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

Submitted electronically via regulations.gov

Re: Docket ID: FDA-2014-D-0090 and FDA-2014-D-0363: Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval; and Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Disease or Conditions.

Thank you for the opportunity to submit comments on two new guidance documents from the Food and Drug Administration (FDA) designed to expedite patient access to new medical devices. These guidance documents generally strike the right balance between accelerating the development of medical devices for patients with serious, unmet needs while also ensuring the safety and effectiveness of new technologies.

The Pew Charitable Trusts is an independent, non-profit research and public policy organization. Pew seeks to enhance medical device safety and foster device innovation that benefits patients.

In January of this year, Pew held a conference with thought leaders from FDA, the Centers for Medicare & Medicaid Services, the medical device industry, and the physician, patient and consumer communities to discuss key issues around facilitating device innovation.[1] Additionally, Pew held a webinar last month to hear the perspectives of product developers, physicians, patients and consumers on these guidance documents. Stakeholder input from both the conference and webinar informed these comments.

The development of promising new technologies to fill serious, unmet medical needs often takes several years—if not longer. In the interim, many patients with life-threatening or irreversibly debilitating conditions lack sufficient treatment options. Accepting the status quo is not a suitable answer for these patients. Part of the solution must include shortening the development time for medical devices that are expected to significantly advance patient care while, at the same time, ensuring that the products will, in fact, improve patient care.

No less important are assurances that the devices used in care are not putting patients needlessly at risk. The development and implementation of robust postmarket monitoring systems and policies are

essential for FDA to quickly identify unsafe or ineffective products and remove those technologies from the market.

A new approach to device development is necessary

One of the lengthiest parts of the device life cycle is the time it takes to conduct clinical trials for new products—typically more than three years. We conducted a preliminary analysis on devices designated by FDA as filling unmet medical needs, and found that the pivotal clinical trials alone—not to mention lab and bench testing—lasted twice as long as FDA review. Existing efforts to speed devices to market, while important, focus on other aspects of the life cycle. Those initiatives include investments in regulatory science, fostering collaboration between FDA and industry and moving product applications to the front of the review queue; none of these efforts directly affect clinical trial lengths. FDA's only program to directly shorten product development times—the Humanitarian Use Device designation—is only for products that treat conditions afflicting fewer than 4,000 patients per year. For the majority of patients with serious medical conditions and no therapeutic options, existing FDA programs do not meaningfully shorten the duration of product development.

A new approach is needed to reduce clinical development times for devices to treat patients with serious, unmet medical needs, while ensuring that needed data on device safety and effectiveness is ultimately collected. FDA can do this by accepting more uncertainty about potential risks of these products at the time they are marketed and then leveraging postmarket tools to collect additional data. This approach would recognize that FDA never has complete knowledge about all the effects of a given technology at the time of approval and must use a total product life-cycle strategy to regulate new devices.

FDA's proposals in these guidance documents have the potential to fill that void, but only if the agency recognizes certain key considerations necessary to meaningfully reduce premarket development times while ensuring the sufficient collection of postmarket data.

Prompt completion of postmarket studies is essential

The success of shifting data typically collected premarket to after approval relies on the prompt collection of postmarket data. Often, despite current FDA requirements for manufacturers to conduct postmarket trials, commencement of those studies is delayed. For example, in May 2011 FDA responded to concerns of high failure rates with metal-on-metal hip implants by ordering manufacturers to conduct postmarket studies assessing adverse events associated with the products. Despite that order, by June 2012 postmarket study plans for less than one-quarter of metal-on-metal hip products were in place.[2]

These types of delays will undermine efforts to shift premarket data to the postmarket setting. Accordingly, FDA must ensure that the postmarket study plans are quickly finalized and the trials efficiently executed. FDA's proposal to require the submission of a Data Development Plan—to articulate the data that will be collected premarket and postmarket—should alleviate some challenges finalizing postmarket study designs. However, FDA should also consider only approving applications

under the policies articulated in these guidance documents once the manufacturer and agency have fully agreed to the postmarket study plan.

