

# **Expanded Access Programs: Points to Consider<sup>1</sup>**

## **BIO Board Standing Committee on Bioethics October 2014**

Patient requests for access to drugs and biologics prior to their approval have long created a dilemma for biotechnology companies. Typically, these requests come from seriously ill patients or their families or caregivers who believe an experimental product could save or prolong their lives. Biotech companies may be challenged by such requests because, in the first instance, they want to respond positively, but at the same time they must consider the impact of such a response on their ability to complete their development of the product, move it successfully through the regulatory process to receive marketing approval, and thus make it available to the many patients whose unmet medical need the product promises to address.

This issue has become increasingly visible and difficult in recent times, as views about the inherent right of patients in certain situations to unapproved products have been expressed by patients and their advocates, state legislators, and some members of Congress. In addition, the increasing use of social media has brought individual cases more prominently into the public eye and rallied hundreds or thousands of people to the cause of each patient. Clearly, the very public pressure on companies — and on the FDA — to fill the requests can become almost unendurable.

The BIO Bioethics Committee has explored the issues surrounding early access to biotech products. This document represents the Committee's deliberations and provides "Points to Consider" for biotechnology companies confronting these issues. It is the Committee's hope that these Points will help companies analyze many of the challenges, including ethical challenges, raised by expanded access programs.

### **Background/FDA Rules on Expanded Access**

FDA has a long history of permitting access to investigational drugs for patients with serious or immediately life-threatening diseases for which there is no adequate available therapy under special types of investigational new drug exemptions (INDs). These are different from "typical" INDs because the treatment uses generally are not designed to answer safety or effectiveness questions about the drug, but rather are intended to treat the patient.

On August 12, 2009, FDA published two rules to clarify the methods by which seriously ill patients may access investigational drugs and biologics when such patients are not eligible to participate in the relevant clinical trials and don't have other satisfactory treatment options.

The rule on "Expanded Access to Investigational Drugs for Treatment Use" clarifies procedures and standards first promulgated in 1987. The earlier rule stated that access to investigational drugs for a broad population could be authorized under a treatment protocol or treatment investigational new drug application (IND) when certain criteria were met. That rule implicitly acknowledged the existence of other kinds of treatment use, *e.g.*, in

---

<sup>1</sup> These Points to Consider were developed by the Biotechnology Industry Organization's (BIO's) Board Standing Committee on Bioethics, and approved on September 3, 2014. This document does not represent BIO policy. It is intended for informational purposes and to further the debate on Early Access Programs.

individual patients, by adding a provision for obtaining an investigational drug for treatment use in an emergency situation.

The 2009 rule provided more information about how experimental drugs can be made available to individual patients and intermediate-size patient populations. It also described the criteria that must be met to authorize the expanded access use. For example:

- the patient or patients to be treated must have a serious or immediately life-threatening disease or condition, with no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- the potential patient benefit justifies the potential risks of the treatment use, and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
- providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the drug or biologic or otherwise compromise its potential development.

The rule is available at <http://edocket.access.gpo.gov/2009/pdf/E9-19005.pdf>.

The other rule, "Charging for Investigational Drugs Under an Investigational New Drug Application," clarifies the specific circumstances and the types of costs for which a manufacturer can charge patients for an investigational drug when used as part of a clinical trial or when used outside the scope of a clinical trial. It is available at <http://edocket.access.gpo.gov/2009/pdf/E9-19004.pdf>.

## Points to Consider

**a. A company's principal goal and commitment is to develop and market approved safe and effective products efficiently, so patients for whom the products are appropriate will have access to them. While effectively carrying out this responsibility, it also may be feasible and appropriate for the company to respond to the needs of individual patients who may not be participants in the clinical studies.**

Some people argue that terminally ill patients have the right to an unapproved product outside the context of a clinical trial if they (and their physicians) believe the product will treat their condition and if they understand the potential risks of taking it. This perspective is based on the principle that patients have the right of autonomy regarding their treatment. According to this view, as long as the patient understands the risks associated with that product — and the product already has demonstrated some evidence of safety — he or she should be allowed access.

