Identifying key bottlenecks in the early stages of antibiotic R&D and exploring public and not-for-profit solutions

A policy brief based on Expert workshop discussions

Organized under the ReAct initiative:
Revisiting Effective Models to Advance the Antibiotic Pipeline (REMAAP)

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About REMAAP
The initiative *"Revisiting Effective Models to Advance the Antibiotic Pipeline" (REMAAP)* seeks to build evidence and broader political understanding of the core challenges in antibiotic research and development and how to effectively address them.

Within the framework of this initiative ReAct organised an in-person workshop in Uppsala, Sweden on November 7-8th 2022. The workshop aimed to take an "end-to-end" approach to antibiotic R&D (from discovery to patient access), with specific attention given to the early stages (discovery and preclinical) of antibiotic research and development. Discussions focussed on identifying the vulnerabilities, challenges, and potential solutions. The workshop gathered leading experts with knowledge particularly of the early stages of antibiotic R&D with backgrounds ranging from microbiology and chemistry, lab experience and compound development, infectious diseases and clinical medicine, economy, policy and history. This document synthesizes the identified challenges and suggests building blocks of more comprehensive solutions.

Background

Resistance to existing antibiotics is increasing worldwide causing an estimated 1.27 million deaths in 2019. Meanwhile, in the last three decades hardly any new antibiotics have been developed as the existing R&D model, which relies on recouping R&D investments through sales revenues, is neither appropriate nor effective for developing antibiotics. Most multinational pharmaceutical companies have exited the field, and today it is primarily academics and smaller biotech companies that are left. To reinvigorate the pipeline and ensure that patients have sustainable access to effective antibiotics when needed, it is widely accepted that new models for both coordinating and financing antibiotic R&D are needed.

Workshop discussions

It was clear from the discussions that the underlying causes and effects of the different challenges are often intertwined and linked to the poor outcomes of R&D investments and efforts. Going forward, addressing the challenges in the early stages will be essential in order to improve final outcomes of antibiotic R&D.

Political platforms, processes, and fora where these challenges should be addressed include:

- Global processes which can address antibiotic R&D and access constraints e.g. the UN General Assembly High Level Meeting on AMR in 2024, and the development of the WHO "Pandemic Accord".
- Regional policy development and funding investments in antibiotic R&D, for example revision of pharmaceutical legislation in the EU and establishment of bodies like the European Health Emergency Preparedness and Response Authority (HERA) to develop medical countermeasures for pandemic preparedness.
- National policy frameworks, initiatives, action plans and investments.

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5 key takeaways

1. Increase governmental ownership of the issue & political leadership required to address the R&D challenges

Political leadership to address the challenges in early antibiotic R&D is currently insufficient. Governments often lack insight into the required funding needs, and how to target funding to the different needs within this phase. Additionally, it is a challenge that the multinational and long-term nature of drug development and the long-term funding predictability that it requires, are poorly aligned.

Suggested ways forward

- Governments should seek to deepen their understanding of the complexity of the antibiotic R&D processes, the constraints of the current market model and the consequences for public health, as well as the key role that public funders can play. This should enable governments to increasingly engage in and own the processes and problems, and thereby also more effectively contribute to the solutions.
- Global alliances and ensuring representation of LMICs when developing solutions is paramount for sustainability in access to and stewardship of new antibiotics.

2. Strengthen global coordination and exchange of knowledge & expertise

The antibiotic discovery field suffers from fragmentation and lack of coordination, collaboration and knowledge-sharing between research groups. This leads to repetition of mistakes, a waste of resources and time, and fewer molecules likely to move forward. Few research entities engaged in discovery and early R&D stages have a full 'end-to-end' understanding of the R&D processes - from early discovery to drug development and patient access. Furthermore, academic research incentives (e.g. to publish work in prestigious journals) are not necessarily well-aligned with drug discovery and public health-driven research agendas.

Suggested ways forward

- New and existing early stage research funding and structures should demand and enable knowledge- and data sharing (including of failing compounds and assays) between experts, as well as providing support and incentives for researchers to take their research to the next phase.

- Existing actors in the field such as ENABLE2 (preclinical research), CARB-X (funder of pre- and early clinical R&D) and GARDP (predominantly focused on late stage clinical R&D and access) operating in different R&D stages should be better and more sustainably supported. Alignment and collaboration between their respective mandates should be strengthened.

