of the risk-adjusted net present value (NPV) of new antibiotic development are three to ten times lower than expected returns in other therapeutic areas, making this an unattractive area for investment.^{vii}
 - The need to conserve the effectiveness of new antibiotics limits the size of their potential market, with tight controls over the use new antimicrobial agents.
 - Where new antibiotics *are* used, returns are still limited because the curative nature of effective antimicrobials calls for short courses of treatment.^{viii}
 - Concern about unclear regulatory demands, low levels of historic reimbursement, the prevalence of generics, the inherent risk of investment in new mechanisms of action and the absence of point-of-care rapid diagnostic tests to better target treatment further limit the commercial attractiveness of investment in antibiotic R&D.
- These challenges have led to widespread calls from government and civil society to “strengthen incentives to conduct research and development of new effective antibiotics.”^{ix}
 - Healthcare leaders have acknowledged that creating a sustainable model for innovation in antimicrobials that meets the needs of both medicine developers and the healthcare systems they serve requires focused collaboration among the constituencies and institutions involved in the development, approval, reimbursement and use of these medicines.
 - Accordingly, the Council has called on Member States and the Commission to “explore ways to promote further public-private partnerships between industry, academia, non-profit organizations and the healthcare system [and] ensure that all actions are appropriately co-ordinated between different stakeholders from the sectors involved.”^x

The need for leadership in restocking the antibiotic pipeline

- Although opinion leaders have done a great deal to raise awareness and concern about the problem of AMR, this activity still lacks focus. There is no consensus among the relevant stakeholders on a course of action, and no process in place to enable them jointly to design such a course.
 - A number of conferences and workshops have brought together leading thinkers from multiple constituencies to discuss the need to promote innovation in antimicrobial R&D. To our knowledge, none of these forums has resulted in agreement on a specific course of action.
 - Conversely, specific policy proposals from industry and professional societies have been made with limited involvement from other stakeholders. As a result, these proposals lack broader support.
- Agreement on and successful implementation of a new model to foster antimicrobial innovation will require a number of questions to be addressed. These include:
 - How to focus incentives on antibiotics that address the unmet needs created by bacterial resistance?
 - How to ensure appropriate stewardship and use guidelines for new antibiotics?

- How to ensure appropriate incentives for the development of related diagnostics, and how to establish the value of such diagnostics?
- How to ensure that the incentives are flexible and equitable in the face of evolving circumstances?
- How to ensure an equitable outcome for companies with antibiotics currently in the pipeline?
- Successfully addressing this complexity must rest on a renewed level of engagement, understanding and trust among the relevant stakeholders, including EC institutions, medical and policy experts, professional societies and those responsible for the authorisation, reimbursement and uptake of medicines in national healthcare systems (regulators, HTAs, payers and providers).
- For antibiotics developers, this process starts with “*a safe place for conversation in which people can actually debate these ideas enough that they truly understand them.*” Then, in moving from understanding to action, developers note “*the need for a binding agent that holds the disparate groups [concerned with this problem] together and drives progress on a faster time scale.*” From the developers’ perspective, “*the key missing piece is trust and the reluctance of government agencies to engage with industry.*”
- Designing and leading networks of leaders to drive progress on complex, multi-stakeholder challenges is Tapestry Networks’ core mission. Tapestry specialises in forming working partnerships between the public and private sectors as well as civil society. These partnerships – which we regard as networks because of the way they are constructed and function – typically address the intersection of private sector innovation and the public interest. The participants in these networks are respected leaders from key stakeholders who realise the status quo is neither desirable nor sustainable.
- Through a related Tapestry-lead initiative – the European Healthcare Innovation Leadership Network – healthcare leaders both public and private from various European countries are addressing the complementary goals of improving patient health outcomes and enhancing the climate for innovation while acknowledging pressures to control healthcare costs.
 - This initiative has resulted in the introduction of multi-country, multi-stakeholder consultations in drug development to better assess and validate the emerging value of new medicines in developers’ pipelines.
 - The consultations, which are being piloted in antibiotics and three other therapeutic areas, bring together medicine sponsors with the European Medicines Agency and health technology assessors, healthcare budget holders, patient representatives and medical experts from five Member States and multiple levels of government.

Endnotes

- ⁱ ECDC/EMA Joint Working Group, *The bacterial challenge: time to react* (Stockholm: European Centre for Disease Prevention and Control, 2009), page v.
- ⁱⁱ ECDC/EMA Joint Working Group, *The bacterial challenge: time to react*, page vi.
- ⁱⁱⁱ European Academies Science Advisory Council, *Tackling Antibacterial Resistance in Europe* (London: European Academies Science Advisory Council, 2007), page 21.
- ^{iv} *Ibid.*, page vi.
- ^v Council of the European Union, *Council Conclusions on innovative incentives for effective antibiotics* (Brussels: Council of the European Union, 2009), page 2.
- ^{vi} Council of the European Union, *Council Conclusions on innovative incentives for effective antibiotics*, page 2.
- ^{vii} *Ibid.*
- ^{viii} Elias Mossialos et al., *Policies and incentives for promoting innovation in antibiotic research*, page 154.
- ^{ix} Council of the European Union, *Council Conclusions on innovative incentives for effective antibiotics*, page 3.
- ^x Council of the European Union, *Council Conclusions on innovative incentives for effective antibiotics*, page 3.