

Accelerating global innovation to address antibacterial resistance: introducing CARB-X

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A global response to the chronic shortfall in antibiotic innovation is urgently needed to combat antimicrobial resistance. Here, we introduce CARB-X, a new global public–private partnership that will invest more than US\$350 million in the next 5 years to accelerate the progression of a diverse portfolio of innovative antibacterial products into clinical trials.

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Antimicrobial resistance has emerged as a major threat to public health^{1,2}. The global response to this challenge must encompass many elements, one of which is the creation of new products. Unfortunately, antibiotic innovation has lagged in recent years. And, unlike other drug classes, which remain as effective now as the day they were first discovered, antibiotics lose effectiveness over time through bacterial resistance. We must innovate just to avoid losing crucial advances in treating infectious diseases.

The recently released final report of the AMR Review, chaired by Lord Jim O'Neill, offered 10 recommendations for global action in response¹. The full report is worthy of attention and action, but we focus on one recommendation, the call for a Global Antibiotic Innovation Fund focused on the creation of new tools directed at antibacterial resistance.

The report acknowledged several promising initiatives in this arena, including ENABLE, funded by the Innovative Medicines Initiative (IMI)'s New Drugs for Bad Bugs programme targeting Gram-negative bacteria; the UK–China antibiotic research partnership announced by the two governments; the Global Antibiotic Research and Development (GARD) partnership, a new non-profit antibiotic drug developer in Geneva launched by the World Health Organization and the Drugs for Neglected Diseases initiative; the work of the Biomedical Advanced Research and Development Authority (BARDA), a US government agency that has supported several key antibiotic products and portfolios; and the long-standing work of charities such as the Wellcome Trust and funding agencies such as the US National Institute for Allergy and Infectious Diseases (NIAID), the UK Medical Research Council and the

IMI. But the report also cautioned that these groups must work together, with the whole being more than the sum of the parts, in new collaborative models that can advance the best science and products, no matter where the team is located.

In that spirit, we are pleased to announce the public launch of CARB-X, a new global public–private partnership for preclinical antibacterial research, with research funds for the first 5 years exceeding US\$350 million (see Further information). Over the first 5 years of CARB-X, the goal is to accelerate a diverse portfolio of more than 20 high-quality antibacterial products towards entry into human testing. Key funders include the US government (BARDA and NIAID), the Wellcome Trust and the AMR Centre, a public–private partnership located at the Alderley Park research facility near Manchester, UK. The entity is called CARB-X as it sprang from the US government's Combating Antibiotic Resistant Bacteria (CARB) initiative, and will directly address several key goals in the 2015 US CARB National Action Plan. Boston University leads the project.

CARB-X: accelerating antibacterial innovation

CARB-X is a global accelerator, designed to provide significant research funding, research support services and business mentoring services with minimal bureaucracy. The goal is to advance products towards clinical studies expeditiously, but with all of the data needed to make good decisions. All funds are non-dilutive, which keeps the product developer moving forwards without additional debt or equity dilution. Research support services will include streamlined access to NIAID, RTI International and AMR Centre preclinical services and project management support with research, but

developers are also able to conduct their own research or engage any contract research organization. Business support services will be provided in partnership with MassBio and the California Life Sciences Institute, located in two of the world's strongest biotechnology hubs, together with the resources at the Wellcome Trust and the AMR Centre in the United Kingdom. At the Broad Institute in the United States, CARB-X will create a new Collaborative Hub in Early Antibiotic Discovery, fostering interdisciplinary work. The combination of funding, research support and business support services is an important part of this translational science effort.

CARB-X is global. Antibiotic resistance is a global problem, and is beyond any one company, cluster or country, so our remit is also global. Innovation is beyond borders and there are no knowledge monopolies, so funds and business support services will be available to product developers from any country, without geographical restrictions. The goal is to accelerate the best products for human health. Although our initial leadership is transatlantic, our structure was deliberately designed to accept additional partners, including those from other regions in due course. In the future, CARB-X will look to expand its scope and impact through the formation of additional partnerships with governments and non-government organizations interested in addressing antimicrobial resistance.

CARB-X is focused on antibacterial products more broadly, not just therapeutics. As the goal is to protect human health from resistant bacterial infections, our product scope will include any therapeutics, preventive measures such as vaccines, diagnostics and other devices. The best infection is the one that never occurred owing to preventive measures such as vaccines. Rapid point-of-care diagnostics that change clinical practice could dramatically reduce inappropriate use. In short, CARB-X has no pre-specified product modalities, so long as the product will have an impact on bacterial resistance and advance human health.

CARB-X seeks innovation, not modest modifications of existing drugs. The initial portfolio goal in the first year will be heavily weighted towards the Gram-negative bacteria posing the greatest threats to human health, together with other urgent and serious threats described in the US Centers for Disease Control and Prevention's 2013 Threat Assessment. We will also explore non-traditional approaches. For subsequent years, we will convene global stakeholders to update these portfolio goals to reflect emerging global bacterial threats. CARB-X itself can be innovative through transparency and collaboration with all other efforts to address antimicrobial resistance.

CARB-X will go live over the next few months with the expectation that the application submission and review process will be fully active by the end of 2016. Interested product developers should check the CARB-X [website](#) for updates. An active programme of presentations at upcoming conferences is also planned.

A remaining need for new incentives

Although this announcement is good news for antibiotic innovation, we note that the most novel recommendation from the AMR Review — the creation of a global system of market entry rewards for antibiotics and alternative therapies — still requires action. In particular, and as emphasized by the AMR Review, there has been a progressive realization of the need for pull incentives that delink R&D rewards from the volume of sales^{3,4}. Antibiotics are in many ways the 'fire departments' or 'fire extinguishers' of medicine³ in that we must pay for the protection offered in advance of need. To create pull incentives that recognize the full social value of antibiotics, market entry rewards and other delinkage rewards are receiving serious study in the IMI-funded research project DRIVE-AB, the US Presidential Advisory Council on CARB and think-tanks such as Chatham House in the United Kingdom and the Duke–Margolis Center in the United States. Even the best research will be for naught if there is no market for the drugs once they are approved by regulators. Nevertheless, until the policy decisions are made to fix the broken economic model for antibiotics after market entry, CARB-X stands ready to stoke the pipeline with innovative antibacterial products that address our most pressing global health needs.

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Competing interests statement

The authors declare [competing interests](#): see Web version for details.

Disclaimer

The authors are the leadership team for CARB-X. The views expressed are those of the authors and do not necessarily represent those of the agencies or entities they work for.

FURTHER INFORMATION

CARB-X: <http://www.carb-x.org>

ALL LINKS ARE ACTIVE IN THE ONLINE PDF

TOC blurb:

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Competing interests statement

J.H.R. is an employee and shareholder of AstraZeneca Pharmaceuticals, non-executive board member, senior advisor and shareholder of F2G Pharmaceuticals; non-executive board member of Adenium Biotech ApS; Expert-in-residence, Wellcome Trust; and operating partner and consultant, Advent Life Sciences. P.J. is executive director of AMR Centre Ltd; non-executive director of Redx Pharma Plc; non-executive director of Yprotech Ltd; non-executive director of Biovictrix Therapeutics Ltd; and owner and director of Intelia Consulting.