



Abigail Alliance for Better Access to Developmental Drugs

www.abigail-alliance.org

501 (C3) non-profit incorporated in Virginia
36 Aspen Hill Drive Fredericksburg, VA 22406
540-899-3766 frankburroughs@abigail-alliance.org

Board of Directors: Doug Baxter: David's Father, Cancer Advocate, Gene Krueger: Abigail's Step Father, Cancer Advocate, Anne Agnew: Booz Allen Hamilton, Prince Agarwal: Cyrano Solutions, Linda Springfield, Cancer Advocate John Rowe, Kianna's Father, Advocate

From: Abigail Alliance for Better Access to Development Drugs
36 Aspen Hill Drive (NEW)
Fredericksburg, VA 22406
540-899-3766 (NEW)

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

Date: March 13, 2007

Subject: FDA Release of Draft Regulations for Treatment Use and Charging for Investigational Drugs
Comments to: FDA [**Docket No. 2006N-0061 and 2006N-0062**](#)

On Monday, December 11, 2006, FDA issued for comment its draft regulations addressing Expanded Access to Investigational Drugs for Treatment Use and Charging for Investigational Drugs. The Abigail Alliance possesses considerable knowledge and expertise regarding the FDA's long-failing policies regarding access to investigational drugs and has conducted a careful review of the draft regulations. Our comments on the FDA's actions follow.

The draft regulations contain no substantive changes to existing FDA policies, and those existing policies have never worked for the large majority of patients with a legitimate need for access to investigational drugs. For many of them that need was, literally, to have a chance at continued life. Instead they died, never getting that chance.

The agency admits that the draft regulations merely write into rule their existing policies. Virtually all of the access and charging mechanisms the draft regulations lay out have been available for years from the FDA, but have fallen far short of meeting the legitimate needs of patients because they are unworkable in the large majority of circumstances for drug companies, doctors and patients.

Given these facts, it is very difficult to view the issuance of the draft regulations as a good faith effort by the agency to address an issue of immense importance to Americans with serious and life threatening diseases. By changing nothing, the agency's now inoperative policies will not become operative, a fact supported by the agency's own projections of almost no expected improvement in program performance in the preamble for the Treatment Use regulation. In reality, the FDA is trying to cement into regulation a set of failing policies that can do nothing but continue to fail.

If the FDA promulgates its draft regulations in their present form, the effect will be decidedly negative for patients with serious and life-threatening diseases, and very difficult to reverse. Changes will be possible only through additional rulemaking, legislation from Congress, or court action. To put this in perspective, FDA took 7 years to begin drafting the proposed regulations after passage of the authorizing legislation in 1997, then once started, took three more years to propose draft regulations which contain nothing new, and now will take even more time before being promulgated.

By issuing the draft regulations, the FDA is taking a very hard line that it intends to change nothing with respect to expanded access, and despite its public relations efforts to the contrary, is sending a clear signal that it is opposed to putting in place any form of expanded access mechanisms that will work for more than a tiny fraction of the patients who could benefit.

The agency has stated in very carefully worded language that it hopes that providing clarity to drug companies (sponsors) and doctors regarding how their programs work will somehow produce small improvements, but the premise is false. Sponsors and physicians who treat serious and life-threatening

diseases already know about the programs because patients make sure they know about them, and for various reasons those sponsors and doctors have found them to be unworkable. It is not a "clarity" problem.

The public should also know that patients have no direct ability under the agency's policies to request or receive an investigational drug. Access hinges on a drug company's willingness and ability to provide the drugs outside clinical trials before their drug is approved. For a variety of reasons, some of which have their roots in the agency's failure to modernize its drug development and approval policies, the FDA's access mechanisms, now written into their draft regulations, remain a largely unworkable minefield for all who try to use them.

