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The Patient Perspective: Putting the Patient at the Center of the Translational Innovation Process

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Abstract

After centuries of physicians believing that they know what is best for patients, this paternalistic approach to patient care is being challenged. The explosion in readily accessible information has resulted in patients being empowered to take on a greater role in decision making, from clinical care to regulatory decision making. The Centers of Excellence in Regulatory Science and Innovation (CERSIs) are collaborating with the US Food and Drug Administration (FDA) to promote patient engagement and advance patient preference research.

PATIENT ENGAGEMENT IN HEALTH CARE

There is increasing interest in using real-world evidence in health care. This provides an opportunity to engage more patients and treat each patient as an individual with a voice. Patient-generated data can be an essential component of real-world evidence, though there are some challenges with utilizing this data effectively.[1] In the past few years, the FDA has increasingly sought to engage patients in the regulatory review process for medical products. These efforts include the Patient-Focused Drug Development Initiative in the Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), which resulted in a series of FDA-led, disease-specific public meetings to obtain patient perspectives. Similarly, the Center for Devices and Radiological Health (CDRH) launched the Patient Preference Initiative in 2013 to "advance the science of measuring patient preferences to inform benefit–risk assessments used in regulatory decision making."[2,3] This initiative has also inspired or commissioned many other proof-of-concept studies of patient preference for preference-sensitive conditions to enable the use of patients' benefit–risk weighted trade-offs as scientific empirical evidence in regulatory decision making.[4–8]

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CONFLICT OF INTEREST

Kuldev Singh is a consultant for Alcon, Allergan, Glaukos, Ivantis, and Sight Sciences. All other authors declared no competing interests for this work.

CASE EXAMPLES

An early example that demonstrated the power of patients to affect regulatory decisions by collecting data on patient perspectives was for disease-modifying therapies for patients with relapsing-remitting multiple sclerosis. Natalizumab, approved by the FDA in November 2004, showed a dramatic positive effect on patient outcomes, but the drug was removed from the market 4 months later due to a rare risk of progressive multifocal leukoencephalopathy (PML). The National Multiple Sclerosis Society commissioned an 810-patient survey to probe the level of risk patients were willing to accept in order to continue to use natalizumab. The survey results identified a segment of users that were willing to accept the PML risk for the benefit they were receiving from the drug, and natalizumab was returned to the market shortly thereafter with a risk management program in place and a black box warning. Other patient preference studies have since shown that patient views can vary significantly, with many patients being less risk-averse than the FDA and their physicians.[4–6,9,10] More recently, the FDA conducted a patient preference study that resulted in a decision aid tool to inform benefit–risk assessments for premarket approval of medical devices. A vagus nerve gastric stimulatory device for weight reduction demonstrated safety in a trial but failed to meet its primary end point for efficacy of a 10% difference in weight loss at 12 months compared with a sham control group. However, this patient preference study demonstrated that a large proportion of obese patients would accept the risks of a surgically implanted device if they lost the amount of weight seen in the clinical trial.[8] This was the first quantitative preference study designed and used to support a regulatory approval decision by CDRH and provided a proof of principle on how patient preference information may be considered in the approval of medical devices. These initial cases have encouraged the FDA to continue conducting research and case studies on using patient preference information, often with the CERSIs.

CERSIs

The FDA-funded CERSIs are working on the development of tools, methods, scientific expertise, and education of new scientists and users of patient preference information as part of its overall mission to advance regulatory science through scientific exchange, innovative research, and education/training. As an example of scientific exchange, in December 2017, the CERSIs jointly organized a workshop with FDA centers (CDRH, CBER, and CDER) to advance the use of patient preference information as scientific evidence in medical product evaluation. This workshop highlighted the immediate need for capacity building and sustainability by outlining a framework of five main priorities to be addressed by collaboration among patients, academics, professional societies, industry, and the FDA. These include: (i) human resource development through training and education, (ii) method development using rapid learning through high-quality research, (iii) use of modern data sharing platforms to drive discovery, (iv) organizational development and collaboration promoting shared communication around the patient perspective, and (v) legal and regulatory changes (Figure 1).

UCSF-Stanford CERSI is playing a key role in this by promoting the use of patient preference information in both physician practice and regulatory decision making,

developing educational initiatives around patient preference, and conducting research studies that further the field. This includes methodology research on using patient-generated data, including projects on developing patient-reported outcomes (PROs) for minimally invasive glaucoma surgery and patient preference measurement for prosthetic device innovations, implantable dialysis devices, and islet cell transplants to support FDA approval decisions (www.ucsfstanfordcersi.org/research). In a bi-coastal collaborative effort, the Johns Hopkins and UCSF-Stanford CERSIs teamed up with the FDA's CDRH and the American Glaucoma Society to accumulate patient preference information and develop a PRO tool to support innovation in minimally invasive glaucoma surgery. Once validated, the online PRO tool will be available to supplement information pertaining to clinical end points, including patient-specific data that will weigh into regulatory decisions. In another project, UCSF-Stanford CERSI is working with CDRH, prosthetists, patients with limb loss, and the Amputee Coalition to develop a choice-based conjoint analysis measure to determine which factors were most important to patients when they weighed the risks and benefits of undergoing an osseointegration procedure for prosthetic devices. This approach provides easy snap on of a prosthetic device and better movement, but a constant infection potential, making its use highly patient preference-sensitive. We developed a video-based, choice-based discrete choice measure to learn the benefit/risk assessment of patients in their decisions to adopt these new technologies, and additional funding from the Burroughs Wellcome Fund is now being used to test this measure in patients and analyze their validity. Similar prototype measures are being developed that will test how patients with type 1 diabetes weigh the benefits and risks of undergoing an islet cell transplant procedure, and how patients with end-stage renal disease weigh the benefits and risks of an implantable bioartificial kidney. The goal of all these projects is to obtain quantitative patient-level benefit–risk assessment data that can be incorporated into the FDA's medical product review processes, thus bringing the patient view directly into regulatory decision making. Furthermore, UCSF and Stanford trainees are actively working on several CERSI research projects, which helps to build capacity in this area. We have also had preliminary discussions with the FDA to develop educational initiatives around patient preference.