- To overcome the fragmentation problems, a sustainably funded centralised coordination entity or hub (for example a network of R&D centres or a consortium of existing actors to coordinate research and discovery) to retain expertise, equipment, and potentially funding should be considered. LMICs partners need to be part of such an entity to ensure global health needs are met and access to the end product is planned for.

The 5 key takeaways


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3. Provide longer-term, sustainable, targeted and coordinated funding

Contrary to the dominating narrative, funding for early antibiotic R&D is still limited, unpredictable, and often not sufficiently long-term. This creates uncertainties that have a discouraging effect on attracting and maintaining researchers in the field. Highly valuable expertise, structures and access to equipment risk being lost when funding ends prematurely. The lack of coordination among funding agencies also creates inefficiencies in the application processes. The lack of more targeted funding and funding conditionalities (e.g. to enable equitable access, knowledge and data-sharing) also hinder progress.

Suggested ways forward

- To yield better results funding must be made long-term and predictable to maintain expertise, structures and institutional memory in the field incl. by funding entities rather than short-term projects.
- Acting as "honest brokers", a consortium of funders (governments and organisations) can coordinate funding efforts to identify gaps, and require more collaboration and information exchange between research groups.
- Funders should include conditionalities to ensure global access to end products and data sharing, also covering early stage funding. Further exploring of where such conditions are best placed to require public health friendly IP management such as licensing (e.g. through a licence and access pool) and use of open knowledge systems is needed.
- Alternative academic incentives to that of publication in scientific journals should also be introduced via a new coordination entity, designed to promote knowledge- and data-sharing (inclusive of failed projects), with the aim to solve the most critical scientific problems.

4. Expand the use of public and not-for-profit models in discovery and early stages of R&D

The commercial prospects of new antibiotics are uncertain. New antibiotics will likely have small markets and/or low or uncertain profit margins. This commercial problem is even more pronounced in poorer countries where prices will have to be lower; for formulations for smaller patient groups like children; and for antibiotics in WHO RESERVE category where stricter stewardship provisions limit their use/sale. Public and not-for-profit funders and developers have been shown to have comparative advantages in advancing antibiotic R&D, especially for areas with lower commercial interest, and for countries that face problems with limited access to new antibiotics. They offer an alternative pathway to the traditional approach where the drug is first developed and marketed in HICs only to "trickle down" to low- and middle income countries many years later.

Suggested ways forward

- The role of public and not-for-profit entities should be expanded into the discovery and preclinical phases of antibiotic R&D, and should be supported by additional pooled funding from philanthropists and governments including from LMICs to broaden ownership.
- A cost and efficiency comparison between not-for-profit pathways and other ways to finance drug development (e.g. through incentives to the private pharmaceutical sector) would be beneficial.

5. Build stronger regional institutions and networks

Exploring models that can more appropriately address the diverse sets of challenges related to antibiotic R&D and access should take into account variations across different geographical regions. A key benefit of regional approaches is to build local ownership, initiatives, leadership, and sustainability, hence moving away from HICs "giving access" to LMICs, and instead shifting the power balance, to build local ownership and encourage initiatives and partnerships.

Suggested ways forward

- Strengthen collaboration and support for new and existing regional institutions and networks such as regional CDCs (Africa CDC, the emergent ASEAN CDC, etc.) involved in antibiotic R&D and responsible for identifying local needs, coordinating clinical trials, networks of manufacturers, regulatory procedures, procurement, production, as well as integrated stewardship policy guidance.

- Additionally, production, with proper conditions, could be out-licensed to middle income countries with production capacity to create ownership.

- Multiple regions can operate in parallel and in collaboration in a "trans-regional" global model and regional coordination bodies can be expanded for building capacity to create an end-to-end knowledge for antibiotic R&D.

The overarching goal of antibiotic R&D should be that **effective antibiotics become affordably, sustainably, and equitably accessible to everyone in need**. Whether this will succeed will depend on whether and how drug development is financed and coordinated. To overcome current fragmentation and misaligned incentives in antibiotic R&D, as well as building on the progress made by some key actors (such as ENABLE2, CARB-X, and GARDP), policy makers at global, regional, and national level should make use of all relevant platforms and processes to accelerate progress towards ensuring a more coherent response.

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