January 3, 2014

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

Re: FDA-2011-N-0898; Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products

Dear Sir/Madam:

The National Coalition for Cancer Research is pleased to submit comments in response to the above-referenced proposed rule issued on November 4, 2013, amending regulations to implement certain drug shortage provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Food and Drug Administration Safety and Innovation Act - Public Law 112-144 (FDASIA).

The National Coalition for Cancer Research (NCCR) is a nonprofit alliance of 23 national cancer research, cancer care and patient organizations representing cancer patients and survivors; children with cancer and their families; cancer researchers, nurses, physicians and pharmacists; as well as cancer hospitals, centers, clinics and specialized research institutions. The organization directs its efforts at making widely known the value of cancer research and the major contributions the National Cancer Program has made to the biomedical sciences and related fields to contribute to the reduction of cancer incidence, morbidity and death, and issues faced by cancer survivors. Through education and advocacy, the National Coalition for Cancer Research is committed to transforming public policy to enable every individual to participate in, and benefit from, cancer research.

NCCR remains highly supportive of requirements that all applicants of covered approved drugs or biological products notify FDA of a permanent discontinuance or interruption in manufacturing of a product that is likely to lead to a meaningful disruption in supply of products in the United States. Such discontinuances and shortages have had a significant negative impact on the ability of health care practitioners to provide timely treatments to cancer patients.

The shortage of some cancer drugs is not just affecting patients currently undergoing standard or non-investigational treatment, but it is also having a significant negative impact on current and future cancer clinical trials. This impact on cancer research is largely due to the fact that placebos are rarely used in cancer clinical trials, and are never used alone if an acceptable treatment is available. Therefore, cancer clinical trials are traditionally designed to test the safety and efficacy of the standard of care against, or in combination with, a new treatment being investigated. When the standard-of-care or investigational drug is in short supply or is no longer being manufactured, it severely compromises high priority clinical trials. These shortages have resulted in important cancer clinical trials being delayed, suspended and/or halting the accrual of new patients into them. We believed the Proposed Rule will assist researchers and patients participating in clinical trials by providing timely notification if agents used in the clinical trials have been discontinued are in shortage, or other circumstances are likely to lead to a disruption in supply of the product in the United States.

We commend the Agency for its actions taken thus far to alleviate or mitigate drug shortages through a voluntary system of notification. The Proposed Rule implementing FDASIA Title X – Drug Shortages – will provide additional clarification and guidance that will benefit providers, researchers and patients, as well as apply uniform implementation of the requirements established therein.

NCCR believes the Proposed Rule accurately reflects both the intent and spirit of that provision of FDASIA. We appreciate the opportunity to expand on our March 14, 2012 letter in response to FDA-2013-N-0124; Food and Drug Administration Drug Shortages Task Force and Strategic Plan; Request for Comments.

Persons Subject to the Proposed Rule

We support the definition of an ANDA, NDA or BLA applicant to be considered the "manufacturer" of an approved product, even if the applicant contracts that function to another entity. It is essential that a uniform process be established for contract manufacturers to notify the applicant of a potential or actual discontinuance or shortage in order to ensure the applicant can comply with the early notification requirements.

Products Subject to the Proposed Rule

The Proposed Rule applies to products "intended for use in the prevention or treatment of a debilitating or life-threatening condition." Furthermore, the Proposed Rule defines a "product" as one "intended for use in the prevention or treatment of a disease or condition associated with mortality or morbidity that has a substantial impact on day-to-day functioning." FDA proposes to equate the terms "debilitating disease or condition" with "serious disease or condition" and define it according to the current definition of "serious" found in 21 CFR §312.300. We believe this is a reasonable approach to take when defining these terms for purposes of this provision of FDASIA. The Proposed Rule also expands upon the definition of "medically necessary" as used in the Manual of Policies and Procedures (MAPP) by applying reporting requirements, whether or not the product is considered "medically necessary" under MAPP. We concur with FDA that doing so will enable the Agency to prioritize the response to specific shortages or potential shortages and enable the Agency to allocate internal resources appropriately.

We strongly support the proposal to apply the Proposed Rule to all biological products, including recombinant therapeutic proteins, monoclonal antibody products, vaccines, plasma-derived products and their recombinant analogs, blood or blood components, and cellular and gene therapy products. Some of these important products are an essential part of cancer treatments and clinical trials, and the system of early notification of the disruption in production or shortage should be applied to these products as they are for drugs.

