DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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STATEMENT

OF

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BEFORE THE

COMMITTEE ON HOMELAND SECURITY AND GOVERNMENT AFFAIRS

U.S. SENATE

"Exploring a Right to Try for Terminally Ill Patients"

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INTRODUCTION

Mr. Chairman, Ranking Member Carper, and Members of the Committee, I am Dr. Peter Lurie, Associate Commissioner for Public Health Strategy and Analysis at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss expanded access to investigational products

As a physician, I have personally witnessed the suffering and the dilemmas facing patients and their families when they are confronted with serious or life-threatening conditions and limited treatment options. Having exhausted other treatments, they may wish to turn to investigational products. Prior to approval, Investigational new drugs undergo clinical trials to assess whether they can be used safely and deliver efficacious results for a particular indication in humans. FDA recognizes that, in many instances, patients with life-threatening diseases are more willing to accept the risk associated with investigational products than other patients, especially if they have no other available options.

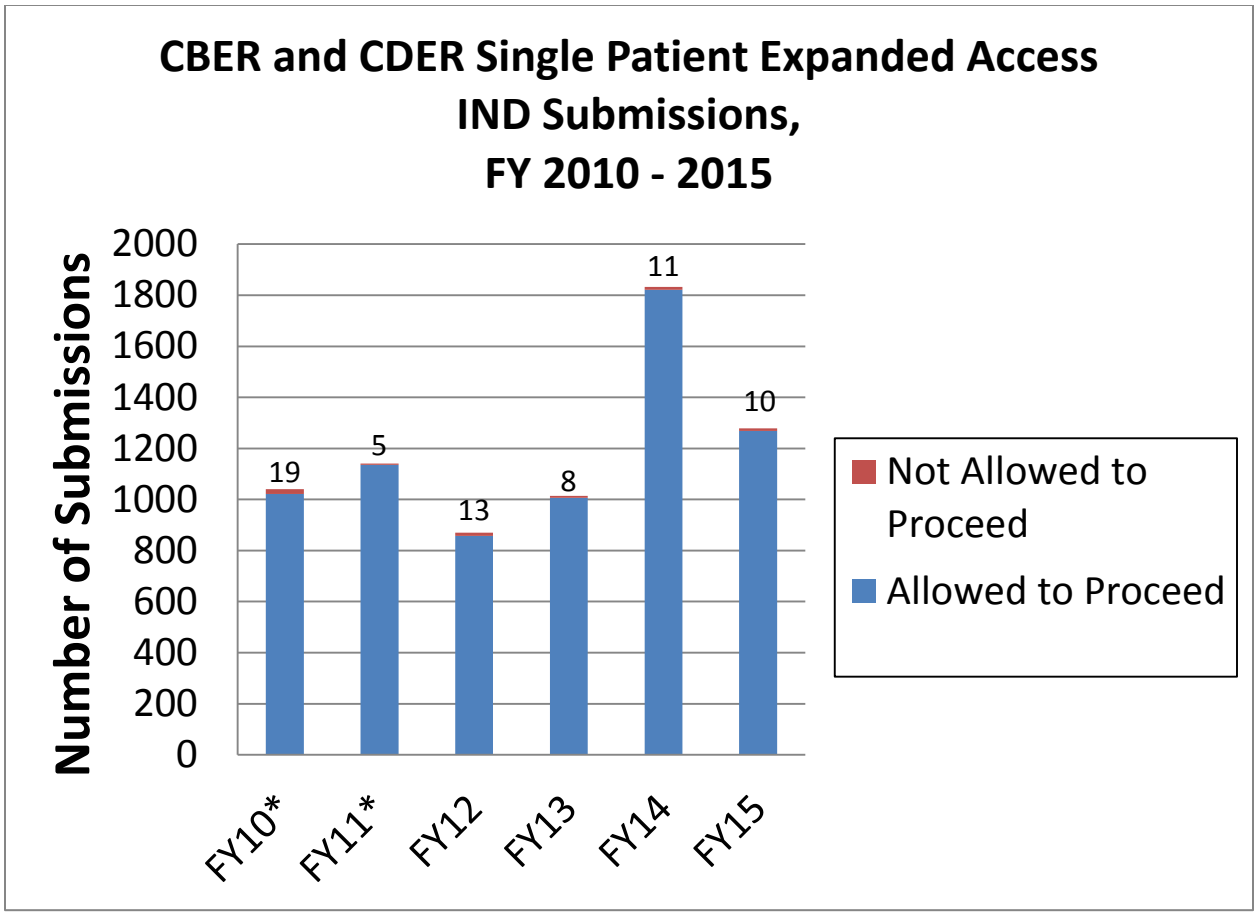
That is why, for over two decades, FDA has had in place a system to help patients gain access to investigational products, and FDA has authorized more than 99 percent of requests between 2010-2015.[1] To be clear: the best way to hasten access to safe and effective products for the largest number of patients is through the clinical trial process. Enrollment in clinical trials helps to ensure adequate protection for patients and leads to the collection of vital data that could eventually result in FDA approval of the investigational product. Once approval is secured, all patients with the condition may receive it, and much wider availability is almost certain to ensue.

