Speed and oversight: FDA Commissioner Gottlieb acts on pledges

In late August, in a rare tide of bipartisan support, the US Congress passed legislation to reauthorize user fee programs for the next five years. The timely reauthorization of the law allowing the agency to collect money from industry to help fund drug reviews also formalizes initiatives to increase generic drug competition already begun at the agency under new commissioner Scott Gottlieb (*Nat. Biotechnol.* **35**, 293–294, 2017). On September 11, Gottlieb delivered a speech promising drug developers new measures to speed up the approval pathway for innovative drugs as well. "We're on an unsustainable path, where the cost of drug development is growing enormously, as well as the costs of the new medicines," Gottlieb said at the Regulatory Affairs Professionals Society 2017 Regulatory Convergence Conference in Washington, DC. "We need to do something now, to make the entire process less costly and more efficient."

Congress, however, refrained from attaching major drug pricing legislation to the FDA Reauthorization Act of 2017 (FDARA). In fact, the new user fee program was remarkably uncontroversial. It passed Congress with near-unanimous support, even amid the heated healthcare reform debate, and despite the administration being at odds with certain generic drugs clauses and taking the position that industry should pay for 100% of drug review costs, for example. "FDARA's not the most exciting law, but that's the story," says Michael McCaughan, founder of health policy analysis firm Prevision Policy in Washington, DC, noting that most of the changes that might have formed the backbone to the present FDARA had already been laid out in the 21st Century Cures Act, which became law in December 2016 (*Nat. Biotechnol.* **35**, 6, 2017).

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FDA Commissioner Scott Gottlieb.

Some of Gottlieb's initiatives have made their way into FDARA, however. The so-called competitive generic therapies path, aimed at reducing regulatory obstacles to generic drug access, ratifies a plan put in place by Gottlieb in May, shortly after he took the helm of the US Food and Drug Administration (FDA). It gives 180 days' exclusivity in addition to priority review for products for which FDA deems there is inadequate generic competition or that are on the agency's drug shortage list. Gottlieb has effectively changed the narrative from 'FDA is dragging its feet and blocking generics' to 'FDA is getting out in front of this problem', says McCaughan. "There will be more generics under FDARA, and that's probably the biggest change under the law," he says. Aside from the push to grease the regulatory wheels for generic drugs (and thus speeding to market more affordable medicines), the new commissioner has been active, at times playing against partisan stereotypes or viewpoints held elsewhere in the Trump administration.

Gottlieb has been vocal in his support for vaccination, even as President Donald Trump

Box 1 FDA cracks down on rogue stem cell clinics

In late August FDA Commissioner Scott Gottlieb said the actions of a few "dishonest actors" in the stem cell therapy and regenerative medicine areas are putting the entire field at risk. He vowed to step up enforcement to "make sure the agency is separating the promise from the unscrupulous hype." At the same time, Gottlieb stated that the FDA must set up a regulatory framework for those working on genuine science to clarify whether a new treatment is subject to FDA regulation or is a legitimately individualized treatment—what the agency calls homologous use, where cells or tissues are taken from, and returned to, a single individual—vand requires no approval. Forthcoming guidance will give industry more clarity about what criteria the FDA will use to define homologous use. Increased enforcement coupled with the promise of clearer regulation is "appropriate and necessary," says Michael Werner, executive director at the Alliance for Regenerative Medicine and a partner at the law firm Holland & Knight in Washington, DC, noting that the commissioner is tackling the two issues, but not conflating them.

The FDA also came down on StemImmune, a biotech located in San Diego. On August 28, the agency seized vials of vaccinia virus vaccine; the company was using the vaccine to create an unapproved stem cell product to treat cancer, according to FDA inspectors. The same day the FDA warned a stem cell clinic that was processing stem cells from fat tissue and using the cells to treat a variety of diseases, including amyotrophic lateral sclerosis, Parkinson's disease and pulmonary fibrosis. "We support FDA stepping up its enforcement of its regulation," says Werner. The potential for the field of regenerative medicine can only be fulfilled with "rigorous oversight from FDA," he says.

reportedly considered a vaccine safety commission to investigate already debunked links between vaccines and autism. As commissioner, he has pushed for lowering the nicotine content and limiting flavoring in cigarettes, and has established a steering committee to seek regulatory strategies to combat the current opioid crisis. Under his leadership the agency requested that Endo Pharmaceuticals (Malvern, Pennsylvania) pull the long-acting opioid Opana ER from the market. In August, Gottlieb decried the "unscrupulous actors" that have exploited uncertainty in the agency's regulation of regenerative medicine products such as stem cell therapy, at the same time calling for modernization of regulations in the space (**Box 1**). And most recently, he signaled the FDA's intent to close loopholes related to the Orphan Drug Act that enabled drug companies to avoid commitments to study drugs in pediatric indications.

Gottlieb is "a physician first," says Marc Samuels, founder and CEO of ADVI, a life sciences and healthcare services consulting firm in Washington, DC. Issues including vaccines, the opioid crisis and smoking transcend partisan or commercial considerations and are "more than just lip service," says Samuels. And as a physician, cancer survivor (Gottlieb was treated for Hodgkin's lymphoma), former FDA deputy commissioner and Centers for Medicare and Medicaid senior policy advisor, he has drawn on various experiences to shape an ambitious agenda. "I think he's done a lot of things that have played very well with the FDA staff and the public health advocates who would have been very ready to criticize him," says McCaughan.

