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

Submitted electronically

RE: Federal Register Notice FDA-2014-N-1698
FDA Activities for Patient Participation in Medical Product Discussions

INTRODUCTION

FasterCures, a center of the Milken Institute, is a non-profit, non-partisan action tank driven by a singular goal -- to save lives by speeding up and improving the medical research system. We thank you for the opportunity to submit these comments in response to Federal Register Notice FDA-2014-N-1698, FDA Activities for Patient Participation in Medical Product Discussions. These comments have been informed through our work to advance patient-centered benefit-risk assessment, including dialogue with our Benefit-Risk Advisory Council, consultations with our TRAIN network of venture philanthropy organizations, formal and informal discussions with stakeholders from across the biomedical ecosystem who convened at our 2014 Partnering for Cures meeting, and conversations initiated during a one-day Benefit-Risk Boot Camp event we hosted in September 2014.

We commend FDA for its initiatives to include patient perspectives in regulatory decision-making, particularly those activities outlined in the Food and Drug Administration Safety and Innovation Act (FDASIA). We believe that a more effective and efficient process of developing and deploying medical products begins by understanding the benefit expectations and risk thresholds of the patients for whom these products are intended. Below we provide both overarching and operational recommendations for ways to deepen and expand the agency's engagement with patients, patient advocates and family caregivers.

Our recommendations have one aim: **to facilitate an intentional evolution from FDA's traditional engagement with individuals who serve as spokespersons for a disease/condition to an evidence-based means of understanding the range of patients' experiences across the lifespan, unmet medical needs, meaningful treatment benefits, risk tolerance, and outcome preferences that is complemented by individual participation of patients and patient advocates in selected roles** (e.g., special government employees (SGEs) serving on advisory committees).

We recognize that such evolution will take time and will require dedicated resource investment and ongoing collaborative efforts by the agency, sponsors of medical product development, and the patient community. A 30-day comment period on a single Federal Register notice is unlikely to elicit the breadth or depth of strategies and tactics to facilitate such evolution and we urge the agency to create a more permanent venue for dialogue and action that can inform patient engagement efforts across the centers, as recommended below.

We have appended a proposal submitted to the U.S. House of Representatives Energy and Commerce Committee that is relevant to the topic of this FR Notice and we will share these recommendations with committee staff as several pertain to topics that have been raised as priorities in the 21st Century Cures Initiative.

PHILOSOPHY OF ENGAGEMENT WITH PATIENTS

We are entering an era of heightened focus on patient-centricity. A legacy of HIV/AIDS activism is the movement's lasting impact on the research system, the regulatory paradigm, and the role of patients and their organizations to catalyze therapies that better meet patient needs. At a federal policy level, Congress created the Patient-Centered Outcomes Research Institute as a provision of the 2010 Patient Protection and Affordable Care Act. The FDASIA legislation enacted in 2012 contains provisions to expand patient perspectives in the regulatory process, including direction to the Secretary of Health and Human Services to "develop and implement strategies to solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussions." *See* FDASIA § 1137. Several FDA publications, including Federal Register notices posted in 2012, 2013, and the Center for Drug Evaluation and Research's Draft PDUFA-V Implementation Plan, "Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making," include the phrase, "FDA believes that the medical product review process could benefit from a more scientific, systematic, and expansive approach to obtaining input from patients who are experiencing a particular disease condition." The U.S. House of Representatives Energy and Commerce Committee has placed "integrating patient perspectives into the regulatory process" at the top of its list of priority reforms for the 21st Century Cures legislation it will introduce in early 2015.

Industry is shifting too. According to a 2012 report by Economist Intelligence Unit, "Reinventing Biopharma: Strategies for an evolving marketplace; The patient-led R&D strategy," a survey of 273 senior executives from the life sciences industry indicates that 53 percent of respondents agree that becoming more patient-centric is a top priority and nearly two-thirds had increased the level of resources expended on learning about patients. Survey respondents forecast increased outreach to patient advocacy groups, through focus groups of patients, and online patient communities over the next three years as a means to gain insights for both R&D strategy (52%) and commercial strategy (47%).

