

March 19, 2007

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Expanded Access to Investigational Drugs for Treatment Use (Docket No. 2006N-0062) and Charging for Investigational Drugs (Docket No. 2006N-0061)

To whom it may concern:

The Food and Drug Administration's (FDA's) Proposed Rules related to access to investigational drugs strike a generally reasonable balance between patient access to such medications, on the one hand, and patient safety and the need to collect data for the drug approval process, on the other. We offer the following comments in an effort to fine-tune the proposal further.

A. Expanded Access to Investigational Drugs for Treatment Use (Docket No. 2006N-0062)

Lack of dissemination plan

A major rationale for this rule is that patients and physicians are not currently adequately aware of the regulations. Such lack of awareness may be related to the sophistication of the patient or differences in utilization of the expanded access options by providers treating the patient's disease. However, the agency appears to believe that simply the publication of the Proposed Rule (and the Final Rule to come) will somehow expand access and utilization in a meaningful way. It is clear to us that Federal Register notices are not the best way of disseminating information to the lay public or their physicians, but the FDA makes no mention of any additional efforts to disseminate the new policies. In that context, the agency's estimates of expanded utilization provided in the Economic Impact Analysis appear overly optimistic.

No definition of "serious" conditions

The agency intends its expanded access initiatives to be restricted to those with "serious or life-threatening illnesses." A reasonable definition of a life-threatening illness is

provided, but the agency has elected not to provide such a definition for “serious” illnesses. Instead, the issue is discussed in the preamble to the Proposed Rule, where serious illnesses are characterized more by what they are not than by what they are. The category of serious “is primarily intended to exclude expanded access to investigational drugs for conditions that are not clearly serious (e.g., symptomatic relief of minor pain or allergic symptoms and other self-limiting conditions not associated with major morbidity).” This leaves very little beyond the bounds of expanded access. The regulation should include a concrete definition of “serious”, and not one that is as inclusive as the preamble appears to contemplate.

Low threshold for “immediately life-threatening” condition category

The agency sensibly states that the degree of evidence necessary to provide a drug under the expanded access provisions should decrease as the seriousness of the disease increases. But, for diseases considered “immediately life-threatening” it has set the floor too low. In some cases, such patients could receive the drug even if there is “no relevant clinical experience, and the case for the potential benefit may be based on preclinical data or on the mechanism of action.” Unless the patient is applying for access in the period between completion of preclinical studies and the initiation of the Phase I trial or the patient is ineligible for the upcoming Phase I trial, it seems inappropriate and possibly dangerous to permit this relatively uncontrolled access to an investigational drug to represent the first human exposure to a drug.

Role of intermediate category

We agree with the concept of creating an intermediate category to bridge the gap between individual access and potentially large treatment IND protocols. The proposal does discuss the potential for patients who would otherwise have received individual access to be “upgraded” to the intermediate category if there were enough applicants for individual access. This would indirectly raise the threshold for access, because the intermediate category has more stringent requirements. The agency even discusses the numerical impact of such reclassification. However, the converse is not considered at all. If patients currently falling into the treatment IND category were reclassified to the intermediate category, the threshold for access would be lowered. Requests for treatment INDs are certainly less common than those for individual access, but treatment INDs can involve thousands of patients. This impact should be considered as quantitatively as possible.

Open-label study crackdown

We are gratified to see that the agency anticipates using this proposal as an opportunity to crack down upon the abuse of the “open-label” trial. As the preamble notes, studies that are actually more reminiscent of treatment INDs have been characterized by sponsors as open-label safety studies, thus affording the study more credibility than it deserves. We hope that this new policy is vigorously enforced.

Public access to data

While the proposed rule has provisions requiring submission of safety and efficacy data to the sponsor (and thus to the FDA), there is no provision for these data to be made public. The public has a right to know the outcomes of these expanded access initiatives, including any evident impact upon outcomes and the incidence of adverse effects.

B. Charging for Investigational Drugs (Docket No. 2006N-0061)

Requirement for prior approval

We support the proposed rule's insistence that affirmative FDA approval be obtained before charging for the experimental drug can occur. In the past, companies could charge if they were not rejected by the FDA within 30 days. The current proposal would rectify that.

Inclusion only of direct costs

As the proposed rule says, the provision of unapproved drugs should ordinarily be considered part of the cost of doing business and so charging for drugs should be unusual. The proposed rule would restrict charges to the direct costs of providing the drug in the context of experimental access. Companies should not be permitted to add in indirect costs or to use the permission to charge as a method for defraying overall development costs.

Effect on poorer patients

We are concerned that the extension of the ability to charge to both the intermediate and individual access options might make it more difficult for poorer patients to receive treatment. The FDA states that companies typically have mechanisms in place for such patients, but the FDA should closely follow whether this continues to be the case.

Thank you for the opportunity to comment on this proposal. We continue to believe that any expanded access to drugs should not occur at the expense of patient safety or the ability to collect data that will permit evidence-based decisions regarding drug approval or labeling.

Yours sincerely,

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