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How Will Trump Change The FDA?

Article By:

Simon J. Elliott

Courtenay C. Brinckerhoff

President-elect Trump's plans for his first 100 days in office include "cutting the red tape at the FDA" and "speed[ing] the approval of life-saving medications." Here, we consider specific steps Trump could take–without or with Congressional approval.

Adopt A Post-Marketing Approval Paradigm

One of Trump's original choices for FDA Commissioner, Jim O'Neill, is said to favor a "post-marketing approval" paradigm to shorten the time it takes new drugs to get to market. (O'Neill does not have a medical background, but did serve as Principal Associate Deputy Secretary at the Department of Health and Human Services under the George W. Bush administration.) The post-marketing approval paradigm would depart from the requirement to show ***safety and efficacy*** prior to marketing that has been in effect since the 1962 Kefauver Harris amendment to the Federal Food, Drug and Cosmetic Act, and would permit a drug to be marketed once it is shown to be ***safe***, with ***efficacy*** demonstrated later.

This change certainly could bring drugs to market sooner, and early sales could provide an income stream to finance the most expensive stage of drug development–the clinical trials required to establish efficacy. But, will consumers–or insurers–pay for drugs that have not yet been shown to work?

It is difficult to imagine a marketplace where insurers (or the U.S. government through Medicaid) pay for drugs before effectiveness has been demonstrated. Additionally, drug companies themselves may be concerned about public relations and liability risks if a drug is not able to meet efficacy endpoints, or turns out to be less safe in larger clinical trials.

Pursue Comprehensive Modernization

Another Trump choice for FDA Commissioner, Dr. Scott Gottlieb, M.D. (who previously served as Deputy Commissioner at the FDA), does not support O'Neill's post-marketing approval paradigm. He instead has proposed a number of alternative reforms, including:

- Prioritizing generic approval

Gottlieb has criticized the Obama administration for making it difficult to obtain approval of generic drugs, leading to a lack of competition in the generic drug market, and higher prices for generic drugs. Gottlieb states that "[t]he FDA should prioritize applications for generic categories where competitors are exiting," and suggests that "[c]ompanies that pursue copies of 'abandoned' generics could receive a voucher that gives them expedited review of another generic drug" to provide "more incentive to market copies of low-volume generics."

- Alleviating burdens placed on generics

Gottlieb also has criticized the FDA for "impos[ing] on generic firms many of the same costly requirements that the agency applies to branded-drug makers," such as requirements made "in a push to reduce the risk of contamination" that "forced generic-drug makers to retool their sterile manufacturing plants and make production lines less intricate." According to Gottlieb, instead of requiring "production lines to be dedicated to one or two drugs … [t]he FDA's safety concerns could be addressed through better quality controls and improving its inspection capabilities."

- Creating a different approval pathway for "complex" drugs

Gottlieb cites the EpiPen as an example of how the FDA's treatment of "complex" drug and drug/device combinations keeps generics off the market. As Gottlieb explains, the drug in the EpiPen (epinephrine) is an old drug, but the auto-injector is protected by patents so a would-be generic would have to use a different auto-injector, but the FDA won't let them do that:

Under the [FDA's] interpretation of [the ANDA] rules, if a patient has to be re-trained to use a generic alternative to a branded product, then the alternative product cannot bear the same labeling as the drug it seeks to copy. As a result, it can't meet the burden of the ANDA process and be approved as a generic equivalent.

According to Gottlieb, the requirement to establish "bioequivalence" for complex drugs can be difficult or impossible when simple pharmacokinetic data is not sufficient to establish that "a copy drug has the same penetration on (and activity at) the biological site that it's targeting." Gottlieb reasons that the current requirements were "crafted at a time when most drugs were simple, small molecule pills," and needs to be updated:

Congress should modernize the generic drug framework to accommodate complex drugs. It could start by giving FDA more discretion to rely on a broader complement of data for evaluating generic copies to complex drugs. This could mean granting FDA the ability to ask for more than just bioequivalence and bioavailability data when it comes to making judgments around sameness as it relates to complex drugs.

- Adopting a risk-based approach to regulation

Gottlieb would like the FDA's efforts to be "much more risk based," particularly in its approach to new technologies such as regenerative medicine and gene editing. Gottlieb suggests the FDA focus on "products that have the potential for latent and widely circulated risks," and not low-risk products like smartphone apps.

I believe FDA needs to more actively consider moving its regulatory processes away from a mostly

clinical orientation and toward one that ties its regulatory functions more closely to the product specific issues as well as the nature of the risk that the agency is grappling with.

For example, Gottlieb recognizes that gene-editing technologies have a potential for latent risk, but does not believe FDA should "use its pre-market requirements as a way to slow technology introduction, on the hope that time alone will reveal any potential dangers." Rather, Gottlieb suggest "a more active approach to risk mitigation once products gain market entry, organizing this oversight based on the nature of the risk that it's trying to resolve."

- Strengthening regulation of laboratory tests through Clinical Labs Improvement Amendments (CLIA)

Gottlieb cites Theranos as an example of the problems with FDA oversight of laboratory tests, and suggests more oversight via CLIA instead.

FDA's review is largely focused on the diagnostic platform itself, which FDA jams into the bucket of being a medical device. …. So when it comes to diagnostics like the blood testing platform that Theranos developed, FDA focuses mostly on the tools, and not the conduct of the lab, or how the many aspects of a diagnostic service are executed.

Yet much of the risk related to diagnostics turns on how the tests are run, not just how they are built. CLIA has a long track record of inspecting labs, and overseeing how diagnostics are performed on patient samples. Ultimately, it was CLIA's oversight that surfaced the most significant problems with Theranos, not FDA's limited review of a single Theranos test.

Drawing on this example, Gottlieb concludes that "the regulation of lab tests is best left to a more robust CLIA, and not FDA," especially "[w]hen the proper function of a novel technology is also tied closely to how it's being used."

- Changing drug pricing mechanisms

Gottlieb disagrees with Trump's proposal to reduce drug prices by importing cheaper drugs, and instead would eliminate "regulations [that] force companies to launch drugs at a single price":

> We … need to make sure that branded drugs … can be priced to reflect the value they deliver to patients. That means allowing drugs to be priced according to clinical circumstances and even the stage of a disease for which they are being prescribed, and the clinical outcomes that they deliver.

Right now, drug makers are largely prevented from offering price concessions based on how a drug is used unless the all of those precise uses are explicitly spelled out in the drug's FDA approved label. So as the publication BioCentury recently noted, if a drug maker wanted to offer discounts based on a drug's ability to shorten or reduce hospital stays it can't — not unless FDA explicitly says that the drug is approved to reduce or prevent hospital stays.

Gottlieb also would like to see antitrust court decisions that favor rebate schemes that benefit everyone except patients legislatively overruled.

Gottlieb’s proposals are ambitious and would require cooperation from industry, other agencies, and Congress–not to mention time to tell if they can be effective.

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