

# CANCER LEADERSHIP COUNCIL

A PATIENT-CENTERED FORUM OF NATIONAL ADVOCACY ORGANIZATIONS  
ADDRESSING PUBLIC POLICY ISSUES IN CANCER

May 7, 2013

Leslie Kux  
Assistant Commissioner for Policy  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

RE: FDA-2013-N-0196, Food and Drug Administration Prescription Drug User Fee Act V  
Benefit-Risk Plan; Request for Comments

Dear Ms. Kux:

The undersigned cancer patient, provider, and research organizations appreciate the opportunity to comment on a structured approach to: 1) the evaluation of benefits and risks as part of the regulatory decision-making process, and 2) the communication of the benefit-risk assessment to the public. We commend the agency for meeting the aggressive deadlines in the PDUFA Reauthorization Goals and Procedures Fiscal Years 2013 through 2017 for implementing a structured benefit-risk assessment process, including standards for the communication of the assessment to the public.

The Draft PDUFA V Implementation Plan, "Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making," says that a framework for benefit-risk decision-making that "summarizes the relevant facts, uncertainties, and key areas of judgment, and clearly explains how these factors influence a regulatory decision," may yield significant advantages. According to the plan, these include: 1) informing and clarifying the regulatory discussion, 2) providing transparency about different regulatory conclusions by different parties using the same information, 3) communicating to the public the basis for FDA regulatory decisions, and 4) documenting a regulatory decision for consideration by the agency when it considers similar benefit-risk questions in the future. These are ambitious goals for a structured benefit-risk assessment, and we will offer below some advice about how to realize some of these objectives.

## ***Ensuring that Structured Benefit-Risk Assessment Does Not Compromise Cancer Drug Review***

Before identifying strategies to optimize the benefit-risk assessment process, we would like to note the potential detrimental effects of this process. As the implementation plan states, the benefit-risk assessment "should support the work of review staff throughout the lifecycle of a drug by capturing the full range of decisions from pre-market review through any regulatory actions that are necessary in the post-market setting." The plan also states that, "a systematic approach should efficiently integrate into a review teams' existing processes and work products." We urge the agency to take steps, if it requires the utilization of the framework

document for structured benefit-risk assessment, to ensure that the document does not require FDA review staff to undertake a process that is parallel to and duplicative of review of safety and efficacy data and regulatory decision-making.

We are concerned that duplication of regulatory activities or requirements could result in a slowdown in the regulatory review process. Cancer patients have benefited significantly from improvements in regulatory review times, and we are concerned that the structured benefit-risk assessment process could serve to undermine that progress because review staffers will shoulder additional responsibilities associated with the structured assessment.

We also note that there are additional provisions in the Food and Drug Administration Safety and Innovation Act (FDASIA) that hold promise of improving the review of cancer therapies, and the implementation of the benefit-risk assessment process should not challenge those improvements in regulatory review. The breakthrough therapy designation, which facilitates greater communication between sponsor and agency in the review process, has been identified as a FDASIA authority that may hold special potential to enhance cancer drug review.

In moving forward with the structured benefit-risk assessment and other provisions of FDASIA that will improve the regulatory review process, FDA must meet the standard it has articulated, which is to integrate these authorities and procedures into “existing processes and work products.”

### ***Optimizing Structured Benefit-Risk Assessment***

The benefit-risk framework document, published on page 7 of the Implementation Plan, has the potential to provide a solid summary of the agency’s rationale for regulatory action. Two decision factors in the document – analysis of condition and current treatment options -- will prompt the agency to identify “evidence and uncertainties” related to those factors that are critical to the informed evaluation of cancer therapies. We believe that the information related to current treatment options will identify the impact of those treatments on the quality of life of patients, including but not limited to the side effects of treatment and the potential late and long-term effects of treatment. This information provides important context for review of new treatments and also serves to identify unmet needs, related to both improved overall survival and quality of life, that reviewers should consider in the regulatory decision-making process. We also recommend, as the framework document is put into routine use, that the analysis of the condition be updated when a new therapy for that condition is evaluated. As knowledge about cancer types, cancer subtypes, and molecular diagnosis deepens, that knowledge should be reflected in the benefit-risk framework document and in regulatory review.

We also believe that the public and FDA review teams will benefit from the evaluation of risk management that the framework document requires as well as from the subsequent publication of that evaluation. It is often suggested that cancer patients have an exceptionally high tolerance for treatment side effects. As patients with some cancer diagnoses find that they have a range of treatment options, they may desire more information about the risks associated with all options and also a consideration of risks of approved therapies in the regulatory review of new drugs. There is promise that the framework document will encourage more rigorous

evaluation of risk management strategies of new and already approved drugs and over time encourage comparison of the risk management strategies of different drugs.

### ***Characterizing Uncertainty in Benefits and Risks***

We commend the decision of FDA regarding the manner in which it will utilize the benefit-risk assessment in FY 2013. The agency indicates that it will focus on: 1) uncertainty about the benefit-risk assessment that is based on pre-market clinical trial data from trials that exclude patients with chronic conditions, who are over a certain age, or who do not meet other enrollment criteria but may be treated with the drug after approval and 2) uncertainty about the meaning of post-market safety signals that may emerge from a wide range of sources and that not be consistent with safety signals from trials. This use of the benefit-risk assessment framework may over time inform the regulatory review process, including the review of cancer drugs, and at the same time provide patients and the public a greater understanding of uncertainties that arise in the review process.

### ***Five-Year Plan***

FDA has indicated that it will adhere to a five-year plan, revising and refining the benefit-risk assessment process as necessary. FDASIA anticipates a five-year process, and we believe that a constant process of refinement of the benefit-risk assessment tool and its utilization will be necessary. There are many unknowns about how the benefit-risk framework will be used and how it will affect the speed and efficiency of the regulatory review process, and a rigorous evaluation process is needed to ensure that the framework assists FDA and is in the best interest of the patients who rely on FDA-regulated therapies.

Sincerely,

### **Cancer Leadership Council**

Bladder Cancer Advocacy Network  
International Myeloma Foundation  
The Leukemia & Lymphoma Society  
LIVESTRONG Foundation  
Lymphoma Research Foundation  
National Coalition for Cancer Survivorship  
National Lung Cancer Partnership  
Ovarian Cancer National Alliance  
Pancreatic Cancer Action Network  
Prevent Cancer Foundation  
Susan G. Komen for the Cure Advocacy Alliance  
Us TOO International Prostate Cancer Education and Support Network