



American Society of Clinical Oncology

## **FDA Final Rules on Patient Access to Investigational Drugs and on Charging for Investigational Drugs**

August 31, 2009

On August 13, 2009, the U.S. Food and Drug Administration (FDA) published two final rules that involve patient access to investigational drugs. One new rule, which is entitled “Expanded Access to Investigational Drugs for Treatment Use,” addresses the FDA’s process for patients to access investigational drugs for treatment use outside of the context of a clinical trial. The second new rule, entitled “Charging for Investigational Drugs under an Investigational New Drug Application,” revises the circumstances under which companies can charge for investigational drugs under both expanded access programs and clinical trials. The rules are available on the [FDA website](#). Both of these rules will become effective on October 12, 2009.

### **Background**

The FDA has permitted expanded access since the 1970s and corresponding regulations have been in place since 1987. However, there has been longstanding uncertainty surrounding the procedures and standards applicable to the FDA’s regulations that govern patient access to unapproved drugs for treatment use outside of the context of clinical trials. As a result, the American Society of Clinical Oncology (ASCO) and the National Coalition for Cancer Survivorship filed a citizens petition in 2006 urging the FDA to issue guidance that would clarify the circumstances under which expanded access programs may be initiated for patients who lack other acceptable treatment options.

The new rules on expanded access and charging for investigational drugs provide additional clarification regarding the procedures and standards applicable in these areas, although the clarification provided within the two rules is only an initial step toward creating a more navigable process. In addition to the final rules, the FDA recently provided some preliminary materials to assist patients and health care providers in understanding the requirements. These materials are available at the following links:

- [Physician Request for a Single Patient IND for Compassionate or Emergency Use](#)
- [For Patients and Patient Advocates: Access to Investigational Drugs Outside of a Clinical Trial](#)
- [For Patients and Patient Advocates: Questions and Answers about treatment of serious and life threatening illnesses, and use of investigational drugs](#)

Education will be key, and the FDA has expressed an intent to develop additional educational materials and clarifying information. ASCO will monitor the progress of this work and update members when the Agency resources are released.



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ASCO is examining the new process carefully and will create educational materials to assist physicians in understanding the process and the FDA's requirements – particularly for health care providers who are unfamiliar with the administrative and regulatory issues associated with investigational agents. ASCO also is posting information for patients on Cancer.net. As ASCO identifies any gaps and ambiguities in the FDA's description of the process, the Society will work with the FDA to address these issues and to communicate the information to the oncology community.

### **Final Rule on Expanded Access to Investigational Drugs**

The final rule recently published on expanded access (see link above) is similar to the proposed rule published by the FDA on December 14, 2006 (available at <http://www.fda.gov/OHRMS/DOCKETS/98fr/06-9684.htm>). Rather than providing a dramatic change in policy, the final rule generally reflects an effort by the FDA to update the regulations to reflect its current practices.

In both the proposed and final rules on expanded access, the FDA continues the policies described in the pre-existing regulations that permit expanded access for large groups of patients under treatment INDs or protocols, as well as permitting access for individual patients in emergency situations. The FDA also clarifies that access to investigational drugs for treatment uses can be considered in a range of circumstances, including 1) single patients (including both emergency and non-emergency situations); 2) small groups (considered to be smaller than typically addressed under a treatment IND); and 3) larger groups under a treatment IND.

The FDA also describes the criteria that will be used in making determinations under the expanded access program. In general, the level of evidence required by the FDA increases as the number of patients increase.

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

- The patient's disease or condition has no satisfactory approved therapy (for example, a rare type of cancer with no known approved treatment, or alternatively, the patient has not responded to treatment with available treatments);
- 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; and
- The expanded availability of the investigational drug will 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.



In the final rule, the FDA made a handful of changes to the 2006 proposed rule. For example, consistent with ASCO's recommendations, the FDA extended the timeframe for physicians to submit written emergency expanded access submissions after obtaining verbal authorization for use from the FDA. The proposed rule required submission within 5 days, and the final rule provides a 15 day period. (ASCO understands the FDA wants to see these materials in a timely manner, but 15 days still seems like a very short timeframe. ASCO will continue to follow this issue, among others).

Additional changes in the final rule, as compared to the 2006 proposed rule, include the following:

- The final rule clarifies that expanded access applies to patients with serious diseases or conditions when there are no comparable or satisfactory alternative therapies to diagnose, monitor or treat the patient's disease or condition. This is different from the proposed rule, which appeared to limit expanded access to patients considered to be seriously ill.
- The final rule includes a new definition for "serious disease or condition." The term is defined as "a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one."
- The final rule clarifies that the expanded access rules apply to the treatment use of both investigational new drugs and approved drugs where availability is limited by a risk evaluation and mitigation strategy (REMS). The proposed rule only indicated that the expanded access requirements would apply to investigational new drugs without reference to approved drugs with limited availability due to a REMS.
- The FDA strengthened language in the final rule by clarifying that as part of a sponsor's responsibility for providing a licensed physician with the information needed to minimize the risk and maximize the potential benefit of the investigational drug, the physician must be provided with the investigator's brochure if one exists for the drug.

Additional information is provided on the links to the FDA website provided above.



## Final Rule on Charging for Investigational Drugs

The final rule on charging for investigational drugs (see link above) is also very similar to the proposed rule published by the FDA in 2006 (available at <http://www.fda.gov/OHRMS/DOCKETS/98fr/06-9685.htm> ).

The proposed and final rules set forth the FDA's policies on charging for investigational drugs in the context of both expanded access initiatives and clinical trials. The FDA describes the applicable requirements for each type of use in which charging is permissible. The FDA also provides clarification of the types of costs that may be recovered when charging for investigational drugs.

In the case of an expanded access program, the rule clarifies that manufacturers may charge for all three types of expanded access (individual patients, small groups of patients and larger groups of patients under a treatment IND or protocol). The rule suggests that the FDA will be more lenient in allowing charging in the context of individual patients and smaller groups (due to the lower risk of interfering with the development of the drug for commercial marketing). The rule provides that only the direct costs of the drug plus the cost of administering the expanded access program can be recovered. For example, costs related to the commercialization of the product may not be included in the charges.

In the context of clinical trials, the FDA believes that under most circumstances the cost of the drug should be borne by the sponsor as part of the normal costs of development. The FDA provides the following three criteria that must be met for sponsors to charge for investigational drugs in a clinical trial:

- Charging is allowed only to facilitate the development of a promising new drug or indication that might not otherwise be developed or to obtain safety information that might not otherwise be obtained. The FDA makes clear that a compelling rationale will be required to satisfy this criterion.
- Charging is permitted only for a trial that is necessary for the development of the drug (either to secure FDA approval for the initial marketing of the drug or to support a significant change in the labeling).
- Charging must be necessary to the conduct of the clinical trial. For example, the cost of the drug may be so extraordinary that the trial could not continue without charging for the drug.

In general, prior written approval from the FDA is required before charging for a drug under an expanded use initiative or a clinical trial. In one significant change in the final rule (as compared to the proposed rule), the FDA removed the proposed requirement that sponsors must obtain FDA approval to charge for a drug that must be obtained from another entity – not affiliated with the sponsor – for use in a clinical trial. This change



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pertains to situations in which: 1) a clinical trial is evaluating a new use for an approved drug; or 2) the clinical trial requires the use of an approved drug for an active control or for combination therapy.

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