EXPANDING THE SCIENCE OF PATIENT INPUT:

Pain Points and Potential

FasterCures
A CENTER OF THE MILKEN INSTITUTE

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ABOUT *FASTERCURES*

FasterCures, a DC-based center of the Milken Institute, is driven by a singular goal—to save lives by speeding up and improving the medical research system. We focus on cutting through the roadblocks that slow medical progress by spurring cross-sector collaboration, cultivating a culture of innovation and engaging patients as partners. This report is released under *FasterCures'* program called Patients Count: The Science of Patient Input, which aims to improve health by expanding opportunities for patients' perspectives to shape the processes by which new therapies are discovered, developed and delivered. Find out more at www.fastercures.org.

ACKNOWLEDGMENTS

FasterCures is grateful to Pfizer for support provided to host the February 2016 workshop and launch this initiative. We also appreciate the time and expertise of the workshop participants, whose insights helped inform this report.

"I'd like to see us **integrate patient-centered practices** in such a way that they are part of strategic planning rather than an afterthought."

GOVERNMENT PARTICIPANT IN PRE-MEETING SURVEY

"The common goal for patient engagement that we identified was to have 'continuous and meaningful engagement with the right patients over the entire course of drug development so that medical products would meet **patients' needs and achieve health outcomes** that matter to them.' We also felt that it was important that patients feel heard and understood and to feel that their engagement and their input matter."

REPORT-OUT FROM ONE OF THE AFTERNOON DISCUSSION GROUPS

"In our experience partnering with pharmaceutical companies, the biggest challenge has been turning patient priorities into action steps. We all agree that medicines that meet patients' needs will better serve everyone's interests, but it's not easy to make it happen. We're all learning, including those of us who bring our experience as patients to the **dialogue about patient-centered research and care.**"

PATIENT ORGANIZATION LEADER

Introduction

Patient engagement can influence plans and policies that shape how medical products move from microscope to marketplace, as well as deepen researchers' understanding of the experience of living with a disease or condition.

Patient engagement has been called the "blockbuster drug of the 21st century."[i] Indeed, studies find that the more engaged and involved patients are with their health and health care, the better the outcomes.[ii] There is now growing interest in engaging patients in another aspect of health care: drug and device development. Borrowing methods from the fields of health economics, outcomes research, epidemiology, social sciences and marketing sciences, a new science of patient input has emerged, embracing data as a means for measuring patient-centered outcomes and quantifying patient preferences.

ENGAGING PATIENTS IN RESEARCH ISN'T JUST A GOODWILL GESTURE: IT CAN MAKE RESEARCH BETTER. Patient engagement can influence plans and policies that shape how medical products move from microscope to marketplace, as well as deepen researchers' understanding of the experience of living with a disease or condition. Together, this can inform research priorities and resource allocation. More importantly, patient engagement can lead to better, safer treatments that target what patients really need and want.

Several factors are driving this paradigm shift from patients as *subjects* in clinical research to patients as *partners* in research. They include patients themselves who are challenging the traditionally paternalistic health-care system; regulatory agencies such as the Food and Drug Administration (FDA); government policy initiatives, including the 21st Century Cures Act; the creation of the Patient-Centered Outcomes Research Institute (PCORI); and nonprofits like *FasterCures*, which are dedicated to integrating patient perspectives in medical product development to speed treatments of high value to patients.

We are at the beginning of this effort, however, with numerous unanswered questions. **To explore current and future challenges, *FasterCures* hosted an all-day workshop on Feb. 17, 2016, as part of its Patient Count: The Science of Patient Input program.**

The goals of the meeting were to:

1. **UNDERSTAND INFLUENCES** that were helping or hindering patient-centered activities
2. **IDENTIFY AND PRIORITIZE TOOLS AND TEMPLATES** to reduce resistance and remove practical barriers to patient engagement
3. **SHAPE THE FUTURE AGENDA OF COLLABORATIVE ACTIVITIES** to enable greater patient-centricity

More than 50 representatives from patient advocacy organizations and other nonprofits, biopharmaceutical and medical device companies, academia and government agencies participated. Reflecting the multi-disciplinary nature of the growing science of patient input, participants were invited to ensure representation from several functional areas and backgrounds, including health economics, regulatory science, patient advocacy, benefit-risk assessment, medical affairs, public policy, communications, public affairs, outcomes measurement and alliance development. Patient group representatives brought experience from diverse communities, including rare and prevalent conditions, diseases with multiple therapies and those with no FDA-approved medical products, and highly engaged patient populations and communities that are not well formed yet. Several participants have had professional experience working in one or more sectors, adding further dimension to their viewpoints and the discussion.

Key Takeaways

"At the end of the day, to us it's all about access for patients and creating drugs that patients value and that can help the public health."

SUE VALLOW, HEAD, PATIENT FOCUSED OUTCOMES, GLAXOSMITHKLINE

The *FasterCures* workshop highlighted both the growing pains associated with patient-centric research and the amazing potential. Among the key takeaways:

1. **DISSEMINATE EXISTING TOOLS AND INFORMATION.**
   There is significant activity in the area of patient-centric research, yet no centralized "home" for information.

2. **IDENTIFY AND COMMUNICATE THE VALUE PROPOSITION.**
   What is the impact of patient-centric research and development on patients and industry? Part of this involves telling the stories of success and painting a picture of what will happen if we engage patients, both internally to key constituents and externally through the media, to shape dialogue and inform practice.

3. **DEVELOP MEASURABLE OUTCOMES.**
   There is an urgent need to recruit and train the cadre of social science experts, inside and outside academia, capable of producing the kind of rigorous patient data and analysis that can be relied upon to inform decisions made by developers, regulators and payers.

4. **CRAFT A COMMON LANGUAGE.**
   Even in this gathering of committed leaders, there was clearly a need for more unified definitions of patient-centricity and patient engagement across the research and development spectrum. Participants called for establishing taxonomies of sources and uses of patient data, identifying sources of bias and developing methods for addressing them and other frameworks.

5. **EXPAND THE CHOIR.**
   All agreed it is important to engage more stakeholders, including academic researchers, legal and regulatory representatives and payers.

6. **BUILD CAPACITY.**
   There is an obvious need for capacity building and training in patient groups, industry and FDA to ensure productive collaboration and, ultimately, a stronger pipeline of medical products that improve the most important dimensions of patients' lives.

LANDSCAPE ANALYSIS

FasterCures Managing Director Kim McCleary clearly demonstrated just how far the field has come with her presentation of an environmental scan of current patient-centricity projects.

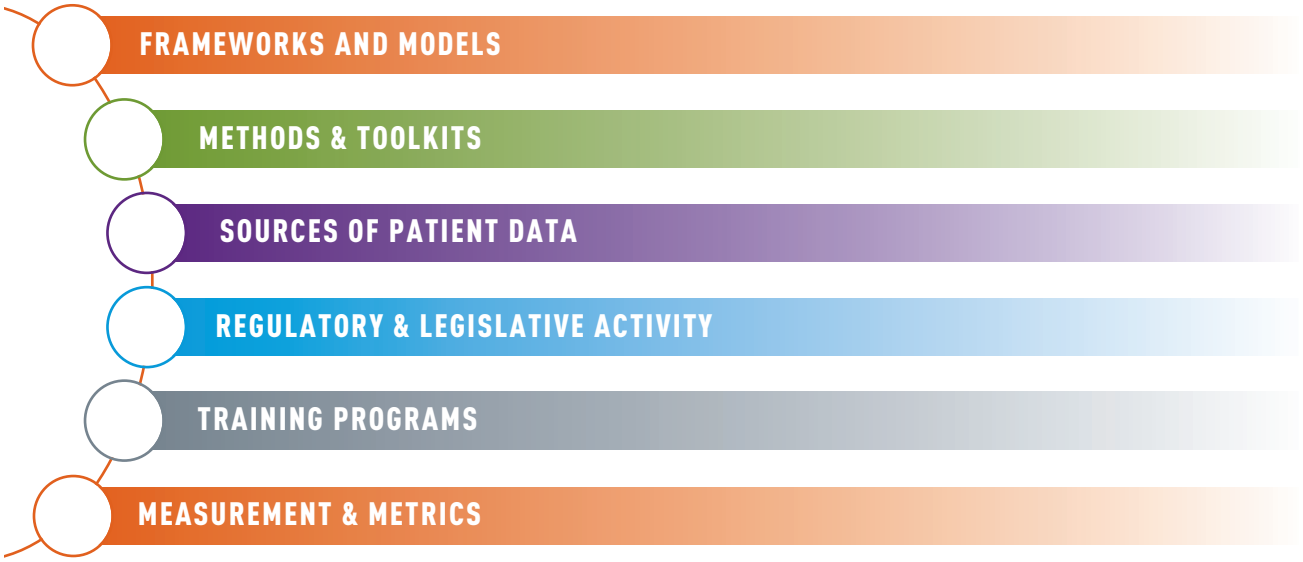
She highlighted more than 70 cross-sector projects in the space led by 35 different organizations and involving more than 100 nonprofits, companies, academic institutions, professional societies and government agencies.

