# At 5 years, CARB-X celebrates progress on antibiotic development

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Chris Dall | News Reporter | CIDRAP News | Aug 13, 2021

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CARB-X Executive Director Kevin Outterson.

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Since its founding in July 2016, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, better known as CARB-X, has poured more than $361 million into the early-stage development of innovative new therapeutics, diagnostics, and vaccines to tackle the world's most dangerous drug-resistant pathogens.

Just don't ask Executive Director Kevin Outterson, JD, to tell which CARB-X-funded project is his favorite.

"I get asked this question a lot, and I can't tell you which of my children is most beautiful," he says.

But what Outterson and others can tell you is that the antibiotic development pipeline, which has been battered in recent years by the broken financial model for new antibiotics, is in better shape because of CARB-X's efforts. Through its 5 years of existence, CARB-X has provided early-stage funding for 92 projects, 10 of which have advanced into phase 1 trials—far exceeding the goals set by the US National Action Plan for Combating Antibiotic-Resistant Bacteria.

CIDRAP News spoke recently with Outterson about what CARB-X has achieved in the past 5 years, the challenges posed by the broken market for new antibiotics, and what lies ahead. The conversation has been lightly edited for clarity and length.

***CIDRAP News: CARB-X just recently celebrated 5 years of funding products to address antibiotic-resistant bacteria. How would you assess those 5 years and CARB-X's impact on the antibacterial pipeline? Is CARB-X doing what it set out to do?***

**Outterson:** When we started, the goal from the US government was really much more modest than what we've achieved. They were thinking of maybe 20 projects during the 5 years, with a couple of those projects graduating into first-in-human trials. After the

market started crushing antibiotic research and development, in particular after the bankruptcies in 2019, it became clear that CARB-X was one of the only significant funders of this pre-clinical work.

So not only have we overachieved our goals, and really have the world's most diverse and innovative portfolio by far, but I think the need for CARB-X was greater than anyone could have imagined back when it was being discussed in the White House in 2015. Sometimes you get lucky with timing, and I think CARB-X being created when it was—so that were up and running when the crisis hit—was really opportune.

***CIDRAP News: CARB-X is currently supporting 60 active projects. Have you been surprised at the number of innovative products that have come through your door? Obviously, there was a certain amount of belief in the science, but has it been beyond your expectations?***

**Outterson:** The quality of the science is spectacular. I tell private investors that it's the opposite of some of the fields that they're investing in. In some other areas, you'll see very early-stage hypotheses that haven't even been tested in animals, and they're looking for a billion-dollar valuation. In antibiotics, there are so many excellent ideas, first-in-class and totally novel approaches, that really, the valuations are remarkably low. So really, we were surprised.

We've had over 1,100 applications, we've funded 92 projects [60 active as of today] and we say no to over 90% of the people that apply to us. We've had applications from more than 30 countries, and we've funded projects in 12 countries. We'll take the best science wherever it is, anywhere in the world.

I think anybody's evaluation would look at the recent clinical [antibiotic] pipeline and say it's not very innovative, taken as a whole. When you look at what we've published about what's inside the CARB-X pipeline…the science teams have done remarkable work. It's not a science problem; it's an economics problem.

***CIDRAP News: What about the wider antibiotic development space? How has it changed since CARB-X was launched? Have you seen the type of progress that you would like to see, and that would really enhance what CARB-X is doing at the front end?***

**Outterson:** I think of us actually as being in the middle of the process. If you had three chains, the first link in the chain would be everyone who funds basic research—NIAID [the National Institute of Allergy and Infectious Diseases] and their equivalent in every other country. The only reason CARB-X had amazing projects to choose from is because 10 years ago, NIAID funded amazing basic science. So we have to remember that.

Then we have this spot, from hit to lead until the end of the phase 1 trials, and then translational work to pre-clinical work to the first-in-human [trials]. We are fairly alone in that space right now.

…After us is where there has been the most exciting development, what happens after they graduate from CARB-X. The most exciting entrant is the AMR Action Fund, [which provides] a billion dollars from a lot of the companies that gave up on antibiotics decades ago. Together with the European Investment Bank and the World Health Organization [WHO] and the Wellcome Trust, [they are] collectively committing to invest in 10 to 12 companies around the stage where one would graduate from CARB-X [phase 2 and phase 3 trials], to try to get two to four antibiotics to market.

That provides a continuation to CARB-X. I was worried for many years that, even if CARB-X did a great job, would these companies just be sitting in a parking lot waiting for private funding? And at least with the AMR Action Fund, we know that, for some subset of them, there's a realistic opportunity [for funding].

