



Testimony

Before the Subcommittee on Health,
Committee on Energy and Commerce,
House of Representatives

For Release on Delivery
Expected at 10:15 a.m. ET
Tuesday, October 3, 2017

INVESTIGATIONAL NEW DRUGS

FDA's Expanded Access Program

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Chairman Burgess, Ranking Member Green, and Members of the Subcommittee:

I am pleased to be here today to discuss our recent report on the Food and Drug Administration's (FDA) expanded access program.¹ As you know, through FDA's expanded access program, patients with serious or life-threatening ailments and no other comparable medical options can obtain access to investigational drugs—drugs not yet approved by FDA for marketing in the United States—outside of a clinical trial when appropriate. FDA receives and reviews expanded access requests, and determines whether to allow them to proceed. Other entities also have roles in the process. For example, manufacturers decide whether to give patients access to their investigational drugs; institutional review boards must approve patients' expanded access treatment plans; and physicians treat the patients with the investigational drugs, and monitor their progress.

FDA's expanded access program has been criticized by some physician and patient advocacy groups for being too burdensome and confusing to the entities involved, which could pose a barrier to individuals' access to investigational drugs. Additionally, manufacturers have raised questions about how FDA might consider data from expanded access use in its process for approving the drug for marketing in the United States. However, stakeholders—including physicians, patients, and patient advocates—have also highlighted steps FDA and other stakeholders have taken to improve the program.

My testimony today summarizes the findings from our July 2017 report examining FDA's expanded access program. Accordingly, this testimony addresses (1) what is known about the number, type, and time frames of expanded access requests received by FDA; (2) what actions FDA and other stakeholders have taken to improve expanded access; and (3) how, if at all, FDA uses data from expanded access in the drug approval process. In addition, I will highlight a recommendation we made to help FDA meet its goal of facilitating expanded access to investigational drugs by patients with serious or life-threatening conditions.

¹GAO, *Investigational New Drugs: FDA Has Taken Steps to Improve the Expanded Access Program but Should Further Clarify How Adverse Events Data Are Used*, [GAO-17-564](#) (Washington, D.C.: July 11, 2017).

To conduct the work for our report, we reviewed regulations and FDA documents, and analyzed FDA data on the numbers and types of expanded access requests it received from fiscal year 2012 through 2015, the most recent available at the time of the review. We also interviewed FDA officials and other stakeholders, including a non-generalizable selection of nine drug manufacturers—selected to represent large and small companies—and patient and physician representatives. The work this statement is based on was performed in accordance with generally accepted government auditing standards. Further details on our scope and methodology are included in our report.

FDA Allowed Nearly All Expanded Access Requests to Proceed from Fiscal Year 2012 through 2015

In our July 2017 report, we found that of the nearly 5,800 expanded access requests that were submitted to FDA from fiscal year 2012 through 2015, FDA allowed 99 percent to proceed.² Almost 96 percent of these requests were for single patients (either emergency or non-emergency), while the rest were for multiple patients. (See table 1.) FDA typically responded to emergency single-patient requests within hours, and responded to all other requests within 30 days. According to a study using FDA data, in the rare cases when FDA did not allow a request to proceed, the most common reasons were incomplete applications, unsafe dosing, the requested drug's demonstrated lack of efficacy for its intended use, the availability of adequate alternative therapies, and inadequate information provided in the application on which to base a decision.³

²The agency reports data separately on four categories of expanded access requests that FDA defines as: (1) single-patient; (2) single-patient emergency, for example, for a patient who is not expected to live long enough for an institutional review board to review a typical single-patient expanded access request; (3) intermediate-size, generally for two patients to potentially hundreds of patients; and (4) treatment for larger widespread populations.

³Jonathan P. Jarow, Steven Lemery, Kevin Bugin, and Naomi Lowy, "Ten-Year Experience for the Center for Drug Evaluation and Research, Part 2: FDA's Role in Ensuring Patient Safety," *Therapeutic Innovation & Regulatory Science*, vol. 51, no. 2 (2016).

Table 1: Total Expanded Access Requests Reviewed and Allowed to Proceed by the Food and Drug Administration’s (FDA) Center for Drug Evaluation and Research and Center for Biologic Evaluation and Research, by Type, Fiscal Years 2012 through 2015.