Nonetheless, FDA recognizes that there are circumstances when patients with serious or life-threatening conditions and no comparable or satisfactory alternative therapy are not eligible for a clinical trial, either because of where they live, their age, or some other disqualifying factor. These patients may consider seeking access to investigational drugs, and FDA's expanded access program is intended to serve them.

To qualify for the program, the patient's treating physician must determine that the patient has a serious or life-threatening condition and no comparable or satisfactory alternative therapy. The physician then approaches the pharmaceutical company to ask for its agreement that it will provide the drug being sought. The company has the right to approve or disapprove the physician's request. If the company agrees to the physician's request, the physician can then apply to FDA for permission to proceed. Should they do so, they are highly likely to be allowed to proceed. As shown in the chart below, FDA has authorized more than 99 percent (7110/7176) of single patient expanded access Investigational New Drug (IND) requests received in Fiscal Years 2010-2015. Emergency requests are usually granted immediately over the phone and non-

[1] FDA has multiple expanded access programs for investigational drugs and devices: single patient INDs and protocols (including emergency applications), intermediate size INDs and protocols and treatment INDs and protocols for widespread use; and – for devices – emergency use, compassionate use, and treatment use (*http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm*). There are far more applications for single patient INDs and protocols, and they are the focus of this testimony.

emergencies are processed in a median of four days. The treating physician is then responsible for obtaining informed consent from the patient and approval from an ethics committee before administering the drug.



Data include emergency and non-emergency single patient IND submissions.
CBER = Center for Biologics Evaluation and Research; CDER = Center for Drug Evaluation and Research
*For FY 10 and FY 11, the reporting period was October 13 through October 12 of the following year.
Source: *http://www.fda.gov/downloads/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/UCM471305.pdf*

Access to investigational products requires the active cooperation of the treating physician, industry and FDA in order to be successful. In particular, the company developing the investigational product must be willing to provide it – FDA cannot force a company to manufacture a product or to make a product available. Companies might have their own reasons to turn down requests for their investigational products, including their desire to maintain their clinical development program or simply because they have not produced enough of the product.

Based on information available, it appears that pharmaceutical companies turn down considerably more applications from physicians than does the Agency. For example, one

company indicated that it had turned down 98 of 160 applications for a single drug in a six-month period.[2] Another company reportedly turned down "hundreds" of applications for its drug over two years.[3] In contrast, over six years, FDA has put on clinical hold 66 applications from the thousands it has received.

With regard to investigational medical devices, FDA also has a process in place for responding to requests for expanded access to these products as. Since 2012, we have approved more than 98 percent of these requests. In 2015, FDA approved 99 percent[4] of expanded access requests received under an Investigational Device Exemption. Unlike drugs and biologics, emergency use of investigational devices does not require prior authorization from FDA, as long as certain criteria are met, such as submitting a report of the emergency use within five working days from the time the sponsor learns of the use.

Since the expanded access program began, FDA has worked to improve it. FDA established an expedited telephone process for daytime and after-hours emergency requests for expanded access, and revamped the regulations regarding expanded access to investigational drugs to make the process and responsibilities of physicians more clear and concise. More recently, in response to feedback from physicians that completing the two expanded access forms was time-consuming, in June 2016, FDA released a single new form (FDA form 3926) for individual patient expanded access. This form is estimated to take 45 minutes to complete and requires just one attachment (the previous one required up to eight). Along with the new form, we released step-by-step instructions on how to complete it. We also released a Questions and Answers guidance that explains what expanded access is, when and how to request expanded access, and the type of information that should be included in requests. At the same time, we released a third guidance that explains the regulations regarding when and how patients may be charged for investigational drugs, notably that the sponsor may recover only its direct costs associated with making the drug available to the patient. Simultaneously, FDA revamped its expanded access website and produced Fact Sheets for physicians and patients. Almost immediately, physicians began to take advantage of the new form. In addition to web pages directed specifically toward patients, physicians and industry, FDA has staff available to assist physicians and patients in understanding how to apply for expanded access.

