NBCC
NATIONAL BREAST CANCER COALITION

grassroots advocacy in action

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September 9, 2003

Mark McClellan, MD, PhD
Commissioner
Food and Drug Administration
14-71 Parklawn Bldg.
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner McClellan:

On behalf of the National Breast Cancer Coalition (NBCC), I submit this response to the Abigail Alliance and the Washington Legal Foundation's Citizen Petition of June 11, 2003. The Citizen Petition calls for a new "Tier 1" approval program that would make available investigational drugs to certain terminally ill patients who are not enrolled in clinical trials. NBCC believes that a policy expanding availability of investigational new drugs for individuals outside of clinical trials will weaken the move towards more and better research, expanded clinical trials, and access to care for all Americans. For these reasons, NBCC opposes the Citizen Petition and strongly urges you to reject it.

As you are aware, NBCC, a grassroots advocacy organization whose sole purpose is to eradicate breast cancer through action and advocacy, is now more than 600 organizations and 60,000 individual members strong. Since NBCC's beginning, the concept of evidence-based medicine has been fundamental to the Coalition. We need to know what works for women with and at risk of breast cancer, and we want all women to have access to what works. Women with breast cancer should not be given false hope by treatments that are unproven. Interventions must be based on the best possible science available, and the best way to achieve that is through well-designed clinical trials. We continue to help develop policies to increase the number of quality clinical trials, and bring the perspective of breast cancer advocates to the design of trials.

The Citizen Petition essentially requests that the FDA relax its regulatory standards for evidence of drug efficacy. The Abigail Alliance seeks to amend the Food, Drug and Cosmetic Act (21 C.F.R. § 312) so that patients with life-threatening diseases and unmet treatment needs would gain access to investigational drugs at an earlier stage in the drug development process than ever before: after a new "Tier 1 Initial Approval." This amendment would effectively allow access to unapproved new drugs outside of a clinical trial, commonly known as "compassionate use," before Phase II. Currently, compassionate use is allowed by the FDA in certain circumstances during Phase III trials, or at the earliest, in certain cases of immediately life-threatening diseases, during Phase II. However, compassionate use is never allowed before Phase II. The Abigail Alliance also seeks an exception for sponsors of drugs under Tier 1

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Approval that would allow them to charge a price higher than cost. Most concerning, is the Abigail Alliance's call for an amendment that would allow limited marketing based on "evidence of efficacy from case history data on a modest number of patients," where "[s]tatistically significant support will not be required." The Abigail Alliance's rationale for these changes is that they will meet the needs of patients with life-threatening disease who are without treatment options. Their legal basis for these changes is that the concepts of different phases in a trial, the use of double-blind studies, and particular levels of statistical power are not mandated by statute. NBCC believes that all these amendments would severely weaken the integrity of the FDA as a scientific body that bases its approval on evidence, and be detrimental to patients.

Public policy should discourage access to investigational drugs outside of clinical trials. Investigational treatments made available outside of clinical trials have the potential to undermine the clinical trials system. There is little incentive for a patient to participate in a clinical trial if she can obtain the investigational drug outside of the trial. This makes trial accrual difficult, and may significantly undermine the ability of the investigators to determine the efficacy and safety of the intervention. That was certainly the case with bone marrow transplant for breast cancer - because it was so widely available outside of clinical trials it was extremely difficult to accrue patients to trials, and it took many years longer than it should have to learn that the high-risk and expensive procedure provides no benefit to women with breast cancer.

Investigational treatments are by definition unproven; even the most promising data in earlier stages of trials often do not hold up. Further, there may be significant safety issues that do not emerge until well into a phase III trial. For example, the cardiotoxicity of Herceptin was not apparent in the phase II data, but emerged in the much larger phase III trial.

Any access to investigational drugs outside of a clinical trial should be in the context of expanded access protocols only, in which distribution of the investigational therapy is fair and data is captured that will add to the scientific base of knowledge about the intervention. Expanded access should not be the norm, rather a protocol may be allowed in particular circumstances and only for individuals who do not meet the eligibility requirements of a clinical trial. If an expanded access program is allowed, access to the drug must be fairly and blindly allocated and all individuals who apply to the program must be followed, and their data reported to the trial sponsor. Expanded access should not be allowed until there is safety data available from a completed phase II trial of the drug, including data that provides some basis for determining that the drug may be efficacious.

It seems compassionate to argue that investigational therapies should be available to seriously ill individuals for whom there is no known effective treatment. An individual may support early access to unproven drugs based on a tragic and emotional personal experience, but policy should not be based on emotion alone. There are significant negative consequences for all patients. The potential risk and harm involved in exposing patients to therapies that have no evidence to support their efficacy is far greater than any perceived benefit.

There are all too few truly effective treatments for most types of cancer. While the public is inundated with information about cancer "breakthroughs" and news of promising new drugs, the reality is that most drugs result in incremental improvement. The research process seems agonizingly slow for those who have run out of treatment options. Pharmaceutical companies, scientists and the media each bear responsibility for creating unreasonable expectations about unproven drugs. This has created a climate where many patients mistakenly believe that access to an investigational drug is their last hope, when most often it is a false hope.

It is compelling to argue that there is little harm in making an investigational therapy available to a seriously ill individual for whom there is no effective therapy, if someone is willing to pay for it. This argument does not hold upon scrutiny. To follow this to its logical conclusion completely undermines research and the concept of evidence based care. Where would the line be drawn? It would mean that any individual should have access to any drug, as long as she is willing to pay for it.

Single patient INDs or INDs with small numbers of patients under Tier 1 approval raise serious issues of fairness. Granting access to investigational drugs with Tier 1 approval to patients who can pay for them at a price higher than cost makes this proposed system highly inequitable. Patients with access to them would likely be very knowledgeable, well-connected, and financially privileged. They would have access to physicians who have the ability to develop a protocol for them, and are willing and able to implement it. This is not the case for most cancer patients. Resources devoted to fighting cancer should be based on the best evidence available. The off-trial process involves a great deal of time and expense for clinicians, regulators and investigators, with very little likelihood of benefit to the patient, or to accumulation of knowledge about the intervention in question, that would benefit all.

We recognize this is an extremely difficult issue. We all want to save lives. We must work together to develop the right public policy that will achieve that goal. This policy must move towards more and better research, expanded clinical trials, and access to health care for all Americans. The National Breast Cancer Coalition is committed to a public policy agenda that will help all women with breast cancer and those at risk. We believe that creating a new program allowing access to unproven drugs as early as after a single Phase I clinical trial will undermine those efforts.

For the reasons above, we urge you to reject the relief sought in the Citizen Petition.

Sincerely,

Fran Visco

Fran Visco
President