CARB-X FAQs

What is CARB-X?

CARB-X is a new global public-private partnership for pre-clinical antibacterial research, with research funds available under a federal cooperative agreement for the first five years up to US$500 million. Over the first five years of CARB-X, our goal is to accelerate a diverse portfolio of more than 20 high-quality antibacterial products towards entry into human testing. Key funders include the U.S. government (BARDA), the Wellcome Trust, and the AMR Centre, a public-private partnership located at the Alderley Park research facility near Manchester, England. The entity is called CARB-X as it sprang from the U.S. government's Combating Antibiotic Resistant Bacteria (CARB) initiative, and will directly address several key goals in the 2015 U.S. CARB National Action Plan. Boston University leads the project.

Why do we need CARB-X for new antibiotics?

We need a diverse and vibrant pipeline of new antibacterial products to prevent and treat drug resistant bacterial infections. Over the past several decades, the number of pharmaceutical companies developing new antimicrobial therapies has decreased. As a result, there has been a significant innovation gap in antimicrobial product development, with no new class of antibiotics invented for the treatment of hospital acquired Gram negative infections in 40 years. From 2007-2012, the number of patents filed for new antibiotics declined by 38.5 percent.

At present, there are a limited number of medium to large pharmaceutical companies still engaged in antimicrobial drug discovery. In fact, from 1998-2013 there were 14 companies that entered antimicrobial drug development, while 36 companies exited (Kinch MS et al., Drug Discovery Today).

Companies increasingly cannot justify that the development of new antimicrobials as sufficiently profitable to warrant the substantial research and development investment required. The reasons for this are multifactorial but include:

1) the short course of antibiotic therapy results in reduced profitability when compared to other drugs (e.g. cardiovascular, mental health) that one must take more frequently,
2) the inevitable development of antimicrobial resistance, a phenomenon that does not occur with many other therapeutic areas, and
3) the use of any new therapy as a last resort in order to preserve the capability to treat drug resistant infections.

Similar market factors have also led to decreased investment in vaccines and diagnostics to address antimicrobial resistance. For diagnostics, these include challenges around the use of, and reimbursement for, differential diagnostic tests that can rule in/out certain infection types, making the business case less certain.

Through the cooperative agreement, CARB-X partners will collaboratively select and provide research support and funds to early-stage developers of antibiotics, which can reduce the business risk inherent

in drug development and, in doing so, incentivize companies to invest in the advanced development to see promising drugs candidates through to regulatory approval.

How will the CARB-X select candidate projects?

Through the cooperative agreement, the strategic direction of CARB-X is governed by a Joint Oversight Committee (JOC) consisting of NIAID, BARDA, Boston University, Wellcome Trust, and AMR Center Senior Leadership. The JOC sets the priorities for CARB-X to support. In Year 1, those priorities are 1) additional therapies for Gram negative bacteria and 2) non-traditional approaches (non-antibiotic) to treat bacterial infections. Product developers wanting to receive support from CARB-X should go to www.carb-x.org or www.medicalcountermeasures.gov for additional information on the individual Accelerators that comprise CARB-X to determine which one is the best fit for that developer. Developers then apply to the Accelerator and undergo a project review process. If selected, the project will receive funding from CARB-X.

How do you know if CARB-X is successful?

The 2015 Combatting Antibiotic Resistant Bacteria (CARB) National Action Plan states that CARB-X should progress two candidate antibiotics into first time in human testing over the five years of the program. CARB-X aims to surpass that goal.

What will each CARB-X partner do under the cooperative agreement?

The Biomedical Advanced Research and Development Authority (BARDA), within the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR) who will draw on its extensive experience of successfully advancing promising medical countermeasures through late-stage development and provide $30 million during the project's first year and up to $250 million during the five-year program.

The AMR Centre, a public-private initiative formed in February 2016 to drive the development of new antibiotics and diagnostics, aims to provide $14 million to support CARB-X projects in year one and up to $100 million over five years. The Wellcome Trust, a global charitable foundation focused on biomedical research, will contribute further funding and its expertise in overseeing projects of this kind.

Boston University in Boston, Massachusetts, will host the CARB-X executive team which will include Kevin Outterson, a leading BU researcher and collaborator in global projects to address antibiotic resistance, along with a team of experts with decades of experience in drug development, including in the area of antibacterial drugs.

The National Institutes of Health's National Institute of Allergy and Infectious Disease (NIAID) leads the U.S. government in determining the causes of infectious and immune-mediated diseases and developing better means of preventing, diagnosing and treating these illnesses. NAID will provide in-kind research support, including preclinical research expertise, to projects that CARB-X supports. NIAID also is providing technical support for CARB-X from their internal subject matter experts in early stage antibiotic drug discovery and product development.

MassBio in Cambridge, as an extension of the successful MassCONNECT program, and California Life Sciences Institute (CLSI) in the San Francisco Bay Area will provide world-class business support and mentoring services to innovative product developers selected for funding. The two accelerators will also share best practices with the Wellcome Trust and AMR Centre, expanding the scope of business support services globally.

Key research programs will occur at the Broad Institute in Cambridge, Massachusetts, including a new, inter-disciplinary Collaborative Hub for Early Antibiotic Discovery with a goal to advance more than three products through shared chemistry services. The Broad Institute also will expand their flexible small grant program, Scientific Projects to Accelerate Research and Collaboration.

RTI International (RTI), a global research support organization headquartered in the Research Triangle Park in North Carolina will provide research support services to product developers in the partner accelerators as well as build and run the computing systems to identify, track and monitor all research programs, including a real-time dashboard management information systems. RTI will evaluate all CARB-X operations, sharing best practices across all partners and supporting continuous quality improvement.

BARDA specific:

BARDA was established to support advanced development. Why is BARDA supporting early stage research and is BARDA actually authorized to support early development?

Antimicrobial resistance is a growing threat to public health and bold solutions are needed to address this innovation gap. BARDA's mandate includes emerging infectious diseases, which includes antimicrobial resistant pathogens, and the Executive Order to combat antimicrobial resistant bacteria directly instructs BARDA to support medical countermeasure development for public health pathogens of urgent or serious public health concern. In addition, sections 319L(c)(2)(D) and 319L(c)(4)(D)(iii) authorize the Secretary to promote innovation to reduce the time and cost of countermeasure and product advanced research and development by awarding contracts, grants, or cooperative agreements, or entering into other transactions, such as prize payments, to promote research to promote strategic initiatives, such as rapid diagnostics, broad spectrum antimicrobials, and vaccine manufacturing technologies. BARDA increasingly recognizes the need to remove any barrier to companies pursing antibiotic development at all phases of development. Under this cooperative agreement, BARDA has joined NIAID in constructing a flexible, novel public-private partnership that utilizes NIAID's expertise in early stage antibacterial drug discovery and development. It is our hope that CARB-X will be even more impactful because of the number of partners who have agreed to collaborate and operate CARB-X under a common strategic vision.

Where is BARDA's funding coming from?

This funding was appropriated in the Department of Health and Human Services Appropriations Act, 2016 (P.L. 114-113). The U.S. government's FY 2016 budget specifically requested funding for this purpose and aligns to the 2014 Combating Antibiotic Resistant Bacteria (CARB) National Strategy and the 2015 CARB National Action Plan.

Why not use the funding to develop products needed for Zika?

The BARDA funding dedicated to CARB-X was requested in the U.S. government's FY 2016 budget specifically for combatting antimicrobial resistance. Other funding, redirected by HHS, is being used to support development of Zika products, although supplemental emergency funding is needed for those products to progress.