***CIDRAP News: How is CARB-X planning to work with the AMR Action Fund so that needed treatments get to the market in a way that ensures fair pricing and accessibility, even in poorer countries?***

**Outterson:** There's a lot of ways for us to collaborate. We need to know what is needed out there in the world, so we listen carefully to the WHO and the CDC [US Centers for Disease Control and Prevention], and we interview clinicians and listen carefully to where the clinical need is. But the AMR Action Fund stands as the intermediary. They want to acquire these projects, by license or acquisition from these small companies that we're supporting, and it is their job to acquire products that they think have a real chance of positively impacting the health of patients.

So we want to know what are the priorities of the AMR Action Fund. What sort of target product profiles are they looking at, what sort of data packages are they interested in? Now, let me tell you, everyone wants to know this. Every company in this space wants this information. But we would also like it, because then we can help nurture our companies over the next years.

…We've always wanted to have these sort of data packages and profiles for these companies to be available for private investment. It's just that, for most of them, this is such a tough market. Without adequate reimbursement after Food and Drug Administration [FDA approval], you can have wonderful science, a great valuation, and a perfect data package, and it's still hard. That's why the action fund was created.

***CIDRAP News: Let's talk about pull incentives. The United Kingdom, Sweden, and other European countries are currently experimenting with models that would change how antibiotics are valued and reimbursed, and the US Congress has introduced legislation—the PASTEUR Act—to that effect. What do you think of these efforts?***

**Outterson:** I think what the United Kingdom has done with their pilot is the best in the world, because they're looking at antibiotics and saying these are infrastructure that requires investments over a generation, and they're willing to pay a subscription. So even if they only need one or two of the pills in the first year, they're willing to pay a subscription because they see the long-term picture, and [recognize] the fact that this is an investment.

If you build a bridge or a dam or a tunnel, you have to pay for the maintenance, or eventually the thing will fail. So the United Kingdom's pilot program is taking the correct approach. It's fully delinked…[they're] going to stop paying based on the volume and start paying based on the social value. That's great.

The European Commission has announced they're exploring pull incentives within Europe. They've put out a tender for a group of academics and industry people to help them define what their options are, and we look forward to seeing how that develops.

The Swedish program is really different. For Sweden, they offered incentives to companies [4 million Swedish Kroner, so a couple of hundred thousand US dollars] that had existing, on-patent antibiotics that weren't available in Sweden….That's an incentive that's really helpful to Sweden, to get them access to a drug that was already available in Europe. It does nothing to incentivize innovation for the next generation of antibiotics.

What they did in Sweden is a great thing. I support it; other countries should look at something similar….But the UK approach is more comprehensive, because it also thinks about the [research and development] ecosystem.

In the United States, the PASTEUR Act—it's proposed, it's not yet law—is similar to the UK system, and therefore is a wonderful thing.

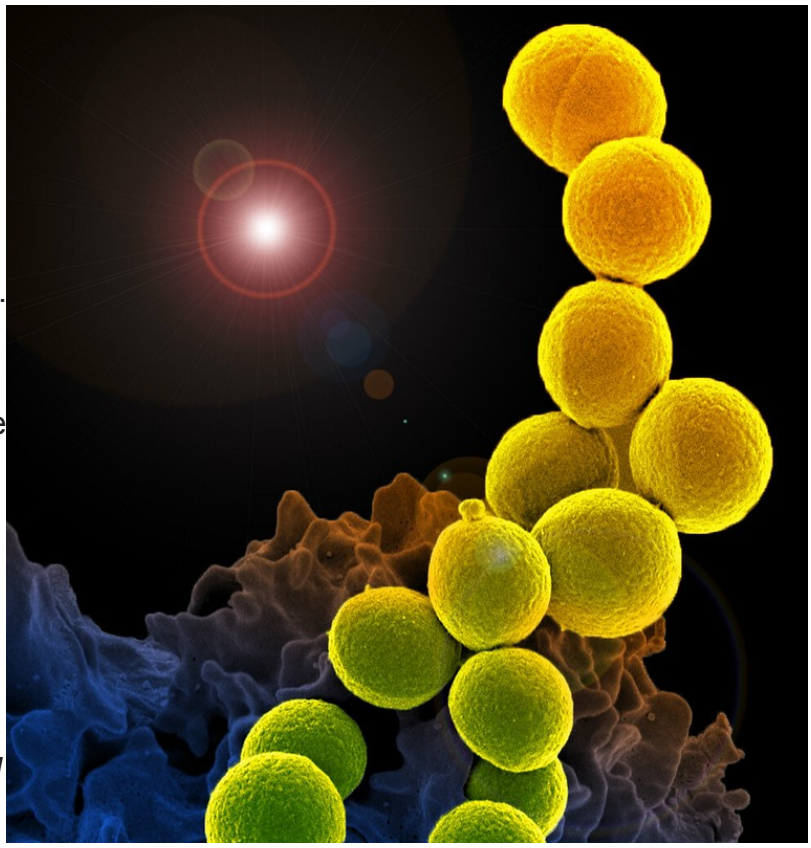
***CIDRAP News: Do you think the Pasteur Act will get passed?***

