Expanded Access to Unapproved Drugs Recast: FDA Simplifies Compassionate Use Application Process

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On February 10, 2014, the Food and Drug Administration (FDA) announced in the Federal Register the release of a new draft guidance that makes changes to its "compassionate use" process to allow a simpler way for licensed physicians to seek expanded access for their patients to drugs that have not yet been approved by FDA as safe and effective.[1] The draft guidance introduces and describes draft Form FDA 3926 (Individual Patient Expanded Access—Investigational New Drug Application (IND)), which is commonly known as a compassionate use request. When finalized, draft Form FDA 3926 will be available for licensed physicians to use for expanded access requests for individual patient INDs.

Notwithstanding the availability of accelerated approval pathways for new drugs, FDA for a number of years has faced criticism from terminally ill patients and their advocates who find it too difficult to obtain access to experimental drugs outside a clinical trial. Indeed, in recent years, this rebuke has led to constitutional litigation against FDA centered on the allegation that FDA's refusal to allow general access to investigational drugs to terminally ill patients, following a Phase I trial that showed the drug was safe for expanded human clinical trials, was a denial of those patients' due process rights.[2]

FDA has been sensitive to this issue since the early years of the AIDS epidemic and in 2009 revised its regulations to establish a broad Expanded Access Program, which includes the compassionate use process. The purpose of the compassionate use process is to make it possible for a patient who has a serious or immediately life-threatening disease or condition to gain access to an investigational drug outside a clinical trial when there is no comparable or satisfactory alternative treatment therapy available.[3] FDA's new draft guidance introduces a time-saving and simplified application form that physicians can use on behalf of individual patients. Previously, physicians were required to use a more complex IND form (Form FDA 1571) which required the submission of 26 types of separate information and 7 attachments. The application form under the old system was originally tailored to companies seeking to begin human clinical investigation rather than expanded access requests from physicians for single patients. As a result, physicians often had difficulty completing the form and associated documents and were forced to spend significant time in making compassionate use applications.

In contrast, the new form (Form FDA 3926) requires only disclosure of the patient's initials and date of submission; clinical information about the patient and the rationale for requesting the proposed treatment (including an explanation why the patient lacks other therapeutic options); treatment information about the investigational drug and its planned use; and a letter of authorization from the drug company allowing the physician to use its product on the patient. The form also contains information about the physician's qualifications and a certification that the physician will not begin treatment for 30 days after FDA receives the application (the time allowed for FDA to review IND

1 80 Fed. Reg. 7,318 (Feb. 10, 2015).

2 A panel of the U.S. Court of Appeals for the D.C. Circuit in 2006 issued a surprising 2-1 decision finding that such patients had a substantive due process right to access potentially life-saving drugs when there were no treatment options. That decision was vacated for rehearing en banc, and the full court rejected such a right, with only the two judges who supported the initial opinion voting in dissent. Abigail Alliance v. Von Eschenbach, 495 F.3d 695 (D.C. Cir. 2007). The Supreme Court denied certiorari in 2008. The issue persists with some critics of FDA now urging the passage of "Right to Try" legislation in several states to make it easier for patients to obtain investigational drugs.

3 21 C.F.R. § 312.310.

submissions) unless the submitting physician receives earlier notification from FDA that the treatment may proceed or procedures for emergency use are met. Informed consent and Institutional Review Board (IRB) requirements must also be obtained consistent with federal requirements.

The draft guidance also notes that FDA will continue to permit treating physicians to request expanded access over the telephone when emergency circumstances exist and patient treatment is needed before the form can be completed and submitted to FDA. In such circumstances, the treating physician may call the appropriate FDA review division, certify that all regulatory requirements are met, and agree to submit the form within 15 days of the agency's authorization of the expanded use access.

Although the simplified process will affect a significant number of patients each year[4] and make the process for obtaining access by physicians more efficient[5], it is important to note that the draft guidance does not change the basic FDA requirements for expanded access for individual patients. These requirements include: (1) that the patient have a serious disease or otherwise life-threatening condition for which there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease of condition; (2) that the potential benefit to the patient outweighs the potential risks; (3) providing the drug for treatment use will not interfere with the clinical investigation that could support marketing approval; and (4) the patient cannot obtain the investigational drug through another IND or to participate in the clinical trial for the drug.

The Federal Register notice and draft guidance can be accessed by clicking here[6] and here.[7]

Although interested persons can comment on a guidance at any time, FDA states that all electronic or written comments on this draft guidance should be submitted by April 13, 2015 to ensure that the agency considers the comment before it begins work on the final version of the guidance.

4 Based on data from 2011-2013, FDA estimates that it will receive approximately 593 requests annually for individual patient expanded access use from approximately 393 licensed physicians and will receive approximately 560 requests annually for individual patient expanded access emergency use from approximately 397 licensed physicians.

5 The FDA notes that using the old form (FDA Form 1571), each physician needed to spend approximately 8 hours to request each individual patient expanded access and approximately 16 hours when requesting expanded access for emergency use. The agency estimates that the new form (Form FDA 3926) will take approximately 45 minutes for the submitting physician to complete.

6 http://www.gpo.gov/fdsys/pkg/FR-2015-02-10/pdf/2015-02561.pdf.

7 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf.

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