The engagement-enabling activities fell into six categories: frameworks, methods and toolkits, sources of patient data, regulatory/legislative activities, training programs and measurement and metrics.

This environmental scan also formed the basis of a new article by Margaret Anderson, executive director of *FasterCures*, and McCleary, published in the April 27, 2016, issue of *Science Translational Medicine*, "On the path to a science of patient input."

The *FasterCures* workshop highlighted both the growing pains associated with patient-centric research and the amazing potential.

FIGURE 1: A LANDSCAPE ASSESSMENT FOUND THAT MORE THAN 70 COLLABORATIVE INITIATIVES TO ADVANCE PATIENT-CENTRICITY FALL INTO SIX CATEGORIES
SOURCE: *FASTERCURES*



Signs of Success

"We need to make sure that patient voices aren't just testimonials, but that patients are involved in the entire process of drug development from the beginning to the end and post-market."

PATRICK WILDMAN, VICE PRESIDENT, PUBLIC POLICY, ALS ASSOCIATION

Those who are committed to fostering patient-centered practices and those still doubtful about the merits of being more patient-centered share a hunger for real-world examples of the differences patient engagement makes. Thus, the workshop began with representatives from four organizations sharing early progress in patient-centered initiatives, as well as concrete steps their organization is taking to better integrate patient perspectives.

THE ALS ASSOCIATION: A Case Study in Patients Informing Priorities

The ALS Association, the nation's largest nonprofit organization with a sole focus on amyotrophic lateral sclerosis (ALS), has a **strong focus on developing treatments that affect disease domains of high importance to patients**. The success of the "Ice Bucket Challenge" brought new resources to the organization that has enabled greater involvement by patients and family members to inform priorities for the organization and more broadly for the field. Patrick Wildman, the association's vice president for public policy, reported on recent progress:

- **HELD AN FDA HEARING ON ALS DRUG DEVELOPMENT.** The association partnered with the Muscular Dystrophy Association for this 2013 meeting, held just after there was a legislative mandate for patient-focused drug development passed in the 2012 Food and Drug Administration Safety and Innovation Act. More than 200 people attended, and more than 1,000 individuals participated online. Sixty participants delivered powerful testimony, and 800 people submitted written comments. Wildman called the meeting a "watershed moment" for this rare disease community, giving patients and family members a new way to engage and to lead in moving the needle toward patient-centricity.

- **CREATING AN ALS DRUG DEVELOPMENT GUIDANCE DOCUMENT.** At the FDA hearing, the community asked FDA to develop a guidance for industry on ALS to aid in drug development. "Soon after, something called the Ice Bucket Challenge happened, and it changed everything for us, including the resources we had available," Wildman recalled.

Following the model that Parent Project Muscular Dystrophy (PPMD) used to develop an FDA guidance document on Duchenne muscular dystrophy[iii], the ALS Association brought together more than 100 stakeholders from throughout the world, including 10 pharmaceutical companies, several other ALS organizations and about 30 patients and family members. They have kept in close contact with FDA throughout the drafting process. The document is focused in several areas: natural history, diagnosis, biomarkers, clinical trial design, benefit-risk assessment and public policy.

The association plans to submit its guidance to FDA officials in April, and the FDA has agreed to hold a public hearing as part of the comment process to again engage broadly with patients, families and caregivers.

"With all of us working together to make sure that patient voices are heard—not just as testimonials—but that they are really involved in the entire process of drug development from the beginning, all the way through to FDA approval and even after a product is on the market. I think we're making a lot of progress in this space thanks to the work that everyone around this table is doing."

ROSLYN SCHNEIDER, GLOBAL PATIENT AFFAIRS LEAD, PFIZER

PFIZER: A Case Study in Neuroscience and Rare Diseases

Roslyn Schneider, Pfizer's global patient affairs lead, illustrated how one of the world's largest pharmaceutical companies is **leveraging staff with complementary skill sets to meaningfully engage with patients and incorporate learnings from that engagement** across the life cycle of medical products.

She focused on the neuroscience and rare disease areas as being early incubators for this work. Schneider outlined steps taken to map current efforts in patient-centered research, identify gaps and begin prioritizing efforts to close those gaps. Among the concrete steps taken:

- **WORKED WITH PFIZER RESEARCH LEADERS** to identify where in the clinical research plan greater patient input would have had an impact as a means to shape future research plans.
- **CREATED NEWLY DEFINED ADVOCACY AND POLICY LEAD POSITIONS** to drive patient-centricity throughout the medicine development life cycle in neuro-science and rare diseases.
- **JOINED THE CROSS-FUNCTIONAL WORKING GROUP** in the rare diseases group to share tactics and learnings from efforts to better engage patients in the clinical development programs.
- **CREATED NEWLY DEFINED ROLES** on the commercial side to drive community engagement in areas of commercial development.
- **ADDED A PATIENT PARTICIPANT** to an external bioethics advisory panel.

Schneider concluded by noting that she is seeing cultural change within Pfizer as a result of these and others efforts to invite colleagues to think of additional ways that patients could inform their work at each action step along the path to a new product.

"The ability to have a well-characterized registry of individuals living with the disease and recruited from the same sites that are going to be executing clinical trials presents a unique opportunity."

HENRY ANHALT, CHIEF MEDICAL OFFICER, T1D EXCHANGE

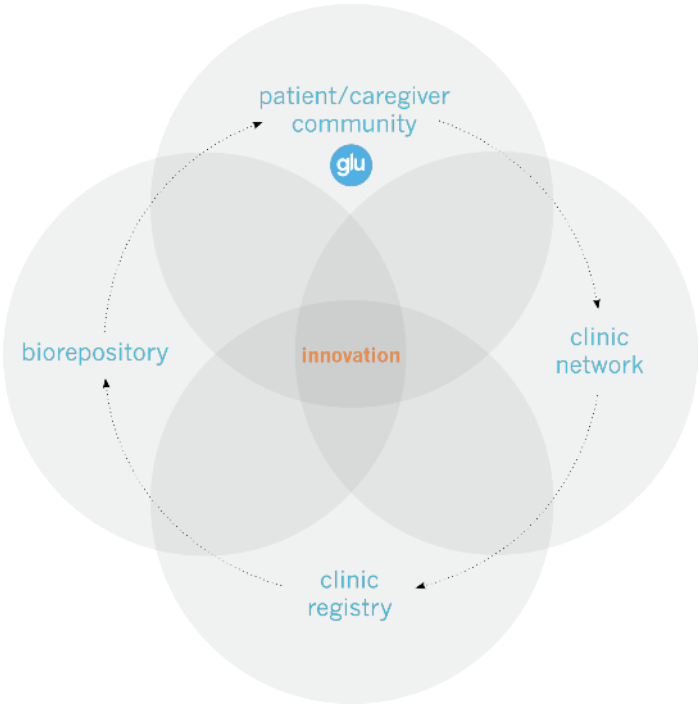
T1D EXCHANGE: A Case Study in Enhancing Networks

As described by Henry Anhalt, chief medical officer, the goal of the patient-centered T1D Exchange is to **improve the lives of people touched by type 1 diabetes by facilitating better care and accelerating the development of new therapies**. He described the challenges that people living with type 1 experience, "swimming upstream against therapeutic inertia" with a condition that is left almost entirely to the patient to manage hour-to-hour, day-to-day. The exchange has developed several patient-centric tools designed to enhance clinical research efforts in this area. They include:

- **A CLINICAL NETWORK.** This involves more than 75 clinics across the United States, a clinical registry with data collected from more

FIGURE 2: THE INTERRELATED APPROACHES T1D EXCHANGE TAKES TO ENCOURAGE PATIENT-CENTRICITY IN RESEARCH

SOURCE: T1D EXCHANGE



than 27,000 patients and a biobank housing a vast collection of biosamples. Together they accelerate the pace of research and discovery and improve patient care. Anhalt observed, "The ability to have a well-characterized registry of individuals living with the disease and recruited from the same sites that are going to be executing clinical trials presents a unique opportunity."

- **AN ONLINE PATIENT/CAREGIVER COMMUNITY.** More than 15,000 patients, caregivers and supporters participate in the community, called Glu. Their discussions lead to "crowdsourced" citizen science that provides a fresh perspective for research as well as clarity around patients' unmet needs. This helps T1D Exchange make a strong case for research in those areas and overcome clinical inertia. Researchers also use Glu to collect patient perspective data in numerous ways, from simple polls and a "question of the day" to robust longitudinal studies. The community has also provided important input into the development of a new continuous glucose monitor, as well as on topics ranging from hypoglycemia to programming for camps for children with type 1 diabetes.

