

Public health principles to ensure sustainable access to novel antibiotics

Tackling antibiotic resistance will not be possible unless there is a sustained, novel and public-health driven commitment by all governments that encourages the continuous development of novel antibiotics and ensures sustainable access when and where antibiotics are needed. The lack of sustainable access to effective antibiotics is a systemic failure, including a failure of the public and private sector to develop new antibiotics, and an unwillingness of governments to leave behind a research and development model that relies on patent monopolies to guide the development of new medicines.

Three years after Heads of State agreed to the UN Political Declaration of the high-level meeting of the General Assembly on Antimicrobial Resistance, a pathway to develop and ensure sustainable access to new and existing antibiotics remains largely elusive. The bankruptcy of Achaogen, a biotechnology company that had successfully launched a new antibiotic, *plazomicin (Zemdri)*, that was included on the WHO's Essential Medicines list only a few months after the company announced its bankruptcy, has added to the shared urgency to build a sustainable model to develop and launch effective new antibiotics.

An End to End Approach: Business as usual or something new?

There seems to be a consensus that a sustainable model is one that functions on an 'end-to-end' basis, e.g. a model that considers the entire chain of actors, investments and regulatory measures that are implicated in developing and bringing novel antibiotics to patients – from early-stage discovery up to the patient receiving the new medicine. There is also consensus that recuperating research and development costs cannot be achieved by relying upon volume-based sales since high volumes of new antibiotics are self-defeating from both a public health and a commercial perspective. High volumes will result in premature resistance, which undermines treatment and shortens the life-span of the antibiotic. Yet even with these areas of shared agreement across governments, consensus falls apart once the specifics of an 'end-to-end' model are discussed.

The central problem is that while there is a recognition amongst some policy makers and experts that new antibiotics can and should be developed through non-traditional approaches that moves away from the traditional drug development pathway and that do not require the largest pharmaceutical companies, many of the recommended approaches from industry, governments and philanthropic funders seek to preserve high prices for new antibiotics. They bend over backwards to place multinational pharmaceutical companies at the heart of the solution, even though it is these companies that have

exited antibiotic research and development over the last two decades, but still advocated endlessly for only using patent monopolies as an incentive for innovation, and which have historically engaged in marketing and pricing practices which discourage sustainable access to antibiotics.

To build a sustainable model, we believe governments must be willing to exercise judgment that is independent of the pharmaceutical industry, and to search for solutions that do not rely upon multinational pharmaceutical companies. We must first acknowledge that the public sector will ultimately have to finance and guide the development of new antibiotics. In doing so, we believe it is possible to construct a sustainable model that works alongside smaller biotechnology companies, generics firms, product development partnerships and global health agencies. It may also require the public sector to assume operational responsibility for particular aspects of an end to end model.

Public money should be dedicated to public need, not private profit

Public funding is already being used to both pay for the development of new antibiotics and their procurement. Yet for some governments and philanthropies, the purpose of using (additional) public funds is to encourage multinational drug companies to participate in or re-enter the development and marketing of new antibiotics, even though these same companies are not commercially interested in the antibiotics market. In fact, we think irrespective of public subsidies or incentives, multinational companies should have a self-interest to prioritize the development of novel antibiotics. This is because without effective antibiotics, core components of the pharmaceutical industry's business may no longer be viable. For example, chemotherapy, an important source of revenue for drug companies, may become increasingly difficult to administer due to the rise of drug-resistant infections.¹ However, public monies should be focused on helping to build a system that is sustainable in the long-term.

If there were no other options, this approach would make sense. Even if large drug companies are partly responsible for the dearth of new antibiotics, if they were the only avenue to replenishing the antibiotic pipeline, all initiatives would have to target them. Yet it is becoming increasingly clear that there are other options. Even those who were previously focused on Big Pharma as the sole or main vehicle to get us out of the antibiotic crisis are now changing their tune. This includes Jim O'Neill, who chaired the UK led AMR Review, has recently indicated that the failure of existing mechanisms, and the private sector in particular, to develop new antibiotics, may necessitate the introduction of one or more state-run utility drug companies to satisfy the urgent need for the development and manufacture of new drugs. Or, in his own words: "just take it away from them and take it over."²

¹ <https://www.bloomberg.com/news/articles/2019-09-05/superbugs-deadlier-than-cancer-put-chemotherapy-into-question>

² <https://www.bbc.com/news/health-47719269>

With sufficient public funding, alongside the continued participation of smaller, innovative biotechnology companies, product development partnerships and generics companies, the development of new antibiotics can not only become viable and sustainable, but will more likely safeguard the public interest.

It is also possible that governments could choose to simply pay for R&D on an end-to-end basis and ensure that public health principles are followed. This could be done through a ‘public option’, wherein R&D could be carried out fully by a public-private entity, through a public sector entity, or through contracting out a private sector entity. Governments could also decide to implement a ‘public option’ for some parts of an end to end model, while relying on private sector investment and expertise for other aspects of drug development. For example, Civica Rx, a US-based public-private partnership to manufacture medicines that are either in short supply, unaffordable (or both), is already actively investing in the manufacture of two existing antibiotics (*vancomycin* and *daptomycin*).