Autonomy in health care decisions is an important bioethics principle that long has been part of American law. It is manifested in the requirement for voluntary informed consent prior to health care treatment and participation in clinical trials. However, in these cases, the principle is applied to ensure that patients are not forced to participate in experiments or to receive treatments against their will, not to guarantee an affirmative right to an experimental treatment. In fact, courts have recognized that there is no affirmative right to an experimental treatment.<sup>2</sup>

Because of their commitment to patients, companies also consider the implications of decisions about making experimental drugs available through expanded access. For example, balanced against an individual's right to decisional autonomy is the company's commitment to efficient completion of the development of products that meet the high standards of safety and efficacy necessary to secure regulatory approval and be available to larger patient populations. There may be a tension between a decision to provide expanded access and the commitment to efficient completion of the drug's development. For example, expanded access may reduce incentives to enroll in clinical trials — thus potentially jeopardizing the ability to complete drug development. In the expanded access setting, which generally is neither as controlled as the clinical trial nor as closely monitored, it also may be difficult for both sponsors and regulators to know how best to interpret information regarding benefit and risk, such as adverse events, that may not have been seen in clinical trials. The potential incongruence between data from expanded access as compared with those obtained in higher confidence settings (controlled trials) may lead to confusion that also may slow development.

**b. Expanded access programs could diminish the integrity of the clinical trial process.**

It long has been accepted that the clinical trial process is the best way to establish the safety and efficacy of drugs and biologics. The regulatory process requires numerous protections for research participants, and strict safety and efficacy standards must be met prior to marketing a product. These rules provide confidence to the public that the drugs and biologics they use are effective and safe and that clinical trials participants are well-informed and protected. These participants often volunteer because they want to contribute

---

<sup>2</sup> *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007) (en banc), cert. denied, 128 S. Ct. 1069 (2008).

to scientific knowledge that could benefit larger populations. Inappropriate and/or excessive use of expanded access could diminish the integrity of this system. For example, it could reduce the incentive for patients to enroll in a trial, especially because of the possibility that in a controlled trial they will not receive the drug but instead a placebo or comparator product. Therefore, if expanded access is excessively or inappropriately available, the effect on clinical trials and, thus, the impact on development and approval of innovative products could be harmful to patients because of delays or even cancellations of important product development programs.

**c. Information from early studies, or data that are not fully analyzed, may not be sufficient to define the benefit-risk calculus for the medicine under study; moreover, such early data may even confuse, mislead, or provide false hope about the effectiveness and safety of a drug or biologic, leading to patient and physician decisions about expanded access that are not fully and effectively informed.**

Appropriate expanded access relies on patients being able to provide informed consent, based on a clear understanding of the potential risks and benefits of an investigational product. This inherently implies that there is sufficient information to make an informed choice even though the product is still in development. Before providing expanded access, companies must ensure that the data available are relevant for a patient's decision and that the patient fully understands the risks and potential benefits. Every attempt should be made to ensure that patients do not have false hope based on early data.

**d. If a company makes unapproved products available outside of clinical trials, it must ensure equity in distribution.**

If a company decides to make an unapproved product available, it must consider the process for determining which patients should have access to it. For example, certain patients may have an advantage over others because they know about expanded access programs, have hired outside counsel, are particularly knowledgeable about product development activities for a particular disease, are media-savvy, or make effective use of social media to rally support. None of these establishes that patient as "more deserving" of expanded access to a product than others.

Therefore, companies need to establish appropriate inclusion/exclusion criteria for their expanded access programs. To the extent possible, these criteria should ensure equity in availability through an expanded access program. These criteria may include the degree of severity of the disease or condition, the physician's assessment of the patient's possibility of benefit as compared with the risk, the particular indication for which the drug or biologic would be used as compared with the indication being studied in the company's clinical trials, the number of doses the company is able to provide over the length of time estimated for the program, the number of patients for whom expanded access may be available, or other criteria. These criteria should be made public and should be easily accessible by patients, physicians, and caregivers (for example, through the company's web site).

Criteria for expanded access should be developed so they may be tailored and applicable to any product the company is developing, to ensure that the company always will be equitable in its treatment of patients, regardless of the therapeutic class or disease area.