Additionally, FDA must have the ability to quickly withdraw approval for a device if the necessary postmarket data are either not collected or demonstrate that the product does not meet the agency's approval standards. While FDA has the ability to deem products misbranded and take administrative actions to withdraw approval, removing products from the market can still take several months—if not longer. In the interim, patients may continue utilizing products that are unsafe or ineffective.

FDA should also consider requiring the initiation of postmarket trials and completion of those studies within a certain timeframe. If manufacturers do not meet those deadlines, FDA should automatically begin proceedings to revoke approval of the device. For example, FDA could inform manufacturers that they have six months to begin patient enrollment in postmarket studies, and three years to complete those trials. Failure to meet those deadlines would result in the revocation of approval.

FDA—and Congress—should evaluate whether FDA has sufficient authorities to promptly withdraw product approvals if the necessary data are not promptly collected or suggest that the product benefits do not outweigh risks. Should FDA lack these authorities, Congress should provide the agency with enhanced abilities to protect the public when manufacturers do not fulfill their postmarket responsibilities.

The importance of a robust postmarket surveillance infrastructure

Effective and prompt execution of FDA's National Medical Device Postmarket Surveillance Plan, which will help identify and address problems with all devices, is particularly essential when FDA has less premarket data on devices at the time of approval.

Key to the agency's postmarket surveillance plan is the adoption of the unique device identifier (UDI) system throughout health care delivery.[3] The UDI system will provide each device with a code corresponding to its make, model and other clinically relevant information.[4] Through UDI capture in electronic health information—including electronic health records (EHRs) and claims—FDA, researchers, manufacturers, payers and providers will have the data necessary to quickly identify safety or quality problems and remove those products from the market.

UDI capture in EHRs can support hospital analyses on product performance in their patients.[5] Similarly, documenting UDI in claims would offer large, longitudinal data sets to analyze device performance—including when patients switch providers or seek care from multiple clinicians.[6] The FDA's Sentinel Initiative, which relies primarily on claims data, could also assess device performance as has been successfully done for drugs. FDA must coordinate with its federal partners to develop a nationwide strategy for UDI adoption in these electronic health data sources.

Implementation of UDI and the rest of FDA's National Medical Device Postmarket Surveillance Plan will provide the critical data needed to better understand the safety and effectiveness of devices, enabling FDA, clinicians, manufacturers and researchers to gather data demonstrating devices' safety and effectiveness and to identify problems with new technologies much sooner.

Registries can support both postmarket surveillance and innovation

Registries—large databases that collect information on a group of patients treated for a particular medical condition—are also vital for tracking device performance over time and can support both postmarket monitoring and efficient premarket data collection.

Typically, medical product registries in the United States have been used to conduct postmarketing surveillance by tracking the experience of a broader patient population for a longer period of time than was studied in premarket clinical trials. For example, FDA has used data from the American College of Cardiology's National Cardiovascular Data Registry to investigate potential safety problems with cardiac devices. FDA should emphasize the potential of registries to collect information on devices when the agency shifts data requirements to the postmarket setting.

FDA should also, though, recognize the ability of registries to expedite patient access to new devices. In these guidance documents, FDA outlines several ways to streamline clinical trials—such as through the use of surrogate endpoints and two-part trials; the agency should add the use of registries to the list of possibilities for facilitating faster product development by serving as platforms for more efficient premarket clinical trials.

A recent clinical trial conducted in Europe demonstrated the ability of registries to quickly and cost-effectively collect large amounts of data. The researchers conducted a "registry-based randomized clinical trial" involving more than 7,000 patients that lost no one during the follow-up period. This unprecedented study only cost $300,000, roughly $50 per patient. Conducting such a study outside of a registry in the United States would cost hundreds of millions of dollars, if not more.[7]

In another example, FDA approved an expanded indication for an innovative heart valve based on the use of an existing registry. FDA instructed the manufacturer and two clinical societies to utilize the registry to collect data in lieu of conducting a clinical trial.[8]

Additionally, registries can provide FDA with assurances that the agency will be able to collect the necessary information on products approved when shifting data from premarket trials. FDA may be reluctant to approve products more quickly if the agency is not confident that safety problems will be detected in the postmarket setting. Registry adoption should mitigate that risk and enable FDA to implement the premarket provisions of these guidance documents.

