CANCER LEADERSHIP COUNCIL

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

August 26, 2013

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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RE: Docket No. FDA–2013–D–0575: Draft Guidance for Industry on Expedited Programs for Serious Conditions – Drugs and Biologics

Dear Dr. Hamburg:

The undersigned organizations representing cancer patients, researchers, and physicians and other health care professionals appreciate the opportunity to comment on Draft Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. The guidance document provides useful information to sponsors, physicians, clinical researchers, and patients regarding four programs that are part of the effort to expedite review of drugs for unmet medical needs. In this document, the Food and Drug Administration (FDA) has preserved "appropriate standards for safety and effectiveness" while defining the programs that direct early attention to drugs for serious conditions.

The guidance document provides important advice simply by describing the four programs – fast track, priority review, accelerated approval, and breakthrough therapy designation – in a single document and explaining the relationships among them. The guidance related to three of the programs is largely unchanged, and the requirements for requesting breakthrough therapy designation and the benefits of that designation are clearly explained.

We offer comments regarding several elements of the guidance document. We commend the agency's flexibility in defining when a therapy may meet an unmet medical need, a status that potentially allows the drug to qualify for fast track and accelerated approval. For example, the agency notes that in situations where there is an available therapy for a condition, a new treatment might be considered to meet an unmet medical need if it is a targeted cancer therapy with a novel mechanism of action that could benefit patients no longer responding to available therapy. This is an important clarification for researchers seeking to develop new targeted therapies.

The agency has also offered useful information about the intermediate clinical endpoint for accelerated approval that was included in Food and Drug Administration Safety and Innovation Act (FDASIA). The user fee law stated that accelerated approval, in addition to being granted on the basis of a surrogate endpoint that is reasonably likely to predict clinical benefit, could be granted on the basis of a clinical endpoint that 1) can be measured earlier than irreversible morbidity or mortality and 2) is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. FDA states that it has limited experience with accelerated approval based on intermediate clinical endpoints but offers sponsors advice on the situations in which such endpoints would lead to accelerated approval and also identifies the possibility these endpoints will support traditional approval. The modification of the accelerated approval regulations pursuant to FDASIA and the current guidance document combine to clarify the use of the intermediate clinical endpoint for accelerated approval.

FDA has provided clear and concise guidance to sponsors regarding the application for breakthrough therapy designation. The designation requires "preliminary clinical evidence of a treatment effect that would represent substantial improvement over available therapies for the treatment of a serious condition." The preliminary clinical information must be credible but not definitive at the time of application. The grant of breakthrough therapy designation triggers the engagement of "senior managers and experienced review staff in a proactive collaborative, cross-disciplinary review."

The cancer community has already observed the benefits of the breakthrough therapy designation. This designation, granted to a number of cancer therapies, has resulted in the active engagement of the Office of Hematology and Oncology Products in the review process for those products. We note that the guidance document urges sponsors with breakthrough therapy designations to be prepared for meetings with the agency throughout drug development and to plan also for a more rapid pace for other aspects of the drug development process, including manufacturing. We trust that sponsors requesting breakthrough designation will be prepared to take full advantage of the commitment of the agency to speedy development and review.

The guidance document identifies circumstances in which a product may lose its breakthrough therapy status. If interim data show a substantially smaller benefit than the response seen in early clinical testing, a drug may lose its breakthrough designation. If breakthrough therapy designation is granted to two drugs that are being developed for the same use and one of the drugs gains traditional approval, the second drug may lose its breakthrough status. The second sponsor could retain its breakthrough status only if it provided evidence of substantial improvement over the recently approved drug. We understand that the approval of the first drug would mean that the "unmet need" has been addressed and there is an available therapy. However, the possibility of loss of breakthrough therapy designation in the middle of drug development creates the sort of regulatory uncertainty that sponsors assert undermines the development process. In addition, it may be difficult for the second sponsor to produce evidence of substantial improvement over a recently approved drug before completion of its trial or trials. We urge the agency to reconsider the policy of termination of breakthrough status in such circumstances.

We appreciate the opportunity to comment on the draft guidance document and look forward to working with FDA in the future to assure the speedy approval of safe and effective cancer drugs.

Sincerely,

Cancer Leadership Council

Bladder Cancer Advocacy Network
Cancer Support Community
The Children's Cause for Cancer Advocacy
Fight Colorectal Cancer
Hematology/Oncology Pharmacy Association
International Myeloma Foundation
Kidney Cancer Association
The Leukemia & Lymphoma Society
LIVE**STRONG** Foundation
Lymphoma Research Foundation
National Coalition for Cancer Survivorship
Ovarian Cancer National Alliance
Pancreatic Cancer Action Network
Prevent Cancer Foundation
Us TOO International Prostate Cancer Education and Support Network

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