

APPLIED CLINICAL TRIALS

*Advocates for Patient Rights Want 'Initial Approval' for Unapproved Drugs
Member of the Abigail Alliance for Better Access to Developmental Drugs answer
questions about Tier I Approval*

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Applied Clinical Trials

Frank Burroughs is president of the Abigail Alliance for Better Access to Developmental Drugs, and Steven Walker is its FDA advisor. They answer questions about their cause, Tier I approval.

Your group has proposed adding a Tier I Initial Approval level to the FDA. What would that accomplish?

Properly implemented, Tier I would allow those with life-threatening illnesses and no remaining approved options an opportunity for access to promising IND drugs. Patients eligible to seek Tier I drugs would be those who have exhausted approved treatments and cannot gain access through enrollment in a clinical trial or expanded access program. The only exception would be cases in which a patient's physician determines that for legitimate reasons, the patient is not a reasonable candidate for a potential trial.

Do you think Tier I was a new idea to the FDA?

We submitted a plan called Early Conditional Approval in January 2003. Based on feedback from the FDA and others, it turned into Tier I Initial Approval, submitted in March 2003. In a meeting requested by the agency shortly after their receipt of Tier I, FDA officials admitted that they had looked at similar ideas in the mid-1990s but did not proceed, apparently due to opposition from insurance firms.

The idea of allowing access is well established. The challenge remains to create a program that succeeds in serving the legitimate needs of terminal patients.

There already exists compassionate use, expanded-access and clinical trial routes for patients to get experimental drugs. What place does Tier I have in all of this?

Tier I will complement the existing access mechanisms. Unfortunately, the existing programs have failed to serve most patients. Simply put, the number of places in these programs is consistently far too small to meet the need. Tier I would create a workable access mechanism for sponsors, the FDA, physicians, and most importantly for patients, while at the same time maintaining the clinical research needed for continued progress.

Some other patient advocate groups oppose Tier 1. Would you care to comment?

Understandably, patient advocacy groups working with patients suffering from the least treatable and most deadly forms of disease tend to support us because it is their constituents being directly affected. Those voicing opposition seem resigned to the notion

that we can either help patients or protect clinical trials, but not both. Tier I is structured to do just that.

Some critics have said Tier I would essentially set up a loophole to let drug companies sell unapproved drugs. Do you agree or disagree?

This is a misleading argument. Any program for early access, by definition, makes the drug available before the completion of clinical trials. But our proposal protects the clinical trial process while better meeting the needs of the terminally ill.

Tier I approval requires continued pursuit of accelerated or regular approval by the FDA. The Tier I restrictions limit availability of drugs to patients already excluded from clinical trials, meaning that a Tier I approval would have little if any effect on clinical trial enrollment, but would make a very positive difference for those that find themselves unable to participate in a trial.

Bypassing clinical trials would not be allowed, nor would it make any sense for the drug sponsor. Tier I is a true restricted approval that would significantly limit the size of the potential market for the drug. These restrictions leave in place strong economic incentives for sponsors to continue pursuit of traditional approval.

The most important point, though, is that the present system itself “bypasses” many thousands of dying patients. The risk/benefit of taking an investigational or Tier I drug should be viewed in the context of the risk posed by their disease.

A patient facing certain death is different from that of a patient with a nonterminal condition or remaining approved treatment options. When the risk of taking a less-well proven drug that might help an individual is weighed against the reality of certain death, allowing access to that drug is not only reasonable, it is their only chance.

How will insurance companies react to Tier I?

Since investigational drugs represent the standard of care for many terminally ill patients, drugs obtained under Tier I approval should be covered. To what extent insurers will actually do so is hard to predict.

One objection we sometimes hear is that of economic inequity—i.e., some patients won’t have access to Tier I drugs for financial reasons, so the program should not exist for anyone. But this same objection could be leveled at just about any component of our health care system.

How you feel about the Tier I objections?

The comments advanced as reasons for opposing Tier I are inconsistent with experience from the few large expanded access programs that have been conducted.

Congress and the FDA decided several years ago to allow access to investigational drugs because it was ethically indefensible to do otherwise. One existing program, called a Treatment IND, even allows the sponsors to charge a “cost recovery” amount to patients

for the drug. Unfortunately, because of regulatory disincentives and a lack of reasonable economic incentives, the programs have failed to serve the needs of far too many patients.

Tier I is very similar in concept to the Treatment IND program, except that instead of being an FDA-approved clinical trial that allows cost recovery, Tier I is a restricted approval that allows companies to charge for the drug. The changes incorporated into Tier I creates an incentive for the company to build manufacturing capacity earlier in its development program, which in turn allows them to supply the drug to those with no other options.

Your group and the Washington Legal Foundation filed suit against the FDA. Has there been any word from the FDA about the lawsuit filed?

The lawsuit was filed after much internal deliberation and discussion because the agency was stonewalling us on the issue. We were asking for a dialogue with the FDA to find a workable solution, and they were refusing to engage in meaningful dialogue. At present, after responding to various motions from FDA and HHS asking the judge to dismiss our lawsuit, we are awaiting an initial ruling.

It is important to understand that the lawsuit is not asking for adoption of Tier I. Put simply, the suit asks the court to confirm that dying patients have a constitutional right to privacy and liberty that is violated by FDA's policies denying access to lifesaving medicines. If the court accepts the constitutional arguments in our lawsuit, Tier I is the kind of program that would likely be considered constitutional.

Are those who have gone through the clinical trial process more qualified to propose an FDA change?

Experiencing the FDA's policy failures firsthand, as many of us have done, is not something we would wish on anyone. But yes, the experience has helped us to understand how well our system works, and more importantly, how it does not work for the patients that need help the most.

In practically every case, Tier 1 supporters pursued treatment in clinical trials, only to find that restrictive entry criteria excluded or delayed their entry to the trials. When they succeeded, their time on the drug in a trial was limited to the period in which they continued to meet the precise disease condition requirements for the trial.

Upon disease progression, even if the drug was still slowing or controlling some aspect of their disease, they were almost universally denied further access to the drug. The few that managed to enroll in more than one clinical trial found that they further narrowed their ability to qualify for other trials by virtue of their lengthening treatment history.

Eventually, locked out of access by any means to the new drugs that might help them, they died. Many came off their last clinical trial in good condition, some still able to live a normal active life, only to rapidly decline because their disease was left untreated.

Many of our members and supporters are the family members and friends of deceased patients. They are the people who fought along side their loved ones, trying to gain access to treatment, only to see it repeatedly denied by an unresponsive system built to serve every interest except that of the patients.

It is these people, the patients fighting a losing battle and those that help them fight, that know best what is wrong with the system, because they have seen its failures from the only viewpoint that really matters.