Clarifications needed to ensure safety and effectiveness

Several other changes to the guidance documents are necessary to expedite the approval of new devices while ensuring appropriate safeguard to protect patients from unnecessary harm.

First, FDA must ensure that shifting premarket data to the postmarket setting only occurs for products when patients with serious medical conditions lack sufficient treatment alternatives. Devices designated for expedited approval should be the exception—not the rule. FDA must work with

patients, physicians, consumers and payers to ensure that the criteria used to select devices appropriately reflect only the highest priorities for improving patient care.

Second, FDA should consider special controls to ensure appropriate utilization of approved devices. Such controls could include special training for physicians before utilizing these products or require physicians to document care in a registry. Such postmarket controls already exist for drugs with the Risk Evaluation and Mitigation Strategies program, and may be appropriate for devices approved when shifting data collection.

Third, FDA should ensure that postmarket studies for devices approved based on intermediate or surrogate endpoints evaluate clinical endpoints. In some cases, changes to intermediate or surrogate endpoints are reasonably likely—but not proven—to correlate with meaningful clinical benefits to patients. FDA must have the confirmatory evidence on the validity of intermediate or surrogate endpoints.

Fourth, FDA must ensure that patients are involved in decisions around expediting approval of new technologies and implementing postmarket controls to further evaluate the safety and effectiveness of new devices. Patients, especially those with serious unmet medical needs, are often willing to accept risks for access to new technologies, but they also rely on FDA to quickly identify problems with those products. Their perspective will be integral to the successful implementation of these guidance documents.

Fifth, FDA and manufacturers must ensure that both patients and physicians are fully informed on outstanding questions regarding the performance of technologies approved when FDA shifts data collection to postmarket trials. Product labels should clearly articulate potential safety or effectiveness concerns studied in the postmarket setting. Both FDA and manufacturers should also proactively inform physicians and consumers—through Dear Doctor letters and other public notifications—on postmarket trial requirements and updated data from those studies.

Finally, FDA approval alone does not guarantee patient access to these devices. Payors—including CMS—also require data to inform their coverage and reimbursement decisions. Just as FDA collaborates with CMS as part of the parallel review program to ensure that premarket data can sufficiently support Medicare coverage decisions, FDA must also involve payors in establishing appropriate data collection plans when shifting evidence collection to the postmarket setting.

Conclusion

The new FDA policies articulated in these draft guidance documents have potential to expedite patient access to devices to cure, treat or diagnose unmet medical needs. The success of these policies, though, relies on the efficient collection of data—both pre- and postmarket. Prompt completion of postmarket trials, adoption of the UDI system and utilization of registries are key factors to the success of these proposals.

Thank you for your consideration of our comments. Should you have any questions or if we can be of assistance, please contact Josh Rising, director of medical devices at The Pew Charitable Trusts, at 202-540-6761 or jrising@pewtrusts.org.

Sincerely,

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[1] The Pew Charitable Trusts. Meeting Summary: Patient Access to High-Risk Devices for Unmet Medical Needs. January 30, 2014. http://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2014/05/19/patient-access-to-highrisk-devices-for-unmet-medical-needs. Accessed July 8, 2014.

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[3] U.S. Food and Drug Administration. Strengthening our National System for Medical Device Postmarket Surveillance. http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/UCM301924.pdf. Accessed February 6, 2014.

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[5] Voluntary 2015 Edition Electronic Health Record (EHR) Certification Criteria; Interoperability Updates and Regulatory Improvements; NPRM. 45 Fed Reg 170 (2014).

[6] Workgroup for Electronic Data Interchange Foundation, "Unique Device Identifiers: Facilitating the Capture and Transmission of UDI," (April 7, 2014).

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