Arnall Golden Gregory LLP

Client Alert

Contact Attorney Regarding This Matter:

William H. Kitchens
404.873.8644 - direct
404.873.8645 - fax
william.kitchens@agg.com

FDA Issues New Regulations on Patient Access to Experimental Drugs

Patients with serious or immediately life threatening diseases, like cancer, who have exhausted all other commercially available treatments, often want to try a promising drug that is still under development. It is understandable that people with a disease with no good treatment options and their treating physicians are very interested in trying a new drug under development, especially if the early results of a clinical trial suggest that the drug shows promise.

As a general rule, these patients have only been able to access experimental drugs as part of an approved human clinical investigation. However, many patients do not qualify for these clinical trials, or they are unable to enroll for various reasons. Indeed, in recent years there has been litigation over the issue of whether patients have a constitutional right, as a matter of due process, to access potentially life saving post-Phase I investigational drugs. Moreover, some commentators have criticized FDA's role in serving as the exclusive gatekeeper over access to drugs in the market and even questioned the propriety of FDA's role in making decisions that limit the availability of new drugs to patients.

In response to these important public health issues, FDA last week issued new regulations to address the issue of patient access to experimental drugs and improve the process for these patients to obtain investigational drugs. Before examining these new rules, it should be noted that FDA has had regulations in place since 1987 (21 C.F.R. Part 312.34) that have allowed patients, in limited circumstances, to gain access to investigational drugs even though the safety and effectiveness of the drug has not been fully established. Moreover, the Food and Drug Administration Modernization Act of 1997 included specific provisions for expanded access to investigational drugs for treatment use if a number of conditions are met. Those conditions require that (1) the patient's physician determine there is no comparable or satisfactory alternative therapy and the risks of the experimental drug are comparable to the risks of the disease or condition; and that (2) the FDA decide there is sufficient evidence of safety and effectiveness to support the use and the use will not interfere with the completion of the clinical trials. The drug sponsor must also submit an appropriate protocol for this expanded access. These existing FDA regulations, although some help for patients with a serious disease, have been confusing and difficult to administer in practice. The new regulations are designed to make the expanded access provisions broader and clearer for the patient and the treating physician, while still preserving the integrity of clinical trials designed to find out whether a drug has a desired effect on some disease or condition.

Arnall Golden Gregory LLP
Attorneys at Law
171 17th Street NW
Suite 2100
Atlanta, GA 30363-1031
404.873.8500
www.agg.com

These changes appeared in the *Federal Register* on August 12, 2009 and incorporate:

- changes in the expanded access rule to explain the procedures and standards for patients who want access to investigational drugs
- changes to the charging rule to explain when a drug manufacturer can charge a patient for an investigational drug, in a clinical trial or expanded access program, and what costs a manufacturer can recover when charging.

FDA emphasized, however, that this need must also be balanced with the need to ensure that ultimately a more complete picture on the safety and effectiveness of the drug has been demonstrated before the drug is commercially available for use in the population at large. Of course, the procedures for human clinical investigation are designed to reach that endpoint.

Below is a summary of the two final regulations:

1. Expanded Access Regulation

To permit treatment of a patient with an investigational drug under an expanded access program, FDA generally must be satisfied that

- The patient's disease or condition has no satisfactory approved therapy. An example of this is a rare type of cancer that has no known or approved treatment. Or, it may be the case that the available treatments did not work for the patient.
- The potential benefit for the patient must justify the potential risks. An example of this is the potential for longer survival with a disease or condition.
- The expanded availability of the untested drug should not interfere with that product's development. For example, access to an investigational drug should not interfere with enrollment in the clinical trials needed to demonstrate the drug's safety and effectiveness.

Among other things, the expanded access regulation will

- explain the several different kinds of access that are possible, including access for individual patients, for small numbers of patients, and for large numbers of patients in what are called "treatment protocols"
- ensure safeguards to protect patients
- preserve the ability to develop meaningful data on the drugs available under expanded access.

2. Charging Regulation

The charging regulation permits drug manufacturers to charge patients for an investigational drug in clinical trials and when it is being made available for expanded access. Charging in clinical trials will be allowed under very limited circumstances, but will be permitted for most expanded access uses.

In some cases, a company is unable to develop a drug unless it is able to charge for the drug in clinical trials. Allowing charging for expanded access helps provide access to investigational drugs that manufacturers

may not be able to offer without being able to charge.

FDA revised this regulation to provide more explicit criteria for when charging should be permitted in clinical trials and for drugs available for expanded access.

Among other considerations, the revisions are meant to:

- make the process of obtaining authorization to charge more transparent
- specify what costs can be recovered by drug manufacturers.

The regulation provides that only the direct costs of the drug can be recovered when charging for a drug in a clinical trial. Because the anticipated cost of drug development must ordinarily be borne by the drug sponsor, in order to charge for an investigational drug in a clinical trial, the drug sponsor must:

- provide evidence that the clinical benefit, if demonstrated in the clinical investigation, will provide a significant advantage over available drugs in the diagnosis, treatment, mitigation, or prevention of a disease or condition
- demonstrate that the data from the clinical trial will be essential to establishing that the drug is safe and effective for the purpose of obtaining initial approval, or will support a significant new change in the labeling of an approved drug, and
- establish that the clinical trial could not be conducted without charging because the cost of the drug is extraordinary to the sponsor (e.g. due to manufacturing complexity or the size or duration of the study).

In the case of an expanded access program, the regulation states that only the direct costs of the drug plus the costs of administering the expanded access program can be covered.

At the same time, FDA launched a new web site, click here where patients can learn about options for investigational drugs. This site explains the various options that patients may use to explore the possible use of investigational drugs with their health care professional.

Topics addressed on this site include:

- factors to consider in evaluating whether to seek access to an investigational drug
- general information on clinical trials and investigational drugs
- information on how to gain access to investigational drugs outside of a clinical trial (expanded access).

Both rules take effect on October 12, 2009. For the full text of the rules, go to:
http://edocket.access.gpo.gov/2009/pdf/E9-19005.pdf and
http://edocket.access.gpo.gov/2009/pdf/E9-19004.pdf

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