**Outterson:** Can you name many other laws that have bipartisan support from the US Congress, from folks with really different backgrounds from both sides of the aisle? I'm not a political expert, but this is something that doesn't feel very partisan. It's been supported by Democrats and Republicans. So I can only be encouraged by that.

Five years ago, I don’t think there were a hundred people who could describe to you what antibiotic delinkage was—this idea of paying for value and not volume. And 10 years ago, there were probably about 5 people. And now we have major governments either doing it, or talking very seriously about doing it. That's amazing progress.

***CIDRAP News: You were one of the authors on a recent paper that found that patients in several high-income countries have limited access to most of the new antibiotics approved since 2010. What is the significance of that study? What does it tell us about the economic challenges that antibiotic developers face?***

**Outterson:** There have been 18 antibiotics and antibacterials approved by either FDA, Health Canada, the European Medicines Agency, or Japan since 2010. That looks like success, right? But there are only 3 high-income countries in which a majority of those drugs are available…The United States, England, and Sweden. So if the bulk of the innovative new antibiotics that have come out in the past decade aren't even commercially launched in the G7 and 7 other high-income countries in Europe, then what is the prospect of these drugs being available in the rest of the world that desperately needs new antibiotics?



…If it doesn't make sense for a company to bother to launch [an antibiotic] in Sweden, or Germany, or Croatia, or Italy, or Canada…then it points to something fundamentally broken. It's not just the normal access battle that we had with HIV drugs, or many other drugs in the past decades. This is an access problem in high-income G7 countries. Something fundamental has to change in the way we pay for antibiotics.

***CIDRAP News: Were the findings of that study deflating for you?***

**Outterson:** I knew that companies were not launching in many countries, but what I was surprised about was how bad the data were. I didn't go into it thinking that Canada and Japan would be last on the list. And I sort of expected other high-income but smaller markets in Europe to come in low. It was interesting. So it's clear from this study that there's a couple of implications you can draw. One is that maybe the drugs that have been approved in the last decade aren't that great.

So how do we approve the quality of these drugs? And for the ones that are useful, how do we make sure that they get to patients?

If you talk to the small companies that get a drug approved, they get requests frequently from these countries where they haven't been able to launch for emergency access to their drug. Somebody's dying in a hospital someplace, and it's a country that doesn't have

commercial launch or approval yet, but they need [the drug], and the company, even though they don't have money and don't have revenues, they still provide it through these emergency access provisions.

…That's not the way we should be running the system, through emergency one-offs. These drugs should be available, they should be on formulary, we should have better diagnostics so we know when we need them, and the companies should be reimbursed appropriately so they don't go bankrupt.

***CIDRAP News: Has the pandemic helped raise the profile of antibiotic resistance and antibiotic development, and is that a good thing?***

**Outterson:** Everyone now knows who Tony Fauci is. The average 4th-grader knows what epidemiology is, or at least can say it. It's disappointing to see the political polarization around these issues, but without a doubt, people are now completely aware that an infectious, transmissible disease can grind our civilization to a halt and cause us all to have to stay inside for months. That is a message we didn't have in our brains a couple of years ago.

But bacteria are different from viruses; they don't mutate as quickly. It's more of a slow-moving glacier, grinding things down before it, as opposed to a fast-moving tornado. So it's not the same, but it is categorically similar.

We know the direction that things are going, we know that resistance will undermine what we use today for modern medicine, and we need to do something about it. It might not be tomorrow that we have this tragedy; it might be 5 years or 10 years. It's hard to predict, exactly. But I think the public and policymakers are aware now of the immense costs, and that a little bit of preparedness can save lives.

***CIDRAP News: What do you hope to see from CARB-X—and the antibiotic development ecosystem—5 years from now?***

**Outterson:** We support today 35 therapeutics. Out of those, all but 1 are entirely new classes, or entirely non-traditional approaches, or new mechanisms of action. I think 15 are all three—so, [they're] highly innovative. I would love to see one of these be the first non-traditional, or the first new class, of therapeutics approved by the FDA, having gone through the AMR Action Fund, and then be awarded a subscription agreement under the Pasteur Act. That would set me up forever.