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REGULATION

Hearing voices: FDA seeks advice from patients

NO DOUBT CAN REMAIN AS TO THE GROWING IMPORTANCE OF THE PATIENT'S VOICE in biomedical research and regulatory science after U.S. President Barack Obama clearly stated that people would not be treated as subjects in the Precision Medicine Initiative but would be partners in the process. He said, "… I'm proud we have so many patients' rights advocates with us here today. They're not going to be on the sidelines. It's not going to be an afterthought. They'll help us design this initiative from the ground up, making sure that we harness new technologies and opportunities in a responsible way" (*1*).

The latest bold commitment comes from the U.S. Food and Drug Administration's (FDA's) Center for Devices and Radiological Health (CDRH), which has opened an announcement in the Federal Regulations establishing a patient engagement advisory committee to advise the FDA commissioner (or designee) on complex issues related to the regulation of medical devices and their use by patients. CDRH's acting associate center director of science and strategic partnerships, Kathryn O'Callaghan, specifically noted during her presentation on 6 October 2015 at the AdvaMed 2015 conference that patient input informs the total medical product life cycle by providing (i) patient-informed needs during discovery and ideation, (ii) patient-informed clinical trial design and patient-reported outcomes in the clinical phase, (iii) patient preference regarding benefit-risk information in regulatory decision-making, (iv) communication of benefit-risk information to patients during product launch, and (v) patient-centered outcomes as products are launched and transitioned to postmarket monitoring. CDRH has also been engaged in a project with the Medical Device Innovation Consortium (MDIC) (*2*) to develop a patient-centered benefit-risk assessment framework and catalog of methods to help patients and providers better understand patient preferences regarding clinical benefits versus risks of devices, including those related to the treatment of obesity (*3*).

CDRH's action to involve people beyond the traditional one-patient-representative-per-panel model for FDA advisory committees is laudable. It is appropriate to give voice to the people who bear the risks and receive the benefits of medical devices because they will create a more robust engagement system. The greatest advances in research and clinical trial design have come from collaborative learning among the diverse stakeholders in the biomedical research ecosystem, and the new engagement advisory committee must assert its influence over all aspects of the medical product life cycle.

Best practices for effective patient engagement in research recognize patients as equal partners in the translational continuum (*4*). As noted by the Clinical Trials Transformation Initiative (CTTI) (www.ctti-clinicaltrials.org) and PCORnet (www.pcornet.org)—a network funded by the Patient-Centered Outcomes Research Network (PCORI; www.pcori.org)—the convening of a stand-alone patient advisory council carries risks, such as siloing the patients from the main activities of the entity or considering their contributions to be less valuable than those of other stakeholder groups. CTTI—a FDA public-private partnership hosted by Duke University with more than 60 diverse member organizations—explored such a model and went beyond it to embrace one in which advocacy leaders and participants in research are part of all organizational activities and project teams working on each step in the translational continuum and systemic improvements in the clinical trials enterprise. It is critical that FDA use CDRH's patient-engagement advisory committee to enable consequential patient participation in all aspects of device development, regulatory frameworks, and follow-up postmarket analysis. The committee structure will include patients and their advocates, as well as nonvoting members from other sectors of the device ecosystem. However, the panel's true potential can only be harnessed by transcending an advisory model and, instead, crafting one in which patients work hand-in-hand with regulators and other stakeholders in a collaborative and iterative manner.

Several examples illustrate how a device community of all stakeholders can be built to meet the needs of the users. Hugo Campos, user of a cardiac defibrillator, has been outspoken about gaining access to the data collected by his implanted device. Advice from Campos

is quite clear: Individuals must be active in their own health management, and to do that, they must have access to all of the electronic data about them and their health. Campos is a patient leader in a number of networks, including PCORnet (www.npr.org/sections/health-shots/2012/05/28/153706099/patients-crusade-for-access-to-their-medical-device-data).