The FDA made clear on March 1, 2007 in its oral arguments before the U.S. Court of Appeals for the District of Columbia Circuit in our lawsuit, *Abigail Alliance v. von Eschenbach*, No. 04-5350, that it believes its power to deny Americans access to potentially life-saving medical care is absolute and cannot be challenged by anyone in any court. In fact, agency lawyers went so as to suggest it would be inappropriate even for Congress to limit the power of the FDA to deny a dying patient access to a promising new therapy being given to hundreds or even thousands of other patients in a clinical trial. Under questioning from the bench, FDA admitted that it believes it could, with impunity and in blanket fashion, ban meat and vegetables, thus starving the entire population. The FDA made the statement as an argument that it need not show any compelling reason for banning meat and vegetables, and could not be judged to have violated anyone's rights in the process, even if the reasons supporting its actions were known to be likely to result in more harm than good.

The agency's non-action in issuing its draft regulations should be viewed in the context of the agency's belief that its power to interfere with the legitimate practice of medicine or even the proper and safe marketing of food is virtually unlimited.

A provision in the preamble preamble to the draft regulations makes the proposals even more cumbersome and difficult for a sponsor who might offer a program, and for patients who might benefit. The FDA states it will now discourage the use of open label safety trials as a way to get investigational drugs to patients for purposes of treatment. Instead the FDA will require that sponsors follow the more rigorous requirements for setting up a Treatment IND. A review of what the FDA will require in the draft regulations raises the bar for approval of a Treatment IND to a level effectively equivalent to the level required to obtain marketing approval.

Open label safety trials have served (albeit too rarely) as a simple, fast, relatively inexpensive way to get an investigational drug to patients who need it while capturing useful supplemental information on drug side effects and efficacy. If FDA is going to discourage open label safety trials as access mechanisms in favor of the more difficult and expensive Treatment IND process, there will likely be even fewer expanded access programs as a result of the FDA's action.

To put this further into perspective, for the thousands of patients who might have benefited from access to an investigational drug during the 90 day comment period for these "stay-the-course" draft regulations, almost none at all were actually able to get a drug they sought, and while the FDA does not track the effect on patients of its failing programs, it is inescapably true that many of those patients did or will die, their diseases left untreated, while the FDA works to make sure that outcome won't change for future patients who find themselves in the same situation.

Maintaining a status quo that isn't working for a vast number of Americans every year who need it to work as a matter of life and death is not a positive or useful rulemaking process.

In our suit, the court no longer questions whether FDA is denying patients access to investigational drugs. The only remaining legal issue is whether they can do it without first showing it is narrowly tailored to a compelling governmental interest.

With its draft regulations, the FDA is tossing to drowning patients not a life raft, but in most cases nothing. It is offering not a full loaf, or half loaf, but a few crumbs -- widely proclaiming them to be "expanded access."

A few days before the comment closing date for the dockets associated with the draft regulations, FDA began to post links to comments submitted to the docket. The FDA is exceedingly slow in posting comments to dockets on its website, and we assume others will be submitted and, eventually, posted. Of those available at the time of docket closing, virtually all of the comments submitted by individual patients, family members of patients, and individual doctors who treat those patients strongly and unequivocally favored increased access to investigational drugs.

So far, only two insurance companies, who appear to fear that they might somehow be required to cover an investigational drug, and a rare disease organization that has long been a defender of the status quo, clearly support the agency's proposal to do nothing.

We think the agency has committed a serious error in proposing draft regulations intended by FDA to perpetuate long-failing programs that fall far short of serving the needs of the people directly affected by those failures; Americans with serious and life-threatening diseases and no remaining treatment options.

As the FDA well knows, those people, through their physicians, almost universally seek access to investigational drugs that have already shown substantial evidence of safety and efficacy in pre-clinical and clinical testing. The FDA also knows those people almost always first attempt to gain access to those drugs by trying to enroll in clinical trials. It is only when all their efforts fail, and that is the case for a great many of them, that they seek a drug outside a clinical trial. They do not seek snake oil or battery acid or something made in a garage with criminal intent. They seek what the FDA would gladly let them try if they could qualify for an FDA approved clinical trial.