There are presently multiple initiatives to better define patient-centricity and the successful practices that support it. As a regulatory agency subject to stringent statutory requirements that define its interface with the public, FDA's engagement with patients will be subject to some unique restrictions. Even so, a set of guiding principles applied across all the agency's patient engagement activities would serve as both a compass and a scorecard for current and future initiatives. At minimum, FDA's patient engagement activities should be:

- **Purposeful** – Engagement should be designed and executed with the intent to inform the agency's mission, strategy, and operations, including policy and regulatory decisions. It should be valued by staff at all levels of the agency as integral to their role in protecting and promoting public health.
- **Reciprocal** – Whenever possible, engagement should be predicated on fostering a mutually beneficial information exchange between patients, industry, regulators, and other stakeholders. To elicit useful types of data, expected outcomes and deliverables should be communicated to the stakeholders. This can occur without violating privacy or confidentiality boundaries that safeguard participants.

- **Dynamic** – Much of FDA's interaction with patients and patient communities is currently episodic or cross-sectional, limited to annual forums or single events. Patient needs within a community and across communities change in response to scientific and technologic advances and other circumstances. Engagement activities should seek to build ongoing relationships and maintain updated information. These activities should be designed in such a manner that patient groups of any size are able to organize themselves and effectively engage.
- **Transparent** – In addition to required reporting on patient engagement activities through vehicles such as publicly available meeting agendas and minutes, the outcomes of patient engagement should be visible to the community, particularly when they affect or influence decisions or policy.

PROGRAMMATIC RECOMMENDATIONS

The following programmatic recommendations aim to infuse current and proposed engagement activities with the characteristics described above. As stated in the introduction, the overarching goal of these proposals is to transition from FDA's traditional model of engagement with designated spokespersons, to an evidence-based model that can effectively integrate the whole patient experience – including needs, risk-tolerance, and outcome preferences – into regulatory decision-making.

Office of the Commissioner

- Establish an advisory body to provide ongoing counsel about, input to, and monitoring of patient participation in regulatory processes and policy. This body, which would include substantial representation from the patient community, would provide guidance outside individual product decisions on the scope and implementation of programs and activities to foster greater inclusion of patient perspectives in regulatory decision-making for product review, post-market requirements, direct-to-consumer promotion, risk communication, and safety surveillance. The Council of Public Representatives to the NIH Director provides one potential model for such an advisory body. As stated by the International Association of Public Participation and referenced by NIH, "the need for public participation is based on the belief that those who are affected by a decision have a right to be involved in the decision-making process. In order to have public participation, organizations like NIH attempt to consult with interested or affected individuals, organizations, and government entities before making a decision. The goal of public participation is to reach better and more acceptable decisions."
- Develop a public-private Partnership to Advance the Science of Patient Input designed to provide a neutral collaborative environment to align interests and resources from the government sector, the private sector, and the public sector. For a more detailed explanation of this proposed partnership, please see our Nov. 12, 2104 proposal to the U.S. House Energy and Commerce Committee on this topic.
- Provide guidance on appropriate interactions between patients and industry to enable collaboration in early stages of R&D and across the lifecycle of product development, clinical trial design, endpoint selection, PRO development, etc. The Economist Intelligence Unit report cited above indicates that industry executive respondents identified "uncertain regulatory requirements" and "regulatory restrictions on contact with patients" as two of the barriers to increasing use of patient-centered data in discovery and development strategy.

Office of Health and Constituent Affairs

- Patient Representative Program: The Patient Representative Program is described by FDA as a way to "bring the patient voice to the discussions about new and already approved drugs and devices and policy questions." We propose expanding and utilizing this program more effectively by:
    - Making Patient Representative training materials available to non-program participants as a means to foster more widespread understanding about medical product development and regulatory processes and the FDA's role.
    - Making full use of patient representative special government employees (SGEs) as described in the program description to serve as "consultant[s] for the review divisions (doctors and scientists who review data to determine whether the medical product's benefits outweigh the potential risks)." We believe that establishing opportunities for patient representatives to inform reviewers about patient perspectives on issues such as unmet medical need, clinical trial design and burden on participants, endpoint and comparator selection, etc. in anticipation of meetings with sponsors across all stages of regulatory decision-making is a necessary supplement to more formal programs such as CDER's Patient Focused Drug Development (PFDD) initiative. All product-specific consultations with patient representative SGEs would be subject to appropriate protections to safeguard confidential information.
    - Seeking means to reduce delays in the screening and clearance processes for assessing conflicts of interest.
    - Clarifying how an individual's affiliation with voluntary health organizations or patient philanthropy groups will be viewed in the selection process for patient representatives. In contrast to the consumer representatives who are required to have "an affiliation with and/or active participation in consumer or community-based organizations," there is a perception that affiliation with a patient organization negatively affects an applicant's chances of being selected.
    - Seeking and utilizing patient representatives with direct experience with the condition that the product under discussion is being developed to treat.
    - Utilizing CDER-hosted PFDD meetings to recruit program participants since the diseases selected for the PFDD program represent areas in which there is some pending or anticipated regulatory action.
    - Providing patient representatives serving on CDRH advisory committees with voting status equal to other advisory committee members.
    - Clarifying the distinction between patient and consumer perspectives to prevent unintended substitution of one for the other when both perspectives might be beneficial to the product review discussions.