THE POWER OF AN ONLINE PATIENT COMMUNITY

When a small pharmaceutical company wanted to collect patient data about injectable glucagon, it turned to Glu, T1D Exchange's 15,000-member online patient community. The response from the community regarding the challenges of using currently available injectable glucagon helped define the patients' unmet need, established the business case for an alternate delivery method for glucagon and spurred support for clinical trials on an intranasal spray form of this vital therapy.

According to Henry Anhalt, "T1D Exchange became the nexus between a small biotech company, a funder, a clinical trial registry, a network of clinics and a patient engagement platform. We were able to bring all the stakeholders together and in an incredibly short period of time completed phase III studies of the product. Soon after, Eli Lilly acquired the worldwide rights to continue development. My hope is that they will deliver this product to market so kids can have sleepovers with their grandparents free from the worry about a scary and unfamiliar injection protocol to administer."

"People feel very isolated, and it can be extremely hard to identify and engage patients and their families. Even though our commitment starts at the top with our CEO, Richard Pops, we have a challenge ahead of us."

NIKKI LEVY, VICE PRESIDENT, PATIENT ENGAGEMENT, ALKERMES

ALKERMES: A Case Study in Involving Patients in Research

As vice president of patient engagement for a global biopharmaceutical company focused on developing drugs to address mental health disorders such as depression, schizophrenia and addiction, Nikki Levy recognizes the challenges these affected communities face, given the stigma attached to these conditions. She also noted the major impact these mental health conditions have on the people around the patient—the family, the caregivers, the community, society. "People feel very isolated, and it can be extremely hard to identify and engage patients and their families. Even though our commitment at Alkermes starts at the top with our CEO, Richard Pops, we have a challenge ahead of us."

Levy stated that until fairly recently, the patient advocacy groups serving these conditions primarily focused on supporting families and individuals and connecting them to resources, rather than involving them in research. Thus, Alkermes has **several initiatives designed to facilitate opportunities to elicit patient perspectives that can inform research**:

- **CAPACITY BUILDING.** The company is working with numerous patient advocacy organizations to help them expand from their historic focus on patient support to providing input into the clinical trial process, including identifying patients for studies. To that end, Alkermes has committed to regular communication and transparency. For instance, a day after two of its clinical trials in depression failed to meet their endpoints, the company's CEO held a conference call with leaders of mental health patient organizations to provide context and to reinforce the company's continued commitment to research in this area.

- **SUMMIT DEVELOPMENT.** The company recently hosted a summit for advocacy groups to learn from one another, make connections with Alkermes' team and encourage greater synergies between organizations.

- **COMPETITIVE GRANTS.** Alkermes is launching a grant program to empower patient organizations to propose creative ways for the company to better incorporate patient perspectives into drug design and clinical trials.

ASSESSING THE CURRENT STATUS OF PATIENT-CENTRICITY

FasterCures **distributed a pre-meeting survey to attendees to assess the current status and understanding of patient-centered research. While not scientifically valid, it provided a snapshot of meeting participants' thoughts on patient-centricity in designing and developing treatments.**

Respondents were asked to use the human lifespan to gauge the maturity of patient-centric medical research. Most respondents said the field was still in its teenaged years, or, as one person wrote: "In the phase of trying new things, but a bit awkward in execution. Still lacking a clear vision of what the future holds and what success will look like, but putting significant effort into trying to move in the right direction."

Another respondent wrote that "the science of patient input affects multiple functions but is not broadly understood," while another said that too often the patient perspective is viewed as a separate issue rather than integrated into the larger discussion about drug and device development. *FasterCures* also polled meeting participants on the greatest challenges to patient-centric research. Among the write-in responses were these:

- **Obtaining buy-in about incorporating patient-centered practices across the organization, not just in a few areas**
- **Making the value proposition apparent**
- **Going from "buzzword" to actually integrating a patient-centered strategy**
- **Translating patient priorities into action items**
- **Integrating patient perspectives, rather than viewing them as a separate add-on**
- **Adapting existing processes and resources to be more patient-centered**
- **Determining which patient-centered practices are relevant**
- **Demonstrating the positive impact of patient-centered practices**

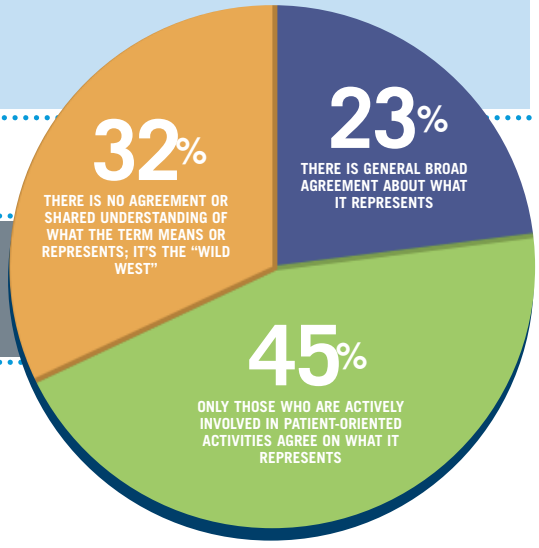


FIGURE 3: PARTICIPANTS' PERCEPTION OF THE TERM "PATIENT-CENTERED" AS REPORTED IN A PRE-WORKSHOP SURVEY

SOURCE: *FASTERCURES*

Science of Patient Input: The Need for a Common Language

"When you're in a meeting like this and people start talking about shared taxonomy and methods, it may not sound sexy, but it tells you we're getting to the heart of the matter. That's something to get excited about."

WORKSHOP PARTICIPANT

Patient-centric. Patient-centered. Patient-focused. Patient engagement. Patient empowerment. These are just some of the terms used to describe initiatives designed to more fully involve patients in R&D and health-care delivery. But, what do they really mean?

"It is completely amorphous," said one participant, who works for a patient advocacy organization. "We need some common definitions and common benefits for everyone." Another participant recognized that this call for common terms was progress itself: "When you're in a meeting like this and people start talking about shared taxonomy and methods, it may not sound sexy, but it tells you we're getting to the heart of the matter. That's something to get excited about."

An industry representative said that while her company's senior management strongly supports the idea of patient-centered research, "they want to know what the real definition is and what the vision is. What does it look like when that partnership really works?" Creating a vision and a communication plan would enable greater implementation and operationalization, she said.

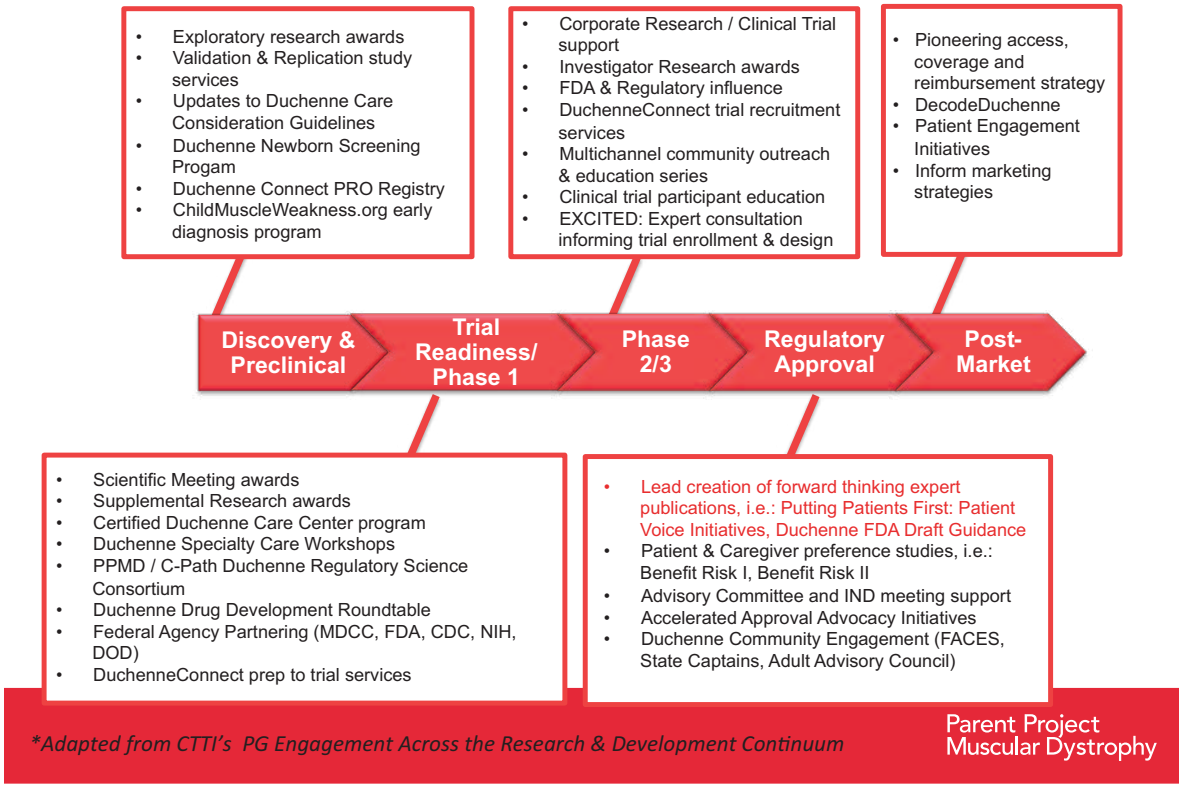
One participant urged that the vision should "identify the outcomes patients want and the treatments that help them achieve their goals and aspirations, and provide those treatments within the context of their current situation and life experiences."

