July 30, 2004

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

Re: Docket No. 2004-N-0181, Critical Path Initiative

Dear Sir/Madam:

The Amyotrophic Lateral Sclerosis (ALS) Association is pleased to submit comments to the Food and Drug Administration as it explores ways to reduce existing hurdles in medical product design and development. We strongly support the Agency in this endeavor and are hopeful that the "Critical Path Initiative" not only will speed the pace of product development, but also bring changes to the development process that will lead to new treatments and cures for diseases like ALS.

The ALS Association is the only national not-for-profit health association dedicated solely to the fight against ALS, or Lou Gehrig's Disease. In addition to serving as a resource for ALS patients and their families, The Association advocates for increased funding for ALS research and other health care reforms that respond to the needs of ALS patients. The ALS Association also is the largest private source of funding for ALS-specific scientific research in the world, having awarded nearly $27 million since 1991 to fund research seeking to identify the cause, means of prevention and cure for ALS.

About ALS

ALS is a fatal, neurodegenerative disease that attacks nerve cells and pathways in the brain and spinal cord, ultimately resulting in a loss of voluntary muscle control, paralysis and death. More than 5,600 Americans are diagnosed with ALS each year and an estimated 30,000 are living with the disease today. Although the average life expectancy for ALS patients is two to five years from the time of diagnosis, many patients are living longer, more productive lives thanks to recent advances in research and improved medical care. Despite these advances, there is no known cause or cure for the disease, nor is there a means of prevention. Moreover, there currently is only one drug on the market, Rilutek, used in the treatment of ALS. Therefore, The Association welcomes any efforts by FDA to examine ways to speed innovation and the development of new products that could benefit ALS patients.

The comments we are providing are intended as a preliminary assessment of our concerns and thoughts on the critical path of the product development process. We look forward to working with the FDA and other concerned stakeholders on this initiative and to providing the Agency additional input as it continues to explore new approaches in the development process.

Encouraging Research and Development of ALS-Specific Products

ALS is designated as an "orphan disease," affecting less than 200,000 patients. As a result, many of the problems associated with the development of products to treat ALS concern the initial stages of the drug development process – providing incentives for manufacturers to conduct ALS-specific product development research and matching ALS researchers with manufacturers willing to develop and market a product. However, we are pleased that the data show that orphan drugs have faster clinical development times, lower costs of development, and more significant end markets than products for common diseases. The regulatory environment established for orphan drugs, including the availability of treatment INDs for drugs to treat seriously ill patients who have no treatment options, tax credits and marketing exclusivity arrangements, has enabled many orphan drugs to reach market quicker than those for more common diseases. Indeed, The Association supports the incentives available through the Orphan Drug Act.

Nevertheless, as FDA itself has noted, there are several areas of the critical path – assessment of safety, proof of efficacy, and industrialization – that hinder product development and which can be improved. We have listed below a few of those areas as well as some that facilitate development as well.

Cooperative Research and Development Agreements (CRADAs)

Many in the ALS community believe that CRADAs have been helpful in speeding the development process by facilitating the transfer of ideas from the research facilities to industry. However, we are aware that concerns exist in the process of gathering toxicology data to help assess safety and in what role the government should play in the pricing of compounds. While The Association has not taken a formal position on what role government should play in pricing, we do believe that incentives, financial and regulatory, are necessary to encourage continued active industry involvement in ALS product development.

Centers of Excellence

Some have suggested that establishing ALS Centers of Excellence could facilitate research and development of ALS-specific products similar to the way such Centers have aided innovation in the development of products for other diseases. In those cases, Centers of Excellence provide industry a multidisciplinary team experienced in the treatment of the disease as well as a substantial pool of patients to participate in clinical trials. Centers of Excellence, as sites which provide care to specific groups of patients and already conduct research on specific diseases, indeed are important resources for information that can be used to assess safety, prove efficacy and design trials. Although individual ALSA Centers have gained considerable clinical trial experience in recent years and should continue to play a significant role in clinical research, ALSA does not believe individual Centers alone have the necessary numbers of ALS patients to produce statistically significant clinical trials. Instead, multi-center trials, as currently is the case,

are likely to be the best means of assuring large enough patient pools to conduct clinical trials that produce reliable results.

Grouping Neurological Disorders as a Collection of Orphan Diseases

ALSA believes that grouping neurological disorders as a collection of orphan diseases would help shorten the development time of a drug and help minimize regulatory hurdles. We also believe that encouraging more discussion between the different neurological diseases will bring benefits to the development process. Such collaboration can exploit the varying expertise of researchers and manufacturers and allow for the sharing of concerns and ideas on all phases of product development, including basic research and clinical trial design. However, while efforts at collaboration may speed product development, the desire to move expeditiously must be tempered by thoroughness. It is critical that the necessary steps are taken to assess safety, establish appropriate dosing and conduct efficacy studies. If this is not done, additional costs and needless delays later in the development process may result and, could deter manufactures from conducting future product development.

Considerations for improved Clinical Trials for ALS

The ALS community is aware of and attempting to address several challenging areas to improve clinical trials. These include diagnosis, outcome measures, recruitment for clinical trials, funding and increased geographic distribution of trial centers to enable the smaller regions to participate in the ongoing trials and. In addition, discussions continue with NIH to encourage more rapid funding for clinical trials, a key concern in a disease such as ALS where patients may only live a few years after diagnosis.

There are several other concerns that we have in the drug development process that have presented barriers to progress, including concerns about insurance reimbursement for participation in clinical trials, low levels of participation, and the lack of willingness of physicians and patients use compounds, among others. These concerns are present, to varying degrees, throughout the development process and can be addressed through increased educational efforts by the medical community, public and private research institutions and manufacturers.

Conclusions

The ALS Association applauds the FDA for its efforts to determine what changes can be made to improve the product development process so that patients will continue to benefit from our nation's increasing commitment to the funding of medical research. Because ALS is an orphan disease, many of our immediate concerns lie in the need to encourage manufacturer involvement in the research that can lead to product drug development rather than in the development process itself. However, we believe changes can be made to improve the development process. To that end, we anticipate providing the Agency additional input on our specific concerns about the critical path in the

development process -- concerns that we hope can be addressed to the benefit of ALS patients and their families.

We appreciate the opportunity to comment on this important initiative.