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Feature Article

Expanded Access to Investigational Drugs New FDA Regulations Provide Effective Framework, but Questions Remain

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You've got a drug in the pipeline that's showing great promise. Results from your clinical trials are making news. What happens when you start getting calls from physicians and desperately ill patients requesting access to the drug prior to final approval? Who takes the call? What is your response?

For patients who are terminally or seriously ill, have exhausted all available therapies, and cannot enter a clinical trial, access to an investigational drug/biologic outside the trial setting via an expanded-access program can represent a new treatment option.

Since the 1970s, FDA-sanctioned expanded-access programs have enabled patients, under specific circumstances, to access drugs or biologics that are still in development. These rules were recently clarified by FDA and new types of access for treatment use added to ensure "broad and equitable access to investigational drugs for treatment."

The regulations now include all circumstances under which access to investigational drugs is permitted, including: individual patients in nonemergency and emergency settings; small groups of patients; and larger groups of patients under what is called a treatment IND.

While the new FDA rules clarify the types of access that are available, there remains flexibility as to exactly how and when these programs can be applied. This flexibility leads to what can be quite divergent and passionate opinions regarding access.

A New Framework

Patient access to investigational drugs was the topic of a recent forum held in Washington, D.C., where representatives from FDA, industry, advocacy groups, the medical profession, and the bioethics community gathered to share their perspectives. It was clear from the forum that each situation in which expanded access may be leveraged has its own unique dynamic and requires thoughtful consideration of patient needs, the company's situation, and regulatory guidelines. And while the new FDA regulations provide an effective framework for access, many questions remain:

- When should access be allowed—after Phase I trials, when safety has been established, or later in the trial process when data on efficacy is available?
- Who should get access? Must a patient be terminally ill? How do we define “terminally ill”?
- In the case of a cancer drug, must the patient seeking access have the type of cancer the drug is being tested against in trials? What is considered fair when choosing which patients can get access and which cannot?
- How do we appropriately balance the needs of desperately ill patients with safety concerns?
- How do we ensure expanded access does not put clinical trial enrollment at risk?

Ultimately, the choice to offer expanded access, or not, is left up to the drug developer. FDA regulations do not force companies to offer access to their investigational drugs. When considering this option, however, companies must undertake a thorough evaluation of important questions such as when to offer access and for which patients.

Determined Patients

Companies should also be mindful that the focus on expanded access is likely to intensify and result in an increased number of requests for investigational drugs. In addition to the updated FDA regulations, the trend toward greater transparency of drug development pipelines and the accessibility of powerful social media tools have led to a more informed, empowered, and vocal population of patients.

Patients can easily access information about investigational drugs via the internet and are leveraging social media tools such as YouTube, Twitter, and blogs in an effort to influence companies from whom they are seeking access and to call attention to their need. When a request for access is turned down, these online tools can easily be used to rapidly and widely publicize the denial. Aggressive use of social media to convey their efforts to obtain access have led to some patient stories making the national news.

There are, of course, situations in which a company believes that offering expanded access is not the proper course of action—the drug may be in the very early stages of development or the patient may have a condition for which the drug is not indicated.

Even if this is the case, the company may very well be on the receiving end of negative publicity as the denial of access often overshadows the reasons for the decision.

When offered by a trial sponsor, expanded-access programs allow physicians to leverage investigational drugs as treatment options for their desperately ill patients in a regulated manner that is completely visible to the drug developer.

A recent article from the *New York Times* ("Bending the Rules of Clinical Trials," October 29, 2009) described the dilemma faced by a physician as she sought a new treatment option for one of her cancer patients who had, at most, three months to live. Existing treatments offered no hope for this patient, and her dire condition would likely disqualify entry into a clinical trial. The doctor revealed that she was ready to consider violating the entry rules of a clinical trial to secure access to a new therapeutic option.

A study by Lidz, et al., ("Competing Commitments in Clinical Trials," *IRB: Ethics & Human Research*, Sept./Oct., 2009) found that a high percentage of clinicians involved in clinical trials believe that ignoring certain trial entry criteria is acceptable if the patient would benefit. While such a commitment to patients is commendable, the study noted that such efforts could compromise trial results, thus delaying the trial process or altering its outcome.

There is no doubt that the clinical trial process is intended to be and should be the primary way by which patients gain access to experimental drugs. In situations where the patient does not meet the trial criteria, however, an expanded-access program can provide well-regulated, well-controlled access to a new therapeutic option. The needs of desperately ill patients can thus be met while the integrity of the clinical trial process is protected.

The debate over expanded access will certainly continue and will have broad implications for all those involved. As patients become more determined in their efforts to seek access, open dialogue and direct confrontation of the issues surrounding this topic must take place among a broad range of stakeholders including patients, physicians, drug developers, FDA, advocacy groups, and policymakers. Our goal must remain clear: Defining and facilitating responsible, controlled access to investigational drugs in a manner that effectively balances the needs of all participants while best serving the needs of desperately ill patients.