SETTING EXPECTATIONS

To clarify its definition of patient-centric research, PPMD, an organization dedicated to ending Duchenne muscular dystrophy, provides industry partners with a graphic illustrating its vision of patient-engaged drug development and where PPMD has assets that can help reduce barriers to entering into patient-centered research and care. This addresses any preconceived notions of patient-centricity the company may have before meeting with PPMD. The tool has helped reduce companies' resistance to patient involvement and shift their perception of PPMD from one that just recruits for clinical trials to one with a more sophisticated approach to fostering research and engaging a more empowered patient community.

FIGURE 4: BROADLY ENGAGING THE DRUG DEVELOPMENT PIPELINE

SOURCE: PARENT PROJECT MUSCULAR DYSTROPHY

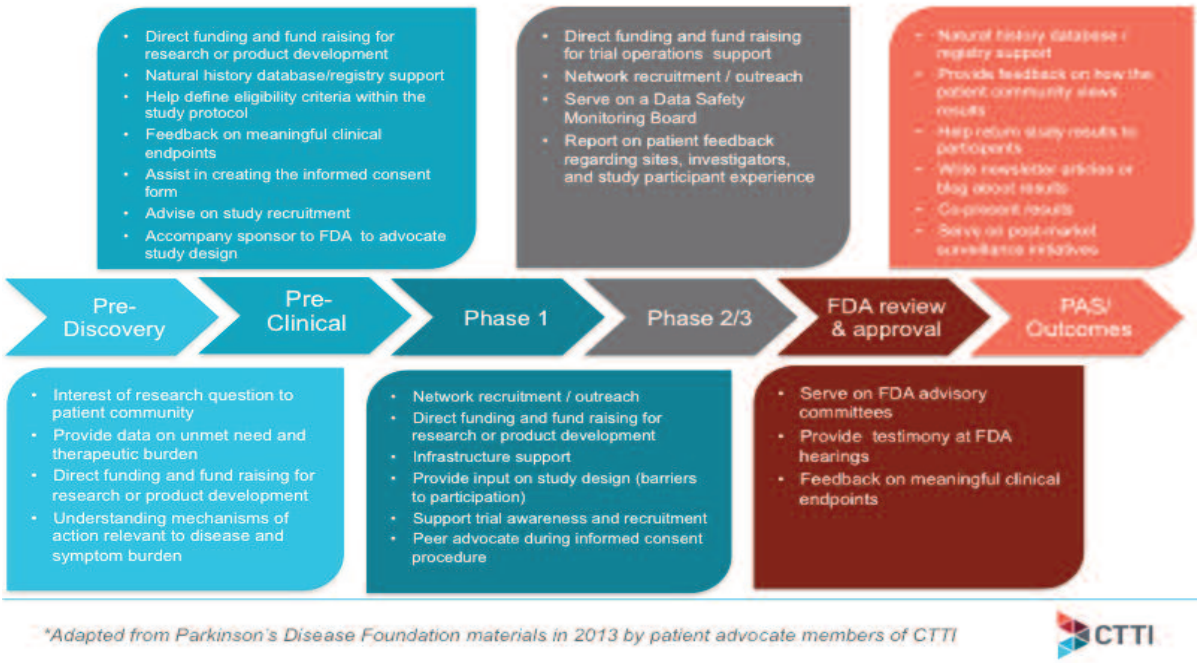


The Continuum of Patient Engagement

THROUGHOUT THE DAY, PARTICIPANTS DISCUSSED VARIOUS APPROACHES TO ENGAGING WITH PATIENTS AND EXPERIENCES INVOLVING THEM IN DIFFERENT ASPECTS OF RESEARCH AND MEDICAL PRODUCT DEVELOPMENT. Frameworks for guiding activities have been helpful, including the model popularized by the Clinical Trials Transformation Initiative (CTTI) with its chevrons indicating steps from pre-discovery research to post-market and ways in which patients and/or patient advocacy organizations might be involved, seen in Figure 5.

Another model for patient engagement was described by Kristin Carman, vice president and director of the Center for Patient and Family Engagement at the American Institutes for Research. She referenced an article she co-authored in *Health Affairs* that illustrates how patients, families and health-care professionals can work in active partnership to redesign the parts of the system that are not working, and she outlined the movement from engaging patients in consultation to involvement, partnership and shared leadership,[iv] as shown in Figure 6. She suggested thinking in these dimensions can help ground the conversation and define the goals of the activity. "It might be consultation in one setting and shared leadership in another, but having a means to categorize the objectives helps people communicate and resolve tensions." She also encouraged patient

FIGURE 5: PATIENT GROUP ENGAGEMENT ACROSS THE RESEARCH & DEVELOPMENT CONTINUUM
SOURCE: CLINICAL TRIALS TRANSFORMATION INITIATIVE



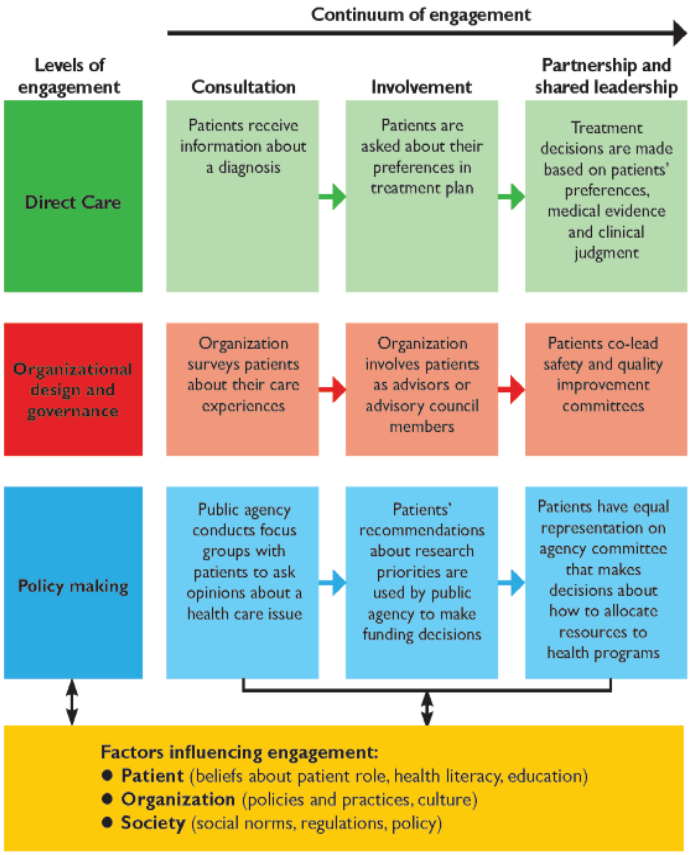
and family participation in defining agendas and decision-making at the point of care, in health-care organizations and in policy-making.

DEFINING COMMON TERMS AND UTILIZING FRAMEWORKS TO GUIDE DISCUSSION CAN HELP ALIGN THE GOALS BETWEEN PATIENTS AND RESEARCHERS, PARTICIPANTS SAID. For instance, when the Cystic Fibrosis Foundation asked the clinical community and patients to define best outcomes related to pulmonary exacerbations, researchers cited restoring lung function while patients wanted to return to their lives and spend less time in the hospital.

This is a good example, one participant said, of the need to drill down and ask patients specific questions. "Then we get to a point where we can start to design studies that are going to have a return on the investment into patient-centricity." Another participant drew on experience working with the HIV community to define patient population subsets, understand their unique challenges to accessing care, and cooperatively defining treatment guidelines and policy measures to help them get the care they needed.

