FDA calls for subscription model to pay for anti-infectives

In September 2018, FDA Commissioner Scott Gottlieb laid out the agency's plan to combat anti-microbial drug resistance, a problem that has become increasingly urgent as companies shy away from developing novel anti-infectives, compounded by the rise in resistant bacteria and the waning efficacy among existing, aging treatments. The agency's strategy includes streamlined regulations and better stewardship, but also new payment and reimbursement mechanisms to encourage industry to embrace drug development. In the past, regulatory carrots, whereby the FDA granted qualifying antibiotics extra market exclusivity and rapid review, such as the 2012 GAIN (Generating Antibiotics Incentives Now) Act, have proven insufficient. The same goes for R&D funding. What's needed are market incentives that decouple economic reward from sales volumes because these medicines will necessarily be used sparingly to slow the development of resistance (*Nat. Biotechnol.* **36**, 555, 2018). "We need to do something soon," says Kevin Outterson, executive director at CARB-X, a global public–private antibiotic R&D partnership. "Most small companies working in the area have less than 24 months of cash".

FDA is exploring a range of so-called 'pull' incentives, including one model in which hospitals would pay a fixed fee, similar to a software license, for access to a drug on a monthly or annual basis. The idea is to create predictable returns for a company and to ensure institutions are not incentivized to use more, or less, of a drug than is clinically appropriate.

This licensing or subscription model isn't perfect. John Rex, Chief Medical Officer and Director at Manchester, England-based antifungal company F2G, says a licensing fee would be complex to implement across all US hospitals. It would also exclude drugs used in the outpatient setting. He instead favors market entry rewards for drug developers. The rewards could be purely financial or related to patent exclusivity, priority review vouchers, or any mix of those. Dozens of flavors of pull incentives have been explored over the years, by groups including DRIVE-AB, an antibiotic-focused project funded by the Innovative Medicines Initiative (a European public–private partnership aimed at accelerating drug development); the World Economic Forum; and the Wellcome Trust, a biomedical research charity based in London.

Drugmakers and researchers eagerly await details of what will emerge from ongoing discussions between the FDA and the Centers for Medicare and Medicaid Services over new reimbursement models. But for CARB-X's Outterson, details of how the pull incentive will work are less important than having an incentive at all. "I'm pragmatic. The pull incentive I like is the one that is significant, and gets passed."

Newscom / Alamy Stock Photo

Scott Gottlieb has served as FDA commissioner under the Trump administration since March 2017.

James Anderson, head of corporate government affairs at Brentford, UK-headquartered GlaxoSmithKline, agrees. "We're agnostic as to the [pull-incentive] model," he says. "It's hugely positive that FDA is so proactive on what needs to happen and has the influence to convene the governmental agencies and political support" required, he says.

Executives at Merck, based in Whitehouse Station, New Jersey, are more circumspect about the licensing model. While supporting the call to action, they prefer tweaks to the current drug reimbursement set-up, rather than an entirely new system. They favor important new anti-infectives being funded through add-on payments, rather than through the current system of 'diagnosis-related groups', which give hospitals a fixed amount for a particular diagnosis as an incentive to use cheaper medicines. Removing anti-infectives from that system would "free up hospitals to use products without consideration of the cost," says Nicole Mahoney, Merck's Director, Global Regulatory Policy. Commissioner Gottlieb did mention technology add-on payments as one potential approach in his September 2018 remarks. But although they'd give manufacturers pricing freedom, such payments on their own may not ensure the responsible use of anti-infectives. This stewardship falls short in many US hospitals, according to Amanda Jezek, senior vice president, public policy and government relations at the Infectious Diseases Society of America, representing infectious disease doctors.

Everyone agrees that there's no single answer to this global problem. "We need a suite of incentives to address the challenge," says Paul Schaper, Merck's executive director of Policy and Government Relations. National markets will require different kinds of incentives to fit their health system. Having three of four reimbursement models across various countries would be fine, according to GSK's Anderson, so long as they're broadly aligned. Such models would "send an important signal" to drug developers that the fruits of their work will be appropriately compensated. "We probably won't get it right the first time. But lessons will be learned, and we can build a better model from them," he says.

Melanie Senior *London, UK*

> **"The single most important thing that has come out of this is that the network that was set up after Ebola has worked."** Mike Beadsworth, director of the tropical and diseases at the Royal Liverpool Hospital, on his team's quick reaction to the finding that three Londoners were infected with monkeypox. (*The Guardian*, 7 October 2018)