- Patient Network: Created in 2012 as part of FDA's Office of Health and Constituent Affairs, FDA describes the Patient Network as a "comprehensive program that works to expand and sustain communication with patients and their community." We believe the utility of this network as a means to involve patients in broader agency policy, and also educate patients about FDA's mission and opportunities to participate in medical product discussions, can be improved by:
    - Assessing whether topics and content at the annual Patient Network Meeting are responsive to the needs and familiarity level of the target audience.
    - Improving outreach and participation at the annual Patient Network Meeting.

- Prioritizing content and improving the design in the bi-weekly e-newsletter, Patient Network News. This could include clearly highlighting opportunities for patient input on issues of broad interest.
- Clarifying the criteria and process for convening other meetings (e.g., Patient Dialogue on Unmet Needs in Diabetes held Nov. 3, 2014; FDA Outreach to the Pediatric Cancer Community held Nov. 18, 2014) and identifying how outcomes of these meetings will be integrated into product reviews and other activities conducted at the center level.

Center for Drug Evaluation & Research

- Patient-Focused Drug Development (PFDD) Initiative: The PFDD meetings are designed to provide "a more systematic approach for the Agency to obtain patients' input on specific disease areas, including their perspectives on their condition, its impact on daily life, and available therapies." *See* Prescription Drug User Fee Act Patient-Focused Drug Development; Announcement of Disease Areas for Meetings Conducted in Fiscal Years 2013–2015, 78 Fed. Reg. 21613 (Apr. 11, 2013). We recommend making more effective use of this program as required under PDUFA-V by:
  - Issuing a detailed plan for how the information gathered through the PFDD will be used by reviewers and FDA in its decisions, including how information will be updated as scientific or therapeutic advances change the disease context and patient experience.
  - Establishing a mechanism for reporting insights across the 20 meetings that might address multiple conditions or populations, in addition to the learnings about individual conditions. Develop and issue a plan to address cross-cutting issues.
  - Clarifying the process for outside groups to hold meetings and outlining what conditions must be met for FDA staff (including reviewers) to participate, as well as addressing the appropriate role for industry to support such meetings.
  - Clarifying a process for proposing alternative methods of providing CDER staff with information about a disease or condition (e.g., data collected from patient registries, natural history studies, surveys, preference studies, etc.) and what data collection standards must be met in order for FDA to utilize the information in its decision-making.
  - Reinstating quarterly meetings of the PFDD Consultation process to provide input on: outcomes to date; improvements in format/structure to be considered; role of individual patients, patient advocates and patient advocacy organizations; utility of data to complement individual testimony; use and dissemination of "Voice of the Patient" reports; how information about a PFDD-highlighted condition or patient experience can be updated as scientific, diagnostic, or therapeutic options change, etc. This group could also be a resource for the FDA's Benefit-Risk Advisory Group and the Change Control Board.
  - Considering the pros and cons of expanding the consultation process to full advisory panel status to provide ongoing input on programs and policies (as planned at CDRH).
  - Encouraging active participation by CDRH in PFDD meetings where devices are currently or potentially integral to treatment armamentarium (e.g., supplemental oxygen in multiple featured conditions, deep-brain stimulation in Parkinson's disease).