One participant from a patient advocacy organization remarked on the difficulty of dealing with different functional teams within a biopharmaceutical company. From the organization's perspective, the individuals and the needs of the R&D teams were completely different and detached from the teams on the commercial side, and it was challenging to align interests even with the same company on the same product because the objectives changed. "They become parallel efforts, which worries us because we believe pulling that information together would be beneficial – to the company, to our efforts on behalf of patients and ultimately to patients themselves."

FIGURE 6: CONTINUUM OF PATIENT ENGAGEMENT
SOURCE: HEALTH AFFAIRS



Building Alliances with Academic Researchers

"Patients serve at the center of all NCATS activities, and we are looking for more substantive and structured ways to include and engage them in order for translation to be more effective and efficient."

SHELLEY BROWN, HEALTH SCIENTIST, NATIONAL INSTITUTES OF HEALTH'S NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

ORGANIZATIONS ARE FOCUSING ON REACHING OUT TO ACADEMIC RESEARCHERS AND HELPING THEM TO UNDERSTAND HOW IMPORTANT PATIENT-CENTRICITY IS. For example, PCORI is changing the incentives for academic researchers who want PCORI funds to conduct research. Engaging patients is a requirement from the application stage on, with funded investigators evaluated throughout the course of the award cycle for how well they're engaging patients in the conduct of research, not just as subjects. Similarly, the National Institutes of Health's (NIH) National Center for Advancing Translational Sciences (NCATS), which is charged with transforming the translational process to bring new treatments and cures to patients more quickly, has required all recipients of its Clinical and Translational Science Awards (CTSA) program grants to include patient and community engagement in all projects, something that potentially challenged the researchers at the 50+ sites around the country. NCATS representative Shelley Brown voiced her interest in learning from what had been done by others to help CTSA investigators succeed: "Patients serve at the center of all NCATS activities, and we are looking for more substantive and structured ways to include and engage them in order for translation to be more effective and efficient." One of the advocacy leaders echoed the opportunity to bridge the knowledge gap. "I suspect that many of the principal investigators don't yet know how to fulfill that requirement," she said. "We have a real opportunity here to step in and work with them."

Some workshop participants expressed concern that academic researchers have been slow to engage patients. One participant remarked that while the NIH has funding available for research focused on patient-centered outcomes in medical research, it receives few grant requests.

Another experienced a similar dynamic with the academic researchers supported by the patient advocacy organization for which she works. “It is surprising to me that within our organization there is a tension from scientist-researchers around the concept of patient-focused drug development. When I talk to researchers about patient engagement and involvement in clinical trials they focus only on patient-reported outcome measures – whether we’re capturing them or not. They’re so focused on science, that it’s very hard to get them to think about other ways in which they might engage patients in the design and execution of their research.”

The FDA Perspective: Where Are We? Where Are We Going?

"People who are living with a chronic disease are experts in that condition."

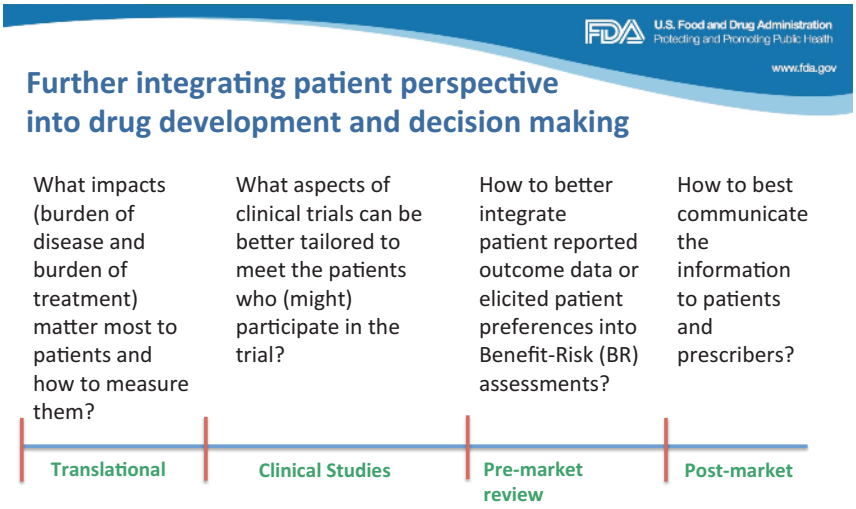
THERESA MULLIN, DIRECTOR, OFFICE OF STRATEGIC PROGRAMS FOR THE CENTER FOR DRUG EVALUATION AND RESEARCH, FDA

The Center for Drug Evaluation and Research

To help participants' understanding of regulatory policy initiatives influencing patient engagement, *FasterCures* invited representatives of the FDA's Center for Drug Evaluation and Research (CDER) and Center for Devices and Radiological Health (CDRH), along with representatives from the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO) to speak about current trends.

Theresa Mullin, director of CDER's Office of Strategic Programs, recounted how CDER codified patient-centricity in biomedical research when it committed to patient-focused drug development in the fifth authorization of the Prescription Drug User Fee Act (PDUFA). The sixth authorization is now under development and the agency, industry and patient organizations have identified "expanding patient perspectives in regulatory decision-making" as a top priority in negotiations.

FIGURE 7: QUESTIONS FRAME FDA'S EFFORTS TO INTEGRATE PATIENT PERSPECTIVES
SOURCE: U.S. FOOD AND DRUG ADMINISTRATION



THE IMPETUS FOR THE AGENCY'S INITIATIVE WAS THE EXPLICIT RECOGNITION THAT PATIENTS ARE UNIQUELY POSITIONED TO INFORM THE FDA ABOUT THE BENEFITS AND HARMS OF TREATMENTS. This, in turn, can help the agency improve its benefit-risk assessment of new drugs. They've learned through the meetings conducted under the Patient-Focused Drug Development initiative that while patients want to be as active as possible in developing new treatments, they are often frustrated that their perspectives are not factored into drug development as endpoints or measures. "We need to get the dimensions of benefit and burden that matter the most to patients incorporated into the data that is collected in trials," she said. "Then we can offer people information about what they really want to know about a drug."

Among the questions FDA is considering as it develops the next generation of patient-focused drug development:

1. How do you engage patients to collect their input on the burden of disease and therapy?
2. Do you have a representative sample of patients involved? What symptoms matter most to patients and how do you measure them?
3. How do you improve the logistics of clinical trials to allow for greater participation?
4. Does the trial have endpoints that matter most to patients? Are these endpoints even feasible?
5. Do they move with treatment?
6. Does the protocol facilitate enrollment?
7. How do you understand individual patient preferences regarding risks and benefits?

"We are challenging our staff to answer the question, 'What is it you wish you could ask patients with this condition?' That has really changed the mindset about patient engagement and how it is relevant to CDRH's work."

KATHRYN O'CALLAGHAN, ACTING ASSOCIATE DIRECTOR FOR SCIENCE AND STRATEGIC PARTNERSHIPS, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FDA

The Center for Devices and Radiological Health

Kathryn O'Callaghan, acting senior advisor for strategic partnerships at CDRH, discussed its Patient Preference Initiative, launched in 2012. Initially the goal was to understand how to integrate patient preferences into the total product life cycle for medical devices. Now the center's goals are much broader: "to promote a culture of meaningful patient engagement and increase the use and transparency of patient input as evidence in the agency's decision making." To do this, CDRH has focused on two main areas of patient-centered science:

- **PATIENT-REPORTED OUTCOMES.** These can be used as endpoints in clinical trials and outcomes to monitor post-marketing performance. They are of increasing interest to payers and regulators, as well as patients. O'Callaghan reported that the agency has seen a more than 500 percent increase since 2008 in pre-market submissions that include patient-reported outcomes as primary or secondary endpoints, including half of all PMA submissions (high-risk devices) received in Fiscal Year 2015.

- **PATIENT PREFERENCE INFORMATION.** This is information gathered to provide the patient perspective on benefit-risk questions like the minimum expected benefit and the maximum tolerated harm. The information can be used to inform which endpoints to study, effect size for regulatory studies and subgroup considerations, and as evidence for labeling changes and expanded indications. CDRH and FDA's Center for Biologics Evaluation and Research issued a draft guidance in May 2015 to stimulate inclusion of patient preference data in pre-market applications for medical devices.[v] A collaboration with FDA, medical device manufacturers and patient organizations through the Medical Device Innovation Consortium produced a framework report and catalogue of methods for conducting patient preference research.[vi]

CDRH has incorporated several patient-centric goals into its 2016-2017 strategic plan[vii] and as priorities for the fourth reauthorization of the Medical Device User Fee Act (MDUFA).

Among them:

- Convene a Patient Engagement Advisory Committee to advise CDRH on including patient participants and integrating patient input into regulatory decision-making, and to serve as experts in patient experience, needs and activities.
- Issue a patient-reported outcomes report on current regulatory usage patterns and gaps.
- Develop a framework for patient input to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention.
- Provide education and training for CDRH staff and industry on the science of measuring and communicating patient input.