In any of the scenarios listed above where the public contributes a substantial percentage of the funding required to pay for R&D, governments should introduce safeguards that can secure a public return on public investment, such as how intellectual property is managed, at what prices the product should be offered and the speed at which the product is registered, manufactured and supplied worldwide.

Public interest principles to address a public health need

In whichever ways new antibiotics are brought to market, the use of public sector funding should preserve certain core principles that protect the public interest. We propose three broad principles.

- 1. Priorities and target product profiles are developed through evidence and scientific consensus:**
With scarce public sector resources and growing levels of resistance, setting appropriate priorities amongst competing needs could be hotly contested between governments, experts and other R&D funders. Priorities should be guided by evidence of what is needed and which investments (if successful) will provide the most significant public health impact. Target product profiles (TPPs) should be developed for new products via consensus amongst scientific experts that ensure products developed according to such TPPs are effective, appropriate and affordable. The World Health Organization has developed a priority pathogen list which provides clear guidance as to what areas of need should be prioritized.
- 2. Full transparency:** There has been a concerted effort to encourage greater transparency within the pharmaceutical sector, especially for the prices paid for medicines. Greater transparency is also needed for other aspects of pharmaceutical R&D including: (1) transparency of the terms and conditions negotiated between funders and recipients of R&D funding; (2) transparency as to the actual cost of R&D for each new antibiotic, (3) full transparency of clinical trial data and (4) transparency of prices paid across the public and private sector. Transparency of contractual terms is

critical as it enables the public to ensure that donor governments seek out a ‘public return on public investment’ (see above). Transparency of R&D costs is crucial because it can ensure that funders neither over pay nor under pay for what is required to fully develop a new antibiotic and to ensure that the developer can achieve a reasonable rate of return on their investment. Transparency of clinical trial data, and in particular to ensure that all trial data (including negative outcomes) is published, is critical to ensure that patient safety is protected and to ensure that scarce investments are only being directed towards products that will have a therapeutic impact. Finally, transparency of prices paid can ensure that prices across and within countries is equitable and affordable and consistent with the ability of patients and health care systems ability to pay.

3. **Full de-linkage:** The UN High Level Declaration, signed by all Heads of State, stated that governments commit to: ‘delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines’.³ We believe that this describes a commitment to what has come to be called ‘full delinkage’ even though that term is not used. In contrast, many funders and companies are only committed to ‘partial delinkage’, which does not ensure affordable access to new medicines and as such, does not fulfil what is stated in the Declaration. It would seem quite clear that ‘affordable access to new medicines’ requires an affordable end product price. While this may not necessarily require the lowest possible price for all countries, we do think that new antibiotics should be introduced at prices that are affordable for all payers in a health care system, whether government, private sector purchasers or households. We also do not think price should ever be used as a means to discourage use of an antibiotic. Furthermore, the successful development of a novel antibiotic should not come at the expense of access to treatments for other diseases. Pharmaceutical companies have suggested that companies should be granted extended monopolies (and thus the ability to charge high prices) for other life-saving drugs in exchange for developing a new antibiotic. In other words, having their cake and eating it too.

Conclusion

An effective end-to-end model that ensures both the development of novel antibiotics and sustainable access is a critical prerequisite to curbing the antibiotic resistance crisis. Substantial and sustained investments must be made by governments and donors to achieve this, not forgetting that countries’ health systems need to be strengthened to ensure that antibiotics are handled appropriately and are accessible to all in need⁴.

³ <https://digitallibrary.un.org/record/842813?ln=en>

⁴ A Global Antimicrobial Conservation Fund for Low- and Middle-Income Countries
[https://linkinghub.elsevier.com/retrieve/pii/S1201-9712\(16\)31173-0](https://linkinghub.elsevier.com/retrieve/pii/S1201-9712(16)31173-0)

Sustainable development of new and affordable antibiotics is currently at a standstill because governments and other donors want to have it both ways. They say the right things about the need to take bold steps to develop and introduce new antibiotics that are available and affordable to all, but they are ultimately unwilling to take even small steps to break with an industry-driven approach. This is in spite of: the failure of industry-led models to develop new antibiotics for the last two decades, the current need for significant public investments to develop new antibiotics, and the on-going crisis of high medicine prices, which has led to both popular and elite demands for concrete measures to reduce drug prices. Governments and philanthropic donors should be leading the way to introduce new approaches that are a break from the past, but one gets the impression that until and unless multinational drug companies are supportive and even fully involved, governments and donors will just keep relying on the failed approaches of the past. Perhaps this would be acceptable if there was limitless time and resources to adopt the right approach, but there are neither unlimited resources nor unlimited time. In deciding the right course of action, it may be better for policy makers to spend less time listening to drug companies and more time contemplating how to really avoid a world without novel antibiotics.