CONCLUSION

The CERSI program is an ideal collaboration between academic institutions and the FDA, allowing the FDA to leverage resources and expertise located within universities to work on FDA-relevant issues and priorities. This partnership is nimble, scalable, timely, and cost-effective, partly because a new research agreement does not need to be established for each new project, and the mechanism allows for enhanced collaboration and simplified transfer of resources. The FDA's Office of Regulatory Science and Innovation provides core funding to support program operations, collaboration, and pilot research projects. FDA centers can provide additional funding for research projects, subject matter expertise, and training for new scientists through fellowships and regulatory science education. Most important, the CERSI program has recognized the importance of putting the patient at the center of all phases of the translational innovation process, including defining patient needs, patient-centered clinical trial design, use of patient preference information in regulatory assessment, and analysis of patient-reported outcomes for postmarket surveillance (Figure

2). Advancing patient engagement at all levels of product development is a shared goal across the spectrum of stakeholders.

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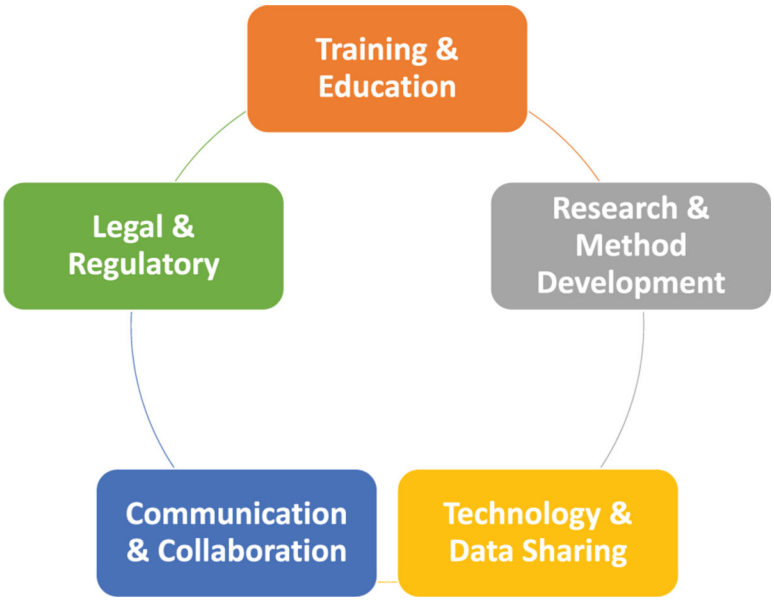

Figure 1.
Framework for capacity building to promote use of patient preference information in regulatory decision making.

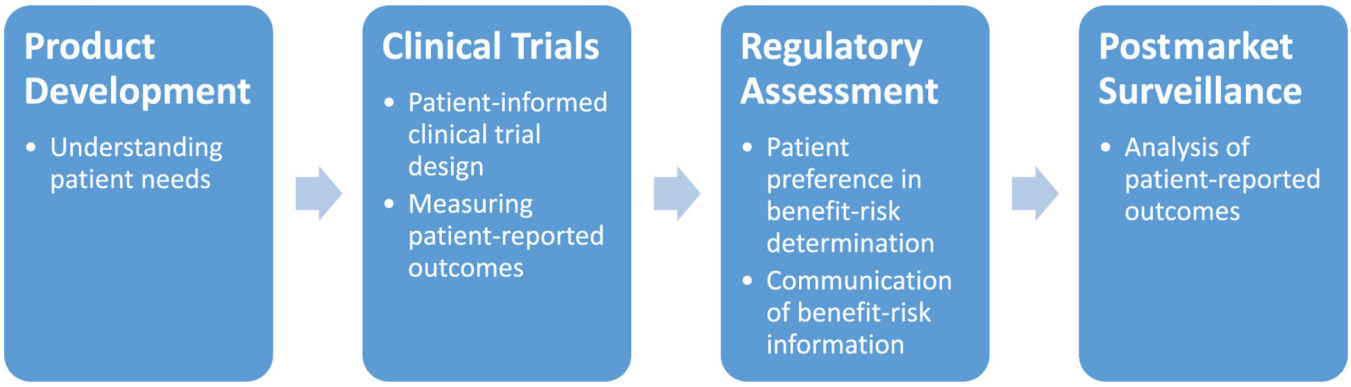

Figure 2.
Patient engagement in the development of medical products.