"We believe that if CDRH is to successfully achieve a mission and vision in the service of patients, we must interact with patients as partners and work together to advance the development and evaluation of innovative devices and monitor the performance of marketed devices."

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
2016-2017 STRATEGIC PRIORITIES

The Industry Perspective

"To start down the path of research and development for a specific product without patient engagement is ludicrous because even if you can get the product approved, you're not going to make it in the market if you don't understand whether it matters to the patient."

ROBERT J. MEYER, DIRECTOR, UNIVERSITY OF VIRGINIA CENTER FOR TRANSLATIONAL AND REGULATORY SCIENCE

WHILE MANY COMPANIES HAVE EXPRESSED A COMMITMENT TO PATIENT-FOCUSED MEDICAL PRODUCT DEVELOPMENT, INDUSTRY IS STILL SEARCHING FOR BEST PRACTICES AND GUIDANCE. "What kind of questions should industry be asking, what kind of questions do patient groups need to be asking and how do those groups work together to ask the questions in the same way in order to achieve a real outcome?" posited one industry representative.

Others participants working in industry highlighted the need for industry to share learnings to help shape best practices. "We could all be learning together, yet much of what happens in our companies after we engage with patients is never shared," said one participant. "We could be making the same mistakes over and over again, or we could be missing out on a better way forward."

The need to gain patient trust was paramount, as was the importance of embedding all activities in sound science with methodology robust enough to influence decision making. At the same time, there was recognition that pilot projects and experimentation with different tactics might need to occur on a small-scale first.

Measuring the impact of patient-centricity was a crucial need expressed by several of the industry participants. Getting buy-in from upper management and budgetary approval often relied on being able to define the return-on-investment. Some of the outcomes important to industry that are potentially improved by engaging with patients included: better understanding of how patients view the benefits of treatment and the harms and risks they pose, more efficient trial design, more feasible and tolerable clinical trial designs from a subject's point of view, more robust recruitment of study participants and higher retention rates, and better adherence to medication regimens.

The pre-meeting survey showed that there was some alignment and some discord between industry participants and patient organization representatives about how and when engagement was desired, as shown in the figure. One factor driving industry's preference for later engagement may be the risk-averse nature of many companies. "There is a significant concern that inviting advocates to come in and talk to the regulatory and commercial teams before a product is approved may constitute pre-approval promotion," one participant said.

Legal and regulatory clarification on this topic would help, several participants noted. The group also recommended inviting legal and

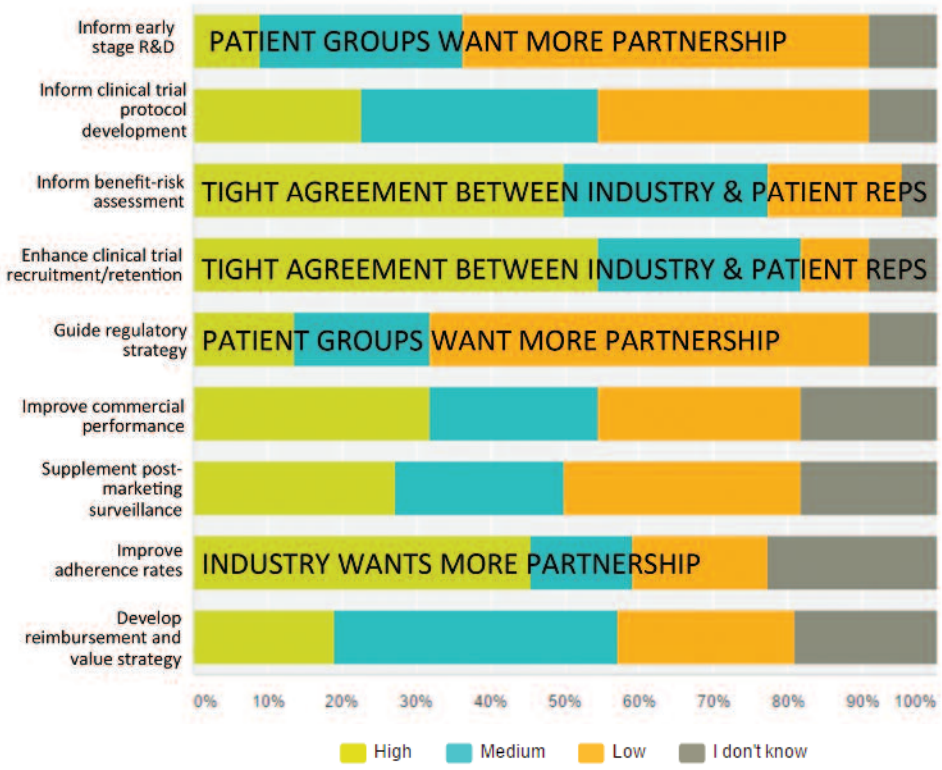
"There is a significant concern that inviting advocates to come in and talk to the regulatory and commercial teams before a product is approved may constitute pre-approval promotion."

WORKSHOP PARTICIPANT

FIGURE 8: PERCEIVED INTEREST IN INDUSTRY FOR INTEGRATING PATIENT PERSPECTIVES AT VARIOUS STAGES OF MEDICAL PRODUCT DEVELOPMENT

BARS REPRESENT ALL PARTICPANTS' RESPONSES; AREAS OF TIGHT AGREEMENT AND DISCORD NOTED WITH TEXT

SOURCE: *FASTERCURES*



"How do we know that the patient input being considered is representative of the vast majority of people who are going to be using devices or drugs? How do we engage those who are under-represented and bring their voices in?"

PATIENT ADVOCACY REPRESENTATIVE

regulatory representatives to future workshop discussions so they can better understand the importance of patient engagement to the ultimate success of new products.

Finally, industry participants expressed concern about staffing and resources at FDA to handle the new science of patient input. "How can we build manpower and expertise across the agency, within the centers and across different review divisions to enable FDA to engage with the patient community and to effectively and efficiently process patient data to inform regulatory decision-making?" asked an industry representative.

DO YOU HAVE THE RIGHT PATIENTS?

Several participants noted that often the patients who participate in advocacy organizations, open meetings and scientific sessions are not typically representative of the entire patient community. For instance, at a recent HIV-related hearing at the FDA, the majority of patient advocates present were white, middle-aged men who had been living with the disease for years, which does not reflect the primary demographics of people living with and at greatest risk for HIV infection.

Theresa Mullin noted that the first of several guidance documents being planned by FDA's CDER will address practical issues to consider and methods to use to try to reach as broad a population of people affected by a condition as possible so that the information collected represents the full range of experiences. "We envision providing examples of what a good product of this extensive outreach looks like," she said. FDA plans to host workshops to gather ideas and input as a step in developing its draft guidance on topics related to patient engagement.

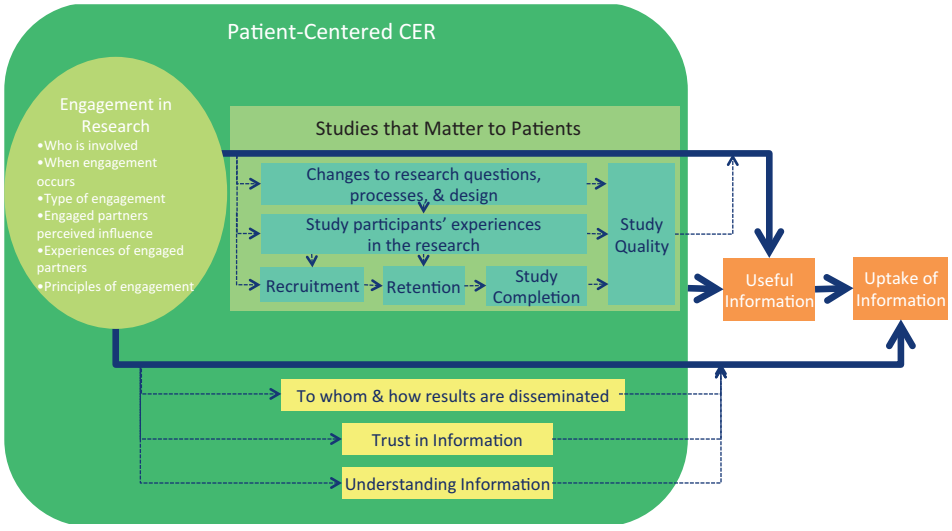
Measuring ROI on Engagement: An Update from PCORI

The establishment of the Patient-Centered Outcomes Research Institute in 2010 through the Affordable Care Act shined a laser beam on the importance of and commitment to patient-centered research. The institute's first funding announcement in 2011 solicited projects specifically focused on incorporating patient perspectives into biomedical research. By the end of fiscal year 2014, PCORI had provided $671 million in research support to 360 projects in 39 states. Every project must have some element of engagement in its design or conduct, and many of them list patients as co-investigators. As part of the institute's multi-level evaluation framework,[viii] principal investigators and patient partners are queried regularly on the challenges they face in collaborating on research and about ways they overcome those challenges.