Type of request		Number reviewed	Allowed to proceed	Percent allowed to proceed
Single Patient	Emergency	2,451	2,436	99.4
	Non-emergency	3,047	3,016	99.0
Multiple Patients	Intermediate-sized	204	194	95.1
	Treatment (widespread)	51	51	100.0
Total		5,753	5,697	99.0

Source: GAO analysis of FDA data | GAO-18-157T

Note: Intermediate-sized requests are generally for two patients to potentially hundreds of patients, and treatment requests are for larger widespread populations.

FDA and Others Have Taken Steps to Improve the Expanded Access Program and Patient Access to Investigational Drugs

We found that FDA and other stakeholders, including a non-profit organization and a drug manufacturer, have taken steps to improve the expanded access process and patient access to drugs. For example, in response to concerns that the process to request expanded access to drugs was complex and cumbersome, FDA simplified its website, guidance, and the forms required for the most common types of expanded access requests. Efforts by other stakeholders include a project to educate and streamline the process by which institutional review boards approve treatment plans for expanded access drug use, and a pilot advisory group to help a drug manufacturer manage expanded access requests.

Some states have also enacted “Right-to-Try” laws to facilitate patient access to investigational drugs. These laws provide liability and licensing protections for manufacturers and providers under state law if an adverse event—such as an adverse reaction to the drug—occurs with patients who were allowed access to investigational drugs. However, some stakeholders we interviewed cited concerns that these laws may not help patients access drugs, in part because they do not compel a manufacturer to provide access.

FDA Reported Limited Use of Expanded Access Safety Data in its Drug Approval Process, and Some Manufacturers Have Asked for More Clarity on This Use by FDA

Manufacturers sponsoring clinical trials must submit safety reports to FDA that include adverse events data resulting from clinical trials, as well as from any expanded access use, to be used in assessing the safety of a drug within the drug approval process.⁴ FDA reported using adverse events data from expanded access use in a few cases during the drug approval process, but not more widely, because expanded access use does not have the same controls as clinical trials. For example, according to a study using FDA data, there were only two instances from 2005 through 2014 in which adverse events from expanded access use contributed to a decision to have a clinical hold put on a drug.⁵ However, several stakeholders we spoke with, including the selected manufacturers we interviewed, raised concerns that FDA is not clear about how it uses expanded access adverse events data in its review of drugs being considered for sale and marketing in the United States.

FDA officials reported that they communicate with manufacturers on how they will use expanded access adverse events data. However, our review of documents FDA uses to communicate with drug manufacturers about the expanded access program found that only one included a reference to FDA's use of these data, and the document did not include specific examples of how the data might be used. Further, some of the manufacturers we interviewed told us the guidance was unclear. These manufacturers noted that the lack of clear information can influence their decision whether to give patients access to their drugs, because of their concerns that an adverse event will result in FDA placing a clinical hold on their drug, which could delay its development. This could impact FDA's goal of facilitating expanded access to drugs for treatment use by patients with serious or life-threatening diseases or conditions, when appropriate.

Based upon this finding, we recommended that FDA should clearly communicate how the agency will use adverse events data from expanded access use when reviewing drugs and biologics for approval for marketing and sale in the United States. FDA agreed with our recommendation, noting that, while there have only been two instances in

⁴The process by which a drug or biologic is developed and considered for approval for marketing in the United States involves a number of steps, which include the clinical testing of the drug's safety and effectiveness on human volunteers.

⁵Jonathan P. Jarow, Steven Lemery, Kevin Bugin, Sean Khozin, and Richard Moscicki, "Expanded Access of Investigational Drugs: The Experience of Drug Evaluation and Research Over a 10-Year Period," *Therapeutic Innovation & Regulatory Science*, vol. 50, no.6 (2016).

which adverse event data have contributed to decisions to temporarily put development of investigational drugs on partial clinical holds, additional clarity on how FDA uses such data from expanded access use may allay manufacturers' concerns.

Chairman Burgess, Ranking Member Green, and Members of the Subcommittee, this concludes my prepared statement. I would be pleased to respond to any questions you may have at this time.

GAO Contacts and Staff Acknowledgments

If you or your staff members have any questions concerning this testimony, please contact me at (202) 512-7114 or dickenj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Other individuals who made key contributions to this testimony include Gerardine Brennan (Assistant Director), Nick Bartine (Analyst-in-Charge), George Bogart, and Carolyn Garvey.

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