

Boundaries of Expanded Access

Patients are demanding drugs—and showing up everywhere from YouTube to the Supreme Court. But to offer access to investigational drugs, companies first need to know the rules

Often, patients with critical or life-threatening illnesses don't qualify for clinical trials. Some are just too sick. Or perhaps their previous medical treatment disqualifies them for the study. Whatever the reason, for many of these patients the wait for drug approval is too long.

Recognizing this situation, governments around the world have established special regulations that allow patients with unmet medical needs—who have exhausted all available treatment options—to obtain drugs prior to their market launch.

Certainly, there is a humanitarian motivation for offering these expanded access programs (EAPs). They were started in the United States more than 30 years ago as a way to give cancer patients access to drugs that were not yet on the market. In 1987, FDA expanded and codified these guidelines, allowing greater access to drugs in development, like HIV/AIDS treatments. Today, patients are pushing the envelope and growing increasingly empowered to demand investigational drugs. For instance, Connie Loughman is a housewife who recently garnered national

attention through a YouTube spot she created, advocating access to a pancreatic cancer treatment for herself and fellow patient Patrick Swayze.

The humanitarian motivation for providing preapproval access is to legally and ethically respond to the needs of desperately ill patients. At the same time, companies need to be aware that these programs create increased visibility for drugs still in development.

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Pharmaceutical companies wishing to expand access to investigational drugs need to be aware of the regulatory guidelines that govern these programs and their promotion—or face stiff penalties and fines. This article provides an overview and offers vital information on the regulatory “do’s and don’ts” of expanded access programs.

Program Options

Expanded access programs operate under stringent regulations that include guidance on who can request a drug, the process by which the drug is accessed, and the type of data that must be collected from participating

patients. In the United States, these programs are defined and enforced by FDA. For patients outside the US, the programs are commonly referred to as named patient programs, and the rules are established and governed by local health and regulatory authorities.

Expanded Access Programs There are several types of FDA-sanctioned EAPs, including treatment protocols, treatment INDs, and single-patient INDs—all of which provide patients who would not otherwise qualify for clinical trials access to investigational drugs. FDA allows all US-based expanded access programs to collect safety and efficacy information.

To create a treatment protocol, a drug company must submit a formal addendum to FDA for an active clinical trial. In that addendum, the company defines the criteria for patient access to the investigational treatment. Then physicians contact the

sponsoring company to request that their patient be included in the treatment protocol.

By contrast, in both treatment INDs and single-patient INDs, physicians drive the request to FDA to allow individual patients access to investigational drugs on an emergency or compassionate basis. They do this by submitting to FDA an application that includes scientific evidence supporting the use of the drug in the particular indication, as well as assurances that all informed consent requirements have been met, that the relevant institutional review board (IRB) has approved the request, and



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that the company agrees to release the drug. FDA may deny the request based on concerns for the safety of the patient.

The pharmaceutical company must agree to the request; FDA does not have the power to compel a company to release a drug for an unapproved use.

Named Patient Programs Named patient programs (NPPs) are similar to US-based EAPs, but with an international component—named patient programs enable physicians and patients to access medicines approved in other countries before marketing approval has been granted in their home country. Many companies typically establish named patient programs to allow patients in clinical trials to continue to access a drug after the trial ends, but prior to marketing authorization.

To gain access to this program, foreign physicians or pharmacists contact the company, or their NPP provider, on behalf of individual or “named” patients. If the patient meets the treatment criteria and all export and import requirements have been met, the drug is shipped to the patient’s pharmacist and dispensed to the patient.

Know the Regulations

Expanded access programs provide significant benefit to critically ill patients. These programs can also benefit manufacturers by creating early visibility for a new product, and initiating physician and pharmacist engagement

An Evolving Landscape

The growing empowerment of patients has driven the demand for expanded access programs, and in turn created a dynamic where companies and regulators are seeking to clarify and evolve the rules of preapproval drug access. In late 2006, FDA issued proposed changes for public comment (although it is not known when the agency will issue a final rule). In 2007, the European Medicines Agency (EMA) issued guidelines on the use of unauthorized drugs by groups of patients via compassionate use programs; however, many groups feel it doesn’t go far enough to offer access to the patients who need it most.

This has created a drumbeat of news, fueling the visibility of the issue and raising questions over how to best address this problem. At the heart of the issue is providing access to early-stage drugs to critically ill patients. Indeed, most EAPs offer access to Phase II or Phase III therapies, but Phase I drugs are not typically made available via EAPs, even if the compound has been found to be safe.

The root of the modern day access movement stems from the Abigail Alliance for Better Access to Developmental Drugs. This Alliance is led by Frank Burroughs, whose daughter Abigail had been diagnosed with cancer of the head and neck. She had exhausted all available therapies, and upon recommendation of her physician, sought access to experimental cancer therapies. Unfortunately, she did not meet the criteria for clinical trials for ImClone’s Erbitux. Abigail eventually died waiting for new treatments. The drugs Abigail sought, based on her oncologist’s recommendation, were later approved.

In 2003, the Alliance sued FDA to gain access to unapproved drugs that have completed Phase I studies. Since then, the case has been dismissed, overturned by the US Courts of Appeals, and tried before the Supreme Court. In early 2008, the US Supreme Court ruled that terminally ill patients have no constitutional right to be treated with experimental drugs. This issue is shifting focus to the US Congress to possibly take up legislation to allow terminally ill patients access to promising test drugs.

with a drug before it launches.

The possibility of a head start in gaining market acceptance for a therapy prior to launch can be particularly attractive for companies. However, whether governed by FDA or another regulatory body, the pharmaceutical industry must remain within the boundaries of the regulations governing pre-launch activity, and cannot actively promote these compassionate use programs.

What does that mean? As an overarching principle, companies can only respond to physicians’ unsolicited requests for more information—which are often asked at medical conferences and in response to news of a company’s late-stage trial. A few companies have also decided to post press releases announcing availabil-

ity of their products via these programs—although others have shied away from that activity.

Solicitation of interest from target physicians, advocacy groups, or patients, however, is not allowed. Companies can’t run advertisements, for example, or have their sales force promote expanded access programs. Crossing this promotional line could result in stiff penalties and negative publicity.

In the end, the growing power of patients means the demand for expanded access programs will only increase. To make the most of the humanitarian and market development benefits, companies must be familiar with expanded access options, the nuances of each, and where those boundaries begin and end. 