With four years of experience, PCORI now has data highlighting the results of patient involvement in its studies, said Jean Slutsky, chief engagement and dissemination officer. **For instance, PCORI can now demonstrate that patient involvement has a significant impact on patient recruitment, retention and design of informed consent to ensure that patients truly understand the benefits and risks of participating as a research subject.** These outcomes align closely to what industry representatives said they need to show in order to gain internal support for patient engagement from upper management.

Slutsky shared an example that researchers designing a study to examine anticoagulant use in patients with history of stroke chose "length of time without an event" as a primary outcome. After receiving feedback from patients, however, they added an outcome that was more important to patients: length of time before hospitalization.

FIGURE 9: EVALUATING THE IMPACT OF PCORI: WHERE DOES ENGAGEMENT IN RESEARCH FIT?
SOURCE: PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE



Priorities for Future Collaboration

Workshop participants divided into small groups to generate ideas for high-priority activities, tools and products that could advance the science of patient input and improve patient-centered decision-making in research, development and regulation of medical products. The initiatives they identified are listed in the table below in order of least challenging to execute to most challenging to execute and as graphically displayed on Figure 10 that follows the table on p. 34.

COMMUNICATIONS INITIATIVES	
GLOSSARY OF TERMS	Collect and harmonize definitions for common terms associated with patient-centricity, disseminate widely and update regularly as warranted.
PROMOTION OF EXISTING RESOURCES	Widely and continuously disseminate existing resources on patient engagement and the science of patient input through a variety of communications channels to various stakeholder audiences and encourage their adoption.
PRESS BRIEFING ON PATIENT-CENTRICITY	Conduct a press briefing for health, science and industry reporters about the aims of patient-centricity and benefits to patients and public health and repeat as warranted.
CASE STUDIES TO BUILD UNDERSTANDING OF VALUE PROPOSITION AND BEST PRACTICES	Document learnings from efforts to elicit and integrate patient perspectives in medical product R&D and regulation; collect and share these case studies as a means to better understand the value proposition for patient engagement and to capture emerging good practices in pursuit of best practices.
ONLINE ARCHIVE OF RESOURCES	Build a user-friendly online archive of annotated resources on patient engagement and the science of patient input such as definitions, frameworks, methods, tools, articles, training materials and policy statements, and update it frequently.

INITIATIVES TO CREATE TOOLS/FRAMEWORKS

SAMPLE PATIENT ENGAGEMENT PLAN	Develop a sample plan for ways to engage individual patients, caregivers, advocates and/or patient organizations at various stages in the total product life cycle of a medical product that addresses the 5 Ws – Why? Who? When? Where? hoW? This would build on the CTTI model for "Patient Group Engagement Across the Clinical Trial Continuum."
MODEL PATIENT-CENTERED TARGET PRODUCT PROFILE	Develop a model Target Product Profile to plan a product development program "with the end in mind" that features a patient-generated description of unmet medical need, symptom/disease domains of highest priority to patients to address and concepts important to patients in the labeling of the product.
FRAMEWORK FOR SOURCES/ USES OF PATIENT DATA	Using *FasterCures*' "From Anecdotal to Actionable" as a starting point, develop a framework for how various sources of patient data (e.g., patient advisory boards, patient registries, online communities) might be used to enrich understanding of concepts such as disease burden, unmet medical need and patient journey.
PATIENT ENGAGEMENT PLAYBOOK	Develop a series of "if/then" statements or decision trees to guide selection of methods/tactics for engaging patients/ advocates at various steps in the development of a medical product. Update regularly as warranted.
FEE SCHEDULE FOR SERVICES PROVIDED BY PATIENT ORGANIZATIONS TO INDUSTRY	Establish a consensus-based schedule of customary and usual fees for routine services provided to industry by patient organizations, with considerations for customizing the fee schedule to reflect unique requirements of a particular contracting arrangement or unique features of the condition of interest. Pilot, revise and promote, and reassess and update regularly as warranted.

TRAINING INITIATIVES

ADAPTATION OF EUPATI RESOURCES TO THE UNITED STATES	Adapt the European Patients Academy on Therapeutic Innovation (EUPATI) educational toolkit and its in-depth Patient Expert Training Course[xii] based on the European Union's systems for regulatory and health technology assessment decision-making to the U.S. system and distribute widely.
REGULATORY/LEGAL ISSUES TRAINING PROGRAM FOR PATIENT ORGANIZATIONS	Create an expert-led training curriculum for patient organization leaders about regulatory policies and statutes that govern medical product development so that they are better able to anticipate challenges and to navigate them when they occur. Deliver the program, evaluate effectiveness, refine and scale to meet need.
ACADEMIC TRAINING PROGRAM FOR SCIENCE OF PATIENT INPUT	Within one or more academic institutions and/or professional societies, develop curricula to enhance understanding by students and degreed professionals in relevant disciplines about the benefits of engaging patients in research and ways in which methods borrowed from the fields of health economics, outcomes research, epidemiology, social sciences and marketing sciences can be applied to elicit, collect and interpret patient perspectives, expectations and preferences. Evaluate effectiveness, refine and scale. Update materials regularly to reflect dynamic state of methods and practice. Consider credentialing to standardize across disciplines.

METHODS DEVELOPMENT

DESCRIPTION OF SOURCES OF POTENTIAL BIAS IN PATIENT INPUT	As a means to identify and mitigate bias in the collection, analysis and interpretation of patient input, describe the potential sources of bias based on scholarly and practical experience. Publish in a widely read academic journal and re-assess based on feedback to the article and as there is more practical experience to draw upon.
DEFINITION OF METHODS AND TACTICS TO ACHIEVE "REPRESENTATIVENESS"	Establish methods for assessing how well or accurately a sample population reflects the broader population to determine its representativeness and provide guidance on how to achieve representativeness in collecting patient input. Thresholds may need to be adapted for different purposes (i.e., internal decision-making vs. regulatory approval).
RESEARCH AGENDA FOR SCIENCE OF PATIENT INPUT	Through a multi-stakeholder consensus-building process, establish a research agenda to prioritize gaps in the knowledge base about the science of patient input that could be best addressed through coordinated research activities. Reassess and update periodically.

INITIATIVES TO ADDRESS LEGAL CHALLENGES

INTEGRATION OF LEGAL/ COMPLIANCE STAFF INTO DIALOGUE	Make consistent efforts to incorporate legal issues and experts on the agendas and faculty of meetings convened about patient engagement and patient-focused medical product development to educate other stakeholders about regulatory statutes and policies and to dispel misinformation.
COLLECTION OF CONFLICT-OF-INTEREST POLICIES	As a step toward redefining ethical and legal boundaries between industry and patient organizations in the context of patient-focused medical product development, collect conflict-of-interest policies in current use by industry sponsors and patient organizations for review and discussion by a multi-disciplinary group that includes relevant stakeholders. Identify next steps to influence policy change.
PRO-BONO LEGAL SERVICES DIRECTORY	Create a listing of contacts within law firms that provide free or discounted professional services to nonprofit patient organizations.
COMPREHENSIVE LIST OF LEGAL CHALLENGES	Assemble a multi-stakeholder group with experience in patient-focused medical product development to define as many of the legal challenges to productive patient organization and industry collaboration that may arise in the total product life cycle.
MODEL PROVISIONS FOR KEY AGREEMENTS BETWEEN PATIENT ORGANIZATIONS AND INDUSTRY	Engage a multi-stakeholder group with appropriate legal expertise to define discrete, regularly occurring scenarios in which patient organizations and industry may mutually benefit from partnering and develop template language that could serve as a model for legal agreements to guide these arrangements.

INITIATIVES TO IMPROVE MEASUREMENT

CHECKLIST/SCALE FOR ASSESSING INCLUSION OF PATIENT INPUT IN PRODUCT DEVELOPMENT	Building on the tools published by CTTI and M-CERSI, develop a comprehensive checklist of steps in total product life cycle of a medical product where patient input could inform decision-making with rating scales to assess patient involvement as high-moderate-low-none. Pilot, refine and update regularly as warranted.
METRICS FOR TRUST, TRANSPARENCY, "MEANINGFUL-NESS" OF ENGAGEMENT	Develop rating scales or other measures to assess concepts of trust, transparency and how meaningful engagement with patients is to research, the process of developing a medical product or delivering a health-care service. Pilot, refine and update regularly as warranted.
COMPREHENSIVE, UNIFIED EVALUATION PROGRAM FOR BENCHMARKING FIELD	To measure and benchmark patient-centricity within an individual institution (e.g., patient organization, company, government agency) and across institutions, develop an integrated set of measurement questions, metrics, methods and sources of data, using the PCORI Evaluation Framework as an illustrative model. Pilot, refine and update regularly as warranted.