A drug extensively tested in the pre-clinical setting that has already shown sufficient evidence of safety and effectiveness in early human clinical testing to go on to large clinical trials approved by the FDA in which hundreds or thousands of individuals are allowed to obtain treatment is not an untested drug, nor is it at all unreasonable to consider that drug a reasonable therapeutic option for someone with no other options. If this were not true, then all of the agency's Phase II and Phase III trials would be medically unethical, and not a single investigational drug would ever be found to meet the agency's standards for approval. Of course, some investigational drugs do work and the evidence that they work frequently emerges in convincing fashion long before FDA approves them, sometimes even as early as the end of Phase I (e.g., Gleevec in CML; Erbitux in head and neck cancer).

The FDA knows that the people who get in to those trials have the same diseases and face the same or very similar risks as patients who don't get into the trials.

In our lawsuit, FDA is now left with a single regulatory claim in justification of its policies – that allowing patients access to investigational drugs outside clinical trials will limit the agency's ability to coerce some of those patients into randomized, double-blind trials with placebo-control arms, or into Phase I trials to test drugs for which no safety or efficacy data in humans exists. The FDA or its amici (friends of the court) have admitted that agency policies do prevent many patients from ever getting in to a clinical trial; consequently, in the context of expanded access it is an admission that even though many patients will never gain entry into a clinical trial because of FDA trial design mandates, denying them access to investigational drugs is necessary, even if it is directly harmful or even fatal to a large number of those people.

Separately, as part of its Critical Path Initiative, FDA admits that its clinical trial paradigm is obsolete and has been outstripped by biomedical science. In a recent speech, the FDA commissioner explained that FDA has been overwhelmed by science. In other words, the FDA's strict mandate that statistically-driven, comparative clinical trials will be run for every drug in order to gain approval, and that a desperate pool of dying patients far larger than is needed to populate those trials must be maintained to ensure timely, complete enrollment, no longer fits the science. But in typical fashion, the FDA has yet to change its policies, or even to begin a formal process for change of its agency-created, obsolete clinical trial mandates.

In proposing the draft expanded access regulations, FDA advances as its primary reason for proposing no changes, that the proper balance must be maintained between allowing access and collecting data; thus the sickest patients – in its view – must continue to be considered little more than resources for research, expendable to ensure enrollment of a small number of them in the agency's mandated clinical trials.

This reduces the agency's belated issuance of a set of status quo cementing regulations to an alarming reality; the FDA is so stagnant and change-resistant that its deepening failure to keep pace with biomedical science is stalling change on virtually everything it does, including allowing accelerating medical progress to reach the patients who, with increasing frequency, die waiting for it.

While it is not at all clear on many fronts that the FDA is capable of fixing any of its problems, it must try, because those problems project onto real people, and in too many cases they are preventing medical progress from reaching them, causing needless suffering, premature death, and abridgement of their fundamental right to pursue life.

The FDA is not at present an agency focused on protecting and promoting the public health. It is an agency wallowing in its own inability to change, to modernize, and to catch up with the science it regulates.

The FDA must do much better than their draft regulations for Treatment Use of Investigational Drugs and Charging for Investigational Drugs promise.

We urge the FDA to withdraw the proposed regulations and immediately start an expedited effort to implement real reform in its policies and practices regarding access to investigational drugs. This time, the agency should listen more closely to the members of the public who have been directly affected by the agency's heavy-handed failing policies, and should consider in good faith our Citizen's Petition on the subject of access to investigational drugs, submitted to the agency on June 11, 2003. The FDA is aware that in violation of its own regulations (which require a response to a Citizen's Petitions within 6 months), ours has been languishing at the agency for three years and 8 months. It can be found on our website at www.abigail-alliance.org, along with information regarding our lawsuit, and should be reviewed by any party interested in the issue of access to investigational drugs.

The Abigail Alliance for Better Access to Developmental Drugs expresses its deep disappointment with the FDA's decision to maintain a failing status quo, and will continue its pursuit of real changes through legislation and the courts to make legitimate access to investigational drugs on behalf of patients with serious and terminal diseases and no other options, a reality.

Abigail Alliance for Better Access to Developmental Drugs

/s/ Steven Walker
Steven Walker

Chief Advisor

/s/ frank Burroughs
Frank Burroughs

President