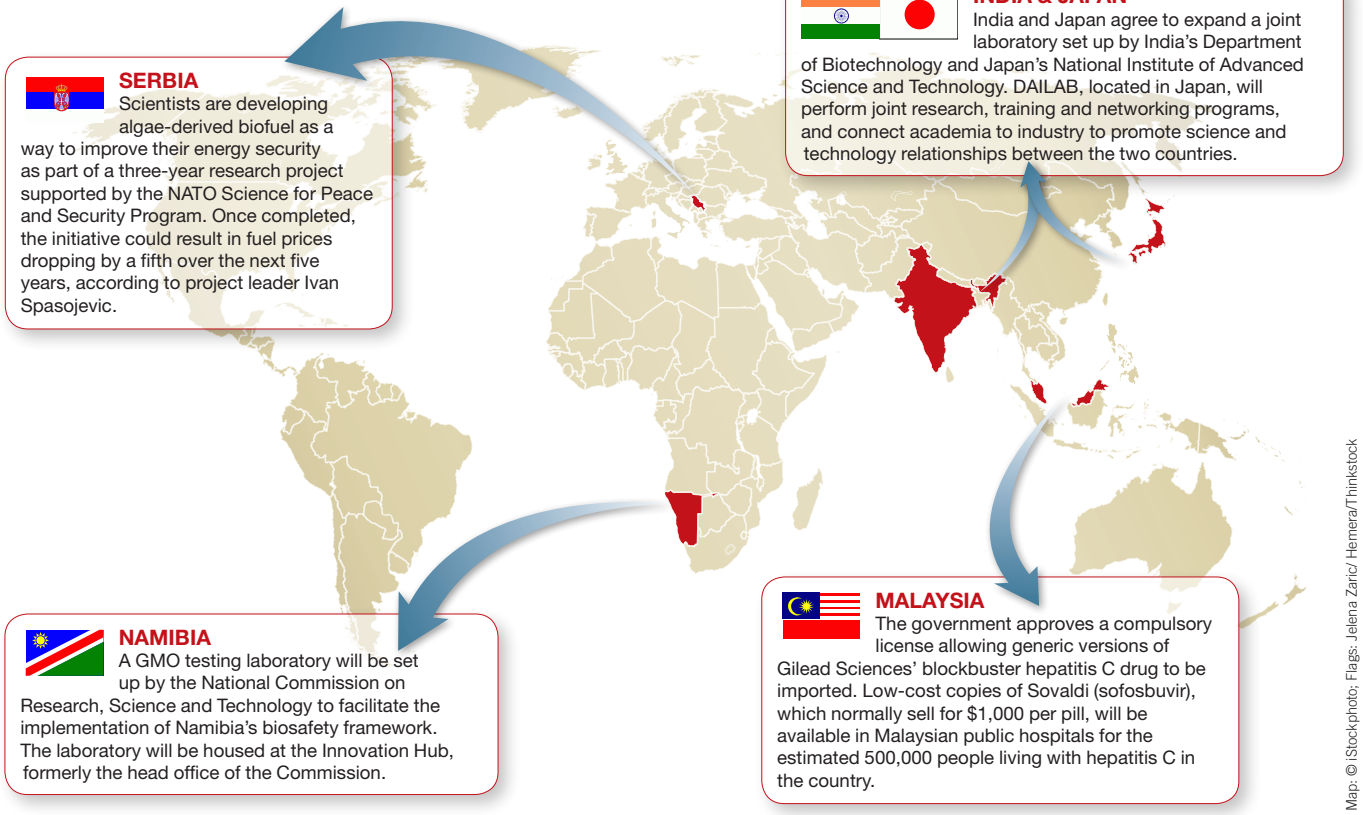
Despite a drop in new drug approvals in 2016, Gottlieb has also inherited an agency that was functioning at a high level, as far as the biopharma industry is concerned. Incentives like the 'breakthrough designation' for drugs that may show substantial improvement over existing therapies or for conditions where no treatment exists have helped to boost industry's regulatory success (*Nat. Biotechnol.* **31**, 945–947, 2014). Gottlieb has pointed out areas where the regulatory process "could be made more efficient," says Samuels, and his basic message for drug developers has been that the agency will have an eye on innovation and try "within the appropriate confines of safety and labeling to get products to patients who need them faster."

Chris Morrison *Yardley, Pennsylvania*

"You can use a hammer to build a house or break a house. You could use this tool to help potentially identify discrimination. But you could also use this tool to discriminate." Sociologist Matthew Salganik of Princeton University refers to a recent study from Stanford AI researchers describing a tool that could predict from a picture whether a person is gay. (*Wired*, 18 September 2017)

"It's a bit like saying it's a good business to go out and buy winning lottery tickets." Daniel Seaton, a spokesman for the Biotechnology Innovation Organization, comments on the skepticism engendered by a recent study setting $757 million as the cost for developing new drugs, because it fails to account for the cost of failures. (*The New York Times*, 11 September 2017)

Around the world in a month



SERBIA
Scientists are developing algae-derived biofuel as a way to improve their energy security as part of a three-year research project supported by the NATO Science for Peace and Security Program. Once completed, the initiative could result in fuel prices dropping by a fifth over the next five years, according to project leader Ivan Spasojevic.

INDIA & JAPAN
India and Japan agree to expand a joint laboratory set up by India's Department of Biotechnology and Japan's National Institute of Advanced Science and Technology. DAILAB, located in Japan, will perform joint research, training and networking programs, and connect academia to industry to promote science and technology relationships between the two countries.

NAMIBIA
A GMO testing laboratory will be set up by the National Commission on Research, Science and Technology to facilitate the implementation of Namibia's biosafety framework. The laboratory will be housed at the Innovation Hub, formerly the head office of the Commission.

MALAYSIA
The government approves a compulsory license allowing generic versions of Gilead Sciences' blockbuster hepatitis C drug to be imported. Low-cost copies of Sovaldi (sofosbuvir), which normally sell for $1,000 per pill, will be available in Malaysian public hospitals for the estimated 500,000 people living with hepatitis C in the country.

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