COMBINATION INITIATIVE

MULTI-SPONSOR PROGRAM FOR PILOTING PATIENT-CENTRIC PRACTICES USING ACTUAL PRODUCT DEVELOPMENT	Create a forum that is protected by appropriate non-disclosure agreements and compliant with anti-trust regulations to enable willing industry sponsors to meet regularly with relevant experts to share experiences and address challenges in integrating patient perspectives into the real-time development programs for one or more medical products. Document and communicate learnings with the broader field as a means to advance understanding and practice of the science of patient input.

FIGURE 10: RELATIVE CLASSIFICATION OF COLLABORATIVE INITIATIVES BY CHALLENGE IN EXECUTION AND CONTRIBUTION TO FIELD

SOURCE: *FASTERCURES*

Moving to Action

The call to action to understand patient perspectives and integrate patients' priorities into the full continuum of medical product discovery, delivery and development has begun to shift culture, strategy and operating plans in many stakeholder organizations. Individuals on the front lines of change are grappling with how to operationalize the new imperative. They are eager to learn from one another and to share information and to exchange intelligence about what's working and what's not as a new science of patient input takes shape and form. Workshop participants reinforced this sense of urgency and importance, and identified 25 high-priority projects to continue to advance the practice of patient-centricity beyond feel-good commitments to solid action. **Through its Patients Count program, *FasterCures* remains steadfastly committed to taking a leading role to enact these recommendations and strongly encourages broad participation by stakeholders across the biomedical ecosystem to realize the potential for continued collaboration and coordinate action.**

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Endnotes

[i] S. Dentzer, Rx For The 'Blockbuster Drug' Of Patient Engagement. *Health Affairs*. 2013;32(2):202.

[ii] J.H. Hibbard, J. Greene, What The Evidence Shows About Patient Activation: Better Health Outcomes And Care Experiences; Fewer Data On Costs. *Health Affairs*. 2013;32(2):207-214.

[iii] FDA issues draft guidance of developing drugs for Duchenne muscular dystrophy (U.S. Food and Drug Administration, Silver Spring, MD, 2015). http://www.fda.gov/Drugs/DrugSafety/ucm448894.htm

[iv] K. L. Carman, P. Dardess, M. Maurer, S. Sofaer, K. Adams, C. Bechtel, J. Sweeney, Patient and Family Engagement: A Framework for Understanding the Elements and Developing Interventions and Policies. *Health Affairs*. 2012;32(2):223-231.

[v] Patient Preference Information – Submission, Review in PMAs, HAD Applications, and *De Novo* Requests, and Inclusion in Device Labeling, Draft Guidance (U.S. Department of Health and Human Services, Center for Devices and Radiological Health, Center for Biologics Evaluation and Research, Rockville, Maryland, 2015). http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf

[vi] A Framework for Incorporating Information on Patient Preference Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology (Medical Device Innovation Consortium, St. Louis Park, Minnesota, 2015). http://mdic.org/pcbr/framework-report/

[vii] 2016-2017 Strategic Priorities (Center for Devices and Radiological Health, Silver Spring, Maryland, 2016). http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM481588.pdf

[viii] Patient-Centered Outcomes Research Institute Evaluation Framework 2.0 (Patient-Centered Outcomes Research Institute, Washington, DC, 2015). http://www.pcori.org/sites/default/files/PCORI-Evaluation-Framework-2.0.pdf

[ix] Patient Group Engagement across the Research & Development Continuum (Clinical Trials Transformation Initiative, Durham, NC, 2015). http://www.ctti-clinicaltrials.org/what-we-do/investigational-plan/patient-groups

[x] Target Product Profile – A Strategic Development Process Tool, Draft Guidance (U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Rockville, Maryland, 2007). http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080593.pdf

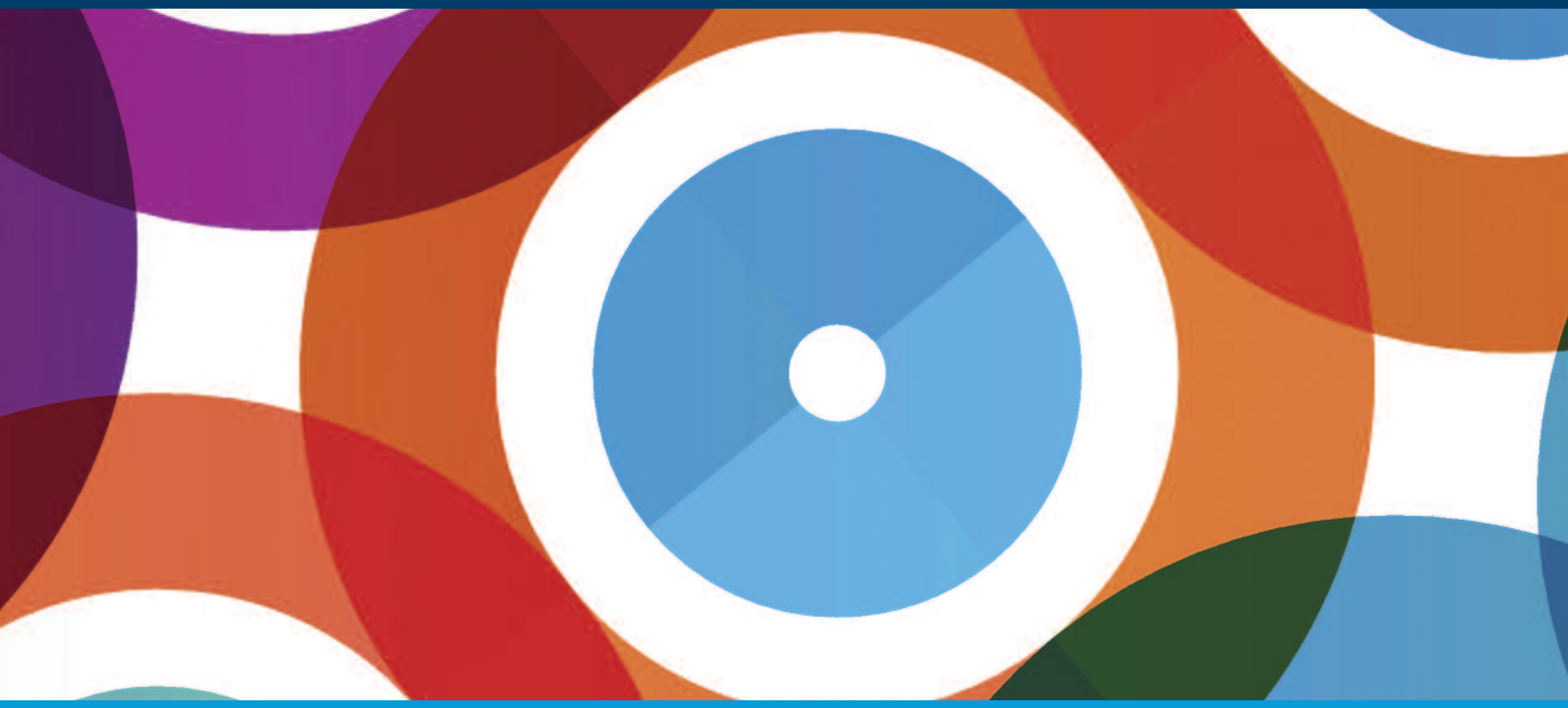
[xi] From Anecdotal to Actionable: The Case for Patient Perspective Data (*FasterCures*, Washington, DC, 2015). http://www.*FasterCures*.org/reports/view/49

[xii] European Patients' Academy on Therapeutic Innovation Training Course (EUPATI, Germany, 2015). http://www.patientsacademy.eu/index.php/en/edu

[xiii] Op cit [Patient Group Engagement across the Research & Development Continuum] (Clinical Trials Transformation Initiative, Durham, NC, 2015). http://www.ctti-clinicaltrials.org/what-we-do/investigational-plan/patient-groups]

[xiv] Assessing meaningful patient engagement in drug development: A definition, framework, and rubric (University of Maryland Center of Excellence in Regulatory Science and Innovation, Baltimore, MD, 2015). http://www.pharmacy. umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/cersievents/pfdd/mcersi-pfdd-framework-rubric.pdf

[xv] Op cit [Patient-Centered Outcomes Research Institute Evaluation Framework 2.0] (Patient-Centered Outcomes Research Institute, Washington, DC, 2015). http://www.pcori.org/sites/default/files/ PCORI-Evaluation-Framework-2.0.pdf]



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