We agree that such notification would allow the Agency to address, prevent or mitigate a shortage of these products, greatly benefiting the public health without duplicating existing reporting systems or creating redundant reporting. We also encourage FDA to develop reliable models for translating market-wide and manufacturer-specific information into national supply projections, keeping the focus on communicating and solving shortages.

Scope of the Term "Product"

We concur with the Proposed Rule definition of "product" to include a specific strength, dosage form, or route of administration of a drug or biological product. In drugs to treat cancer, particularly chemotherapeutic agents, the strength and dosage form of drugs and biological products administered to patients is particularly sensitive and will vary among patients as dosing is frequently based on weight or

body surface area. Early notification of a specific strength or dosage discontinuance or shortage is essential to the establishment and maintenance of a treatment protocol for patients. Through early knowledge of a potential or actual discontinuance or shortage of a particular strength or dosage, treating physicians will have time to modify a patient's treatment protocol, if necessary and try to minimize product wastage.

Notification

We agree with the list of reportable discontinuances or interruptions of a covered drug or biological product as outlined in the Proposed Rule. The two exceptions to the notification requirements outlined in the Proposed Rule (routine maintenance or power outages) are reasonable. We also agree that, in either case, if interruption in the manufacturing of a drug or biological product could lead to a shortage, then it would be considered to be reportable and notification to FDA would be required.

Timing, Submission and Content of Notifications

The proposed minimum contents of the notification to FDA of drug shortages will be valuable to physicians, pharmacists and patients in order to modify their prescribing patterns to adjust to the shortage.

In addition to the contents listed in the Proposed Rule, we strongly encourage the Agency to include in its notifications submitted under section 506C(a) of the FD&C Act if the drug or biological product is being used in an FDA- or NICI-approved clinical trial. As previously noted, placebos are rarely used in cancer clinical trials, and are never used alone if an acceptable treatment is available. We encourage FDA to consider establishing a method of tracking the impact of drug shortages on clinical trials. Since the clinicaltrials.gov website already provides a listing of all clinical trials, researchers could indicate trials that are terminated, suspended or closed due to a drug shortage. Furthermore, historical data showing the impact could be collected. The early notification system established in FDASIA will provide valuable information about a disruption in the manufacturing of a drug, increased demand for the drug or discontinuance of the manufacturing of a drug. Timeliness of such notification is of critical concern to cancer researchers. It would be helpful if the information contained in the FDA's drug shortage website could be categorized by specific classes of drugs in shortage that are relative to a particular area of research, such as oncology. By doing so, FDA could quickly notify researchers of drug shortages in classes frequently used by researchers in a particular specialty. Furthermore, we recommend FDA collaborate with the National Institutes of Health and the pharmaceutical and biotechnology industries to encourage researchers to incorporate into their clinical protocols contingency plans for addressing how the trial will proceed in the event of a shortage of a study drug, including other sources for the drug or alternative drugs that could be used as substitutes when the protocol permits substitutions. We commend the Agency for including this recommendation in its Strategic Plan for Preventing and Mitigating Drug Shortages, issued in October 2013.

Public Lists of Products in Shortage

We commend the Agency for its efforts to collaborate with industry to address underlying quality or manufacturing issues that could lead to a shortage in order to help ensure patient access to vital safe and effective drug and biological products. The FDA practice of maintaining a current list of drugs and biological products in shortage has been extremely useful, and we applaud the Agency for reorganizing the drug shortage list on its website to include six categories of information about each product on the list. As with our recommendation regarding the timing, submission and content of notifications, we recommend the Agency also include information on its drug shortage website about whether the drug or biological product listed is being utilized in an FDA-approved clinical trial, as well as link to the clinicialtrials.gov website for each clinical trial in which the subject product is being utilized.

Should you have questions, or if we may provide additional information, please feel free to contact Mark Smith, our Policy Counsel, at msmith@libertypartnersgroup.com or (202) 442-3700.

The National Coalition for Cancer Research appreciates the opportunity to provide these comments. We hope the Agency will pay special consideration to our comments and recommendations regarding the impact of the Proposed Rule on clinical trials. We commend the efforts already undertaken by FDA, and look forward to working with you in our mutual effort to prevent or mitigate drug shortages.

American Association for Cancer Research
American Cancer Society Cancer Action Network
American Childhood Cancer Organization
American College of Radiology
American Society of Clinical Oncology
American Society of Hematology
Association of American Cancer Institutes
Coalition of Cancer Cooperative Groups
CureSearch Childhood Cancer Foundation
Friends of Cancer Research
Gateway for Cancer Research
Hematology/Oncology Pharmacy Association
International Cancer Advocacy Network
International Myeloma Foundation
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