- Structured Assessment of Benefit-Risk: CDER's PDUFA-V Benefit-Risk Implementation Plan reflects the intention to utilize the PFDD as a means to inform the analysis of the condition and current treatment options, the first two rows of the FDA's framework. The public has not yet had an

opportunity to see a completed benefit-risk framework for an approved product as was anticipated by the end of FY2014 based on the implementation plan. However "Voice of the Patient" reports for several of the PFDD-highlighted conditions do include the condition-specific rows of the framework using information collected during those meetings and through the public docket. The structured assessment of benefit-risk can be further strengthened with patient input by:

- Deepening patient perspectives beyond description of the condition and treatment context to include information about patients' benefit expectations and risk tolerance. Doing so will likely require adjustments to the way in which the PFDD meetings solicit patient perspectives about expected benefits and tolerable harms and risks as well as augmenting this program through means articulated above. It may also require CDER to provide greater clarity about the path for sponsors, patient organizations and other stakeholders to introduce rigorously conducted studies and appropriately collected data about patient-centered outcomes.
- Clarifying how review teams will incorporate patient perspectives on at least the first two rows of the framework for conditions that are not included as part of the PFDD process and for which there is not an externally hosted meeting of a similar nature in which FDA participates.
- Expanding on the PFUDA-V implementation plan for using the completed framework as a communication tool with the public, both for products that are approved (when the framework becomes part of the approval letter and/or advisory committee background package) and products that are not approved.

- Study Endpoints and Labeling Development (SEALD): The "Roadmap to Patient-Focused Clinical Outcome Measurement in Clinical Trials" identifies the first step to qualifying a clinical outcome assessment ("COA") as understanding patient/caregiver perspectives on definition of treatment benefit, benefit-risk tradeoffs, and impact of disease. However, it is unclear how SEALD staff will evaluate a COA applicant's analysis of this foundational information aside from its participation in CDER's PFDD meetings, which will only address 20 conditions. A meeting convened by the Brookings Institution in July 2014 on Patient-Reported Outcomes in Drug Development underscored the relatively slow progress in incorporating PROs into drug labels in spite of a 2009 guidance issued by FDA. This meeting and one planned by FDA for spring 2015 examine the challenge of capturing the patient perspective across the drug development continuum. As CDER examines its process for qualifying COAs, particularly PROs, we encourage strong consideration of methods to expand measures of patient-centered outcomes to incorporate physical function and quality of life, such as the European Medicines Agency has used in its PRO qualification process. *See* "Reflection paper on the use of PRO measures in oncology studies," European Medicines Agency (June 14, 2014).

- Rare Diseases Program: The stated mission of CDER's Rare Disease Program is "to facilitate, support and accelerate the development of drug and biologic products for the benefit of patients with rare disorders." One of the ways in which it seeks to accomplish this mission is by working "collaboratively with external and internal rare disease stakeholders to promote the development of treatments for rare disorders." However, information on the program's web page provides no further description of how patient/caregiver stakeholders can engage in programmatic activities. Section 903 of FDASIA authorizes the involvement of rare disease experts in the review of applications for therapies for rare diseases. We recommend that patient and caregiver representatives be considered for inclusion in

this program as their expertise and experience is vital to the consideration of the benefit-risk assessment, although their training may fall outside the formal channels recognized in the statute. Patient/caregiver representatives may be the most capable consultants on issues outlined by the statute including disease severity, unmet medical need, willingness and ability of individuals with the rare disease to participate in clinical trials, and an assessment of benefits and risks of the applicant's therapy and other treatment options. *See* FDASIA § 903(b).

- Stakeholder meetings for PDUFA-VI: The upcoming series of regular stakeholder meetings as required under the FDA Amendments Act provide an important opportunity to receive input on patient priorities. We encourage CDER to broadly announce these meetings and to utilize technologies such as webcasting to make them available to as wide an audience as possible.

Center for Devices and Radiologic Health

- Patient Preference Initiative: We urge CDRH to broadly share outputs of its contract with the Medical Devices Innovation Consortium, especially the catalog of methods, framework (and industry feedback), and research plan to encourage adoption among device developers and to stimulate development of a similar framework and plan by pharmaceutical and biotech companies.
- Patient Engagement Panel of Medical Devices Advisory Committee: We applaud CDRH's plans to establish this forum to provide input on the products of the MDIC contract and to shape development of guidance or other policy on incorporating patient views into the total product lifecycle of medical devices.
- CDRH Advisory Committee: We urge CRDH to seek authority to provide patient representatives serving on the CDRH Advisory Committee with full voting status so that this perspective is afforded equal weight to other forms of expertise on the committee.

We thank FDA for the opportunity to submit these comments and welcome the opportunity to explore them in greater detail with agency staff. *FasterCures* is committed to being a ready, reliable, and informed partner with the agency to help realize the promise of greater patient participation in regulatory decision-making as a means to improve public health.

Sincerely,

Margaret Anderson
Executive Director