However, even patients with serious or life-threatening diseases and conditions require protection from unnecessary risks, particularly as, in general, the products they are seeking through expanded access are unapproved – and may never be approved. Moreover, FDA is concerned about the ability of unscrupulous individuals to exploit such desperate patients. Thus, with every request, FDA must determine that the potential patient benefit from the

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[2] Caplan AL, Ray A. The ethical challenges of compassionate use. *Journal of the American Medical Association* 2016;315:979-80.

[3] Usdin S. How Chimerix, FDA grappled with providing compassionate access to Josh Hardy. *BioCentury on BioBusiness*, March 31, 2014. Available at*: http://www.biocentury.com/biotech-pharma-news/regulation/2014-03-31/how-chimerix-fda-grappled-with-providing-compassionate-access-to-josh-hardy-a7* (accessed September 11, 2016).

[4] 99.04% of 208 evaluable submissions received. More information is available on this website: *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm.*

investigational drug justifies the potential risks and that the potential risks are not unreasonable in the context of the disease or condition to be treated. For this reason, even as it permits more than 99 percent of applications to proceed, FDA makes meaningful changes in 11 percent of expanded access IND applications to help ensure patient safety, including changes in dosing, safety monitoring, and informed consent.

While we welcome suggestions that might improve the expanded access process, we would caution against any changes that would reduce FDA's role in expanded access or that might undermine the crucial clinical trial development process. As noted, enrollment in clinical trials remains the best option for patients wishing to gain access to investigational medical products as it assures adequate protection for patients and leads to the collection of data that could eventually result in FDA approval of the investigational therapy and thus widespread availability. Criticism that effective therapies are being kept from Americans is unfounded; FDA is committed to new drug development. In 2014, consistent with a trend that has been in place for many years, 60 percent of new molecular entities were approved in the United States before any other country.[5] In calendar year 2015, FDA approved 45 new molecular entity drugs. About 47 percent of these drugs were approved to treat rare or "orphan" diseases that affect 200,000 or fewer Americans.

It is therefore critical that we maintain and not undermine the clinical trials process that has served Americans so well. Most fundamentally, the Agency is concerned that some legislative proposals could undermine FDA's ability to protect and promote the public health through science-based regulation of drugs and devices. FDA's expanded access process strikes a careful balance between helping to facilitate patient access to investigational therapies, while providing patients with appropriate human subject protections and preventing interference with the product's development program. Upsetting this balance has the potential to expose patients to unreasonable risks and stymie the development of medical products that could benefit us all. Notably, FDA often has safety information unavailable to the public that is an important consideration in these decisions.

Finally, prohibiting the Agency from reviewing adverse events that occur in expanded access use would be detrimental and raise significant ethical issues. Given that the Agency is charged with assessing the safety and effectiveness of medical products, the Agency cannot ignore valid scientific information. Of course, the Agency understands that adverse events that arise during expanded access use must be interpreted with caution. However, over the last decade, spanning almost 11,000 expanded access requests, there were only two instances in which a clinical hold was placed on commercial drug development due to adverse events occurring under expanded access INDs or protocols. In both instances, the development of the drugs continued after issues were addressed and the holds were lifted. FDA also recently published a guidance entitled *Expanded Access to Investigational Drugs for Treatment Use –Questions and Answers.* This guidance makes clear that the Agency understands that expanded access is a very particular context (sicker patients, multiple illnesses, concurrent medications, etc.) and that FDA takes that context into account when interpreting adverse events.

[5] Scrip Magazine (1982 -2006), Pharmaprojects/Citeline Pharma R&D Annual Review (2007 -2014).

CONCLUSION

Clinical trials remain the best option for patients wishing to gain access to investigational products and bringing new, innovative products to market through the approval process remains the best way to assure the development of and access to safe and effective new medical products for all patients.

For those patients who cannot participate in trials, and are left in the difficult, heart-wrenching position of having no other therapeutic options, FDA is proud of its expanded access process for individual patients. It has stood the test of time and serves over 1,000 patients each year. FDA continues to work to improve the program and expects the new short form and the associated streamlined process to continue to help patients who cannot participate in clinical trials.

I am happy to answer any questions you may have.