July 31, 2013

Margaret A. Hamburg, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

Dear Commissioner Hamburg,

We appreciate the Food and Drug Administration's (FDA) proposed Guidance for Industry – Expedited Programs for Serious Conditions – Drugs and Biologics. When Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA), it included Section 901 which modernized Accelerated Approval. Congress did this with the goal to "expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions."

In requiring FDA to develop guidance, Section 901 also mentioned that FDA "…shall also consider any unique issues associated with very rare diseases." Despite this, the guidance does not mention Orphan Drugs, rare diseases, or very rare diseases. The guidance also does not specifically mention the challenges that rare diseases have due to having a small population set making traditional approval difficult or the lack of data available on some diseases because of its rarity. Accelerated Approval was modernized to offer a pathway forward for this community which has so many unique challenges.

FDA's evidentiary criteria, as proposed, are too limited. FDASIA requires that FDA,

> "…shall consider how to incorporate novel approaches to the review of surrogate endpoints based on pathophysiologic and pharmacologic evidence in such guidance, especially in instances where the low prevalence of a disease renders the existence or collection of other types of data unlikely or impractical."

Despite this, the guidance presents a rather restrictive set of evidentiary criteria. FDA needs to develop and clearly define the degree of evidence and the robustness of evidence correlating to the surrogate endpoint. FDA must also develop what level of evidence is acceptable when clinical outcome data may not be available due to the rarity of the disease.

Finally, the guidance that FDA issued does not move Accelerated Approval forward as a legitimate pathway for drug approval within the rare disease community. FDA states that whether an "…endpoint is reasonably likely to predict clinical benefit is a matter of judgment." FDA also states that it will exercise judgment on a "case-by-case basis." Accelerated Approval was established over 20 years ago and its use has been limited. FDA needs to provide a clear workable framework for the rare disease community to be able to use Accelerated Approval on a consistent basis with transparent uniform criteria.

There are 30 million Americans that suffer from one of 7,000 rare diseases. Most of these diseases have no treatment options. It is important that FDA ensure that the Accelerated Approval pathway is a vibrant and activate pathway available to this community.