Each of the coauthors of this editorial has firsthand experience with devices that are under the purview of CDRH. Patrick-Lake was a participant in a device clinical trial, designed without patient input, in which she received an investigational implanted cardiac device. That trial was later aborted because of low and slow enrollment. In the case of Patrick-Lake's investigational device exemption (IDE) study, no data were shared with study participants or published, the science was not moved forward, no product reached the market, and millions of dollars were wasted. She has since dedicated her career to bringing the patient voice to research design and regulatory frameworks through her work at CTTI and Duke University, on PCORI grants, and through service on leadership and advisory committees at FDA, PCORnet, MDIC, the Medical Device Epidemiology Network Initiative (MDEpiNet), and the Precision Medicine Initiative Working Group of the Advisory Committee to the NIH Director. Specifically, at CTTI, Patrick-Lake now leads a multistakeholder project team that created evidence-based best practices for effective engagement with patient groups around clinical trials (www.ctti-clinicaltrials.org/files/PatientGroups/PGCTrecs.pdf); the project team is now measuring the value and impact of patient group engagement methods on clinical trials. These experiences have led her to a place of conviction regarding the value and mutual benefits a device community with truly engaged patient partners could bring to sponsors of research, investigators, regulators, and, most importantly, patients.

Genetic tests are regulated as devices and thus receive oversight from CDRH. Coauthor Terry created a genetic test for mutations in the ABCC6 gene that cause the rare connective tissue disorder pseudoxanthoma elasticum. This test was considered to be a laboratory-developed test and, therefore, did not require FDA approval at the time. Still, PXE International, the advocacy group directed by Terry, elected to submit the test to CDRH for approval in 2005 in order to (i) evaluate the test in accordance with the most rigorous assessment available; (ii) provide individuals using the test with assurance that it was held to the highest available standards for analytic and clinical validity; and (iii) enable distribution of the test in kit form so that it was affordable and widely accessible.

Unfortunately, throughout the years 2005 and 2006, the bar for the number of individuals that had to be genotyped to achieve CDRH's requirements for approval kept moving higher, which eventually led the company that provided pro bono assistance to PXE International to decide that it was taking too much of a loss. The community of patients provided clear input regarding their needs: an affordable, reliable genetic test for this rare disease. Although CDRH did its best at the time, the decision-making process was not able to reflect the needs of the community, nor was it able to calibrate the requirements based on the size of the community. In this case, having engaged and articulate patients participate in all aspects of the development process was not enough to find a regulatory pathway that would enable dissemination of an affordable and accessible test kit. Certainly, subsequent discussions at CDRH and recommendations in the genetic testing community have resulted in a more nuanced proposed tiered structure that reflects the needs of the community (*5*). Terry also drives several patient-preference projects, using a platform called Platform for engaging everyone responsibly (*6*), aimed at gathering information for FDA. This advisory committee will engage patients at the same time as the emergence of medical device innovation, integration of digital health technologies, new models for clinical trials, and patient engagement (*7*). Terry is also a cofounding steering committee member of the Coalition for 21st Century Medicine, a multistakeholder group dedicated to developing and making available diagnostics designed to improve health.

However, an advisory committee can constitute a token attempt to appear more patient-centric. Today, it is fashionable to include people as partners, but patients do not just want to have a seat at the table any more; they want to help plan when and where the meal will take place, what will be on the menu, and who else will be invited.

Clearly, we applaud the many advocates and patient groups taking a more active role in research. However, it is also inappropriate and potentially detrimental to shift to the other extreme: elevating patients to a privileged place above all other stakeholders. The CDRH patient engagement advisory committee has an opportunity to model appropriate patient engagement in its charter and the philosophy of the committee itself. Device development

should be a team effort. Researchers, clinicians, industry, patients, and regulators are all stakeholders with a strong vested interest in the end result: more innovative medical devices, successful clinical trials, and improvements in health.

It is critical that all stakeholders who will be affected by CDRH oversight of devices contribute comments to FDA's announcement on the patient-engagement advisory committee by the submission deadline, 20 November 2015. The FDA is offering an opportunity to comment on topics such as (i) how patients can and should be engaged in the pre- and postmarket phases, (ii) how patient-preference data should be used to guide the regulatory process, and (iii) what patients understand about informed consent in clinical trials.

Stakeholders can submit comments electronically or in the form of a written letter to the FDA Division of Dockets Management (*8*). Comments should be identified with the docket number FDA-20150N03166.

– Sharon F. Terry and Bray Patrick-Lake

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8. Submit electronic comments at www.regulations.gov/#!documentDetail;D=FDA-2015-N-3166-0001. Mail written comments to the Division of Dockets Management (HFA-305), FDA, 5630 Fishers Lane, Room 1061, Rockville, MD 20852, USA.

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