Abigail Alliance for Better Access to Developmental Drugs

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November 19, 2003

Dr. Mark McClellan
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Docket No. 2003P-0274/CP1 – Response to submission of Sept. 18, 2003, from NORD regarding "Tier 1 Initial Approval"

Dear Commissioner McClellan:

We have recently obtained a letter dated September 18, 2003, from the National Organization for Rare Disorders (NORD) that was submitted to the docket for the referenced petition ("the NORD letter"). The NORD letter is based on a number of misconceptions and errors regarding the details of our Tier 1 Initial Approval concept as it is proposed in the petition.

The NORD letter states that Tier 1 approved drugs would be available in Phase I clinical trials, Tier 1 approval would be granted without any evidence of safety and effectiveness, and that the purpose of Phase I trials is solely to evaluate toxicity, not efficacy. All three comments are incorrect. Tier 1 approval would not be available until completion of a Phase I trial (effectively not before Phase II) and would not be granted without meeting a defined standard for evidence of safety and efficacy. Phase I clinical trials are often designed with secondary endpoints intended to capture early evidence of efficacy, and it is likely that Phase I trials would be designed with more robust elements intended to establish early evidence of efficacy if Tier 1 approval were an available option. In fact, an increasing number of investigational drugs are showing early evidence of efficacy in Phase I trials, a trend that is likely to continue in light of increasing knowledge regarding the causes of life-threatening diseases, and a constantly improving ability to invent drugs to target those causes.

The assertions in the NORD letter that Tier 1 Initial Approval would impact enrollment of randomized, placebo-controlled trials are also unfounded. With a Tier 1 approved drug, access to the drug would be conditioned on the patient having been found ineligible for a clinical trial for the drug, or considered by their physician to be a poor candidate for

an open and enrolling clinical trial. These protections of clinical trial enrollment are more definitive than those that exist for our current access mechanisms for investigational drugs. Further limitations, if desirable, could be considered as part of the rulemaking process.

The remainder of the concerns raised in the NORD letter are similar to those raised in two previous submittals to the docket ("the Mayer letter" and "the Visco letter"), and are addressed in our separate responses to those letters.

The primary effects of implementing Tier 1 will be to empower the Food and Drug Administration ("the FDA") to more effectively accomplish its mission of protecting *and promoting* the public health, and to spur wider availability of best available care in the form of new treatment options for patients that presently have no option but certain death from their diseases.

The Abigail Alliance for Better Access to Developmental Drugs applauds the important work and valuable services provided to the private sector and patients by NORD in their efforts to bring investigational drugs to patients with no other options, and hope that they will apply their experience and skills to assisting private-sector sponsors and with Tier 1 drug programs.

Sincerely,

Abigail Alliance for Better Access to Developmental Drugs

Steven Walker
Advisor on Regulatory and FDA Issues

Frank Burroughs
President

cc: A. Meyers, NORD
M. Hardin, NORD