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# *New FDA policies ease access to experimental medications*

New guidance documents issued in June 2016 by the FDA offer pharmaceutical companies more clarity about how to handle requests for their experimental products from physicians treating seriously-ill patients. The guidance makes it easier for physicians to submit requests to access experimental drugs, but also poses new potential risks for companies.

At issue is the FDA's expanded access program – often referred to as the compassionate use program – which gives physicians and their patients access to experimental drugs outside of clinical trials. The program's aim is to help patients who have exhausted other treatment options.

The expanded access program has been subject to two lines of criticism. Patients argue it is time-consuming and difficult for their doctors to fill out lengthy, complex forms required by regulators to enroll patients into expanded access programs. Companies, meanwhile, have expressed concerns about how much they are allowed to charge patients and whether serious side effects experienced by patients using a compassionate use medication could prompt regulators to place a hold on testing of the drug in all patients.

The FDA's three new guidance documents on expanded access provide clarity for patients and the industry. First, a new application form, Form FDA 3926, makes it easier to obtain regulatory approval to begin an expanded access program for a single patient. Previously, physicians used a form designed for pharmaceutical companies setting up large-scale clinical trials. The new form is shorter, easier to fill out, and waives several existing requirements intended for companies. The oversight of an Institutional Review Board still is required for expanded access programs.

A second Q&A guidance offers an extensive overview of the expanded access program. In it, the FDA notes that single-patient programs can be combined into an intermediate-size expanded access program if interest grows, allowing the company to simplify program oversight. The guidance also makes clear that the FDA cannot compel a company to make its experimental drug available to patients.

Finally, a third guidance, *Charging for Investigational Drugs Under an Investigational New Drug Application*, establishes how companies are permitted to recoup the costs from patients for running expanded access trials. Companies must request FDA approval to charge for an investigational product, and must show that they are only charging an amount equivalent to, or less than, their "direct costs" of providing the drug, including manufacturing it and conducting the programs. An accountant must certify the costs as being accurate.

## *At a glance*

The FDA's expanded access process is meant to allow desperately ill patients to obtain early access to drugs that have not yet been approved by regulators.

The process involves enrolling the patient or patients into an existing clinical trial, or setting up a new clinical trial.

Pharmaceutical companies are not obligated to allow patients to enroll in these trials.

New guidance from the FDA makes it easier for patients to enroll in trials by shortening and expediting the FDA trial application form.

Other guidance explains how companies may charge patients money for investigational drugs, but only the cost of production.

The guidance documents may lead to new challenges for companies, including an influx of applications from patients, and new pressures from the FDA during the new drug approval process.

## *Expanded access criteria*

| | |
|---|---|
| ***Health status*** | The patient has a serious or immediately life-threatening disease or condition, and there is no satisfactory therapy to treat the disease. |
| ***Potential benefit*** | The potential benefit to the patient justifies the potential risks of the treatment within the context of patient's disease or condition. |
| ***Non-interference*** | Providing the investigational drug will not interfere with the initiation, conduct or completion of other clinical investigations of the drug. |
| ***Trial type*** | Programs can be set up for a single patient, a small (intermediate) group of patients or a widespread group of patients. |
| ***Approval*** | A drug company must consent to the program, as it cannot occur without the company providing the experimental drugs. The FDA and an Institutional Review Board also must approve of the trial, with the latter overseeing the trial. |

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## *Industry implications*

**1) An easier process will bring more pressure from patients.** The FDA's new process for applying for expanded access may pose challenges for some companies. The shorter, easier form likely will encourage greater use of the expanded access pathway, placing greater pressure on companies to provide access to their experimental drugs. This could cause some companies to shift some focus from their main clinical trials, causing delays. Depending on how many patients are enrolled in an expanded access program, a willing company may not have enough manufacturing capacity to supply drugs to additional patients. In addition, even if the company has an ample supply of the drug, and the willingness to provide it, the drugmaker may have little certainty that its drug would help, rather than harm, a particular patient, especially if that patient is in relatively poor condition due to disease complications.

The cost of providing those drugs may be prohibitive for some companies. This is especially true of start-ups, which may not have the capital or infrastructure available to provide the drugs or the staff to review and oversee the additional requests for access. Though companies are permitted to pass on some of those costs to patients, some may not wish to do so, as insurance companies could use those costs – the costs to manufacture a drug – as an input for future pricing and reimbursement negotiations. The FDA generally approves almost all expanded access applications, indicating that most future applications are likely to be approved as well.

***Expanded access approval rates for drugs and biologics***

| | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|
| ***Number of expanded access applications received*** | 1,300 | 1,097 | 1,213 | 2,013 | 1,430 |
| ***Number of expanded access applications approved*** | 1,293 | 1,081 | 1,200 | 1,999 | 1,416 |
| ***Percent of expanded access applications approved*** | 99.5% | 98.5% | 98.9% | 99.3% | 99.0% |

*Source: PwC analysis of FDA expanded access data for CDER and CBER. All years fiscal.*

**2) Consider how to better communicate with patients and physicians.** Companies also must consider how best to interact with patients and their physicians during this process. Companies must weigh the risk of allowing their products to be used in an expanded access trial against concerns about side effects, costs or their abilities to focus on getting their product approved by the FDA for all patients. However, savvy patients and advocates have taken to social media to pressure companies to permit them to enroll in expanded access programs. Some have even generated public criticism against FDA and the manufacturer. This, in turn, can attract unwanted attention by the media and legislators. These patients are often extremely ill, making empathy and compassion natural reactions to their causes.

Companies should make sure they are prepared for such cases, and have policies available to ensure they are not caught off-guard. Companies should enhance their external communications to provide physicians and prospective patients the information they need about expanded access policies and the philosophy behind their decision-making. Some of this information may be published to the government's ClinicalTrials.gov database, but companies should publicize their philosophy and process for expanded access online to ensure patients can find answers to their questions. Certain trade groups already require their members to make information about their expanded access programs public as well. Companies can benefit from patient enrollment in expanded access programs, allowing them to obtain new insights into the needs of patients and find new potential targets for future drug development.

**3) Regulators may feel less pressure to grant immediate approval.** As companies seek approval to market their drugs, some make the argument that desperate patients need quick access to them. Companies typically argue for immediate, full approval of their drugs. However, the FDA's new, easier application process for expanded access may ease pressure on the agency in cases where the clinical data supporting the application for approval is still being gathered and reviewed, but the needs of desperate patients to access the drug are compelling.

Instead, the FDA might ask that the company make greater use of expanded access for desperate patients while conducting additional clinical trials. This could delay approvals for some companies' drug products. The regulators' guidance permitting companies to provide the drug "at cost" also may reduce financial pressure on the companies while that further testing is ongoing.

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