Enhancing the Incorporation of Patient Perspectives in Clinical Trials
Meeting Summary

March 18, 2019
Tommy Douglas Conference Center
10000 New Hampshire Avenue, Silver Spring, Md.

BACKGROUND AND OBJECTIVES

How can clinical research deliver value to patients? How can we design studies that better meet the needs and priorities of study participants? The Clinical Trials Transformation Initiative (CTTI) recently hosted a public workshop, "Enhancing the Incorporation of Patient Perspectives in Clinical Trials," to seek ideas for best practices and key considerations for enhancing the incorporation of patient perspectives on clinical trial access, design, conduct, and post-trial follow-up. Working in collaboration with the U.S. Food and Drug Administration (FDA), this event was held Monday, March 18, from 9:00 a.m. to 5:00 p.m. at the Tommy Douglas Conference Center in Silver Spring, Md. Intended as an opportunity for patients, investigators, and other groups to have their voices heard and, ultimately, help shape better processes for planning and conducting clinical trials, this workshop gathered input from patients, caregivers, industry, academic researchers, and expert practitioners on the challenges and barriers to patient participation and retention in clinical trials. Over 150 people attended the event in person while an estimated 723 people watched the meeting via webcast.

Perspective	# In person Attendees Indicating Perspective*
Academia	**11**
Individual Patient or Caregiver	**32**
Clinical Investigator/Site	**11**
Government/Regulatory	**23**
Industry	**71**
Patient Advocacy Organization	**36**
Other	**22**
**Attendees had option to choose more than one perspective*	

The meeting was organized into five sessions:

- Welcome and Keynote Speech
- Enhancing Awareness & Access
- Design & Conduct of Patient-Centric Trials

- Post-Trial Communication & Engagement
- Key Themes & Looking Forward

This workshop met an FDA commitment that is part of the sixth authorization of the Prescription Drug User Fee Act (PDUFA VI). In addition, the FDA announcement of this public workshop included a request for public comment, and comments submitted to the docket for this event are summarized in the appendix. A docket is a repository through which the public can submit electronic and written comments on specific topics to U.S. federal agencies such as the FDA. The event materials and archived webcast are available online at: https://www.ctti-clinicaltrials.org/briefing-room/meetings/enhancing-incorporation-patient-perspectives-clinical-trials

THEMES

Workshop speakers expressed that patients are looking for value in clinical trial participation. In addition to managing difficult diseases, patients have numerous obligations to work, family, and community. The significant time often required for participation means that patients must carefully evaluate whether a study will truly add value to their own lives or others'. Then when patients do take the time to identify research opportunities, they encounter inclusion/exclusion criteria that pose substantial barriers to enrollment. And among those who enroll, far too many are never informed of their trial's results—yet patients want and deserve this information.

Throughout the workshop's three sessions, speakers emphasized that substantial progress can be made in addressing these challenges, and studies improved overall, when studies are designed with patient input and when patient needs and barriers are acknowledged. Finally, throughout the workshop, attendees emphasized that trust is key throughout the study process and that tools and resources for patient engagement work best when they are paired with trusted community partners.

KEYNOTE

Donna Cryer, President and CEO of the Global Liver Institute, delivered a keynote presentation challenging attendees to reflect on what she considers a broken system in which barriers to patient engagement are still numerous despite years of collective effort. Cryer said that patients and caregivers are still not considered full partners in the clinical trials enterprise. She urged researchers and sponsors to increase access by "bringing trials to us, designing trials with us, conducting trials for us, and allowing post-trial follow-up by us." She pointed to the rare disease community as a model for patient engagement for other disease areas to emulate. Many rare disease advocacy organizations have funded research, created registries, and matched patients to opportunities. She also advocated for a greater understanding that patient

involvement throughout the study process results in more relevant questions, richer data, faster enrollment, better retention, and broader dissemination.

SESSION I: ENHANCING AWARENESS AND ACCESS

Barriers and Challenges

The first session highlighted the need to raise awareness about clinical research and lower the barriers to participation for patients looking for opportunities. This session began with three patient perspectives on barriers and challenges from: Donna Appell, Hermansky-Pudlak Syndrome Network; Steven Hall, Cystic Fibrosis Patient Advocate; and Jamil Rivers, Breast Cancer Patient Advocate.

Donna Appell is a nurse by training and the mother of a daughter with Hermansky-Pudlak Syndrome (HPS), a rare genetic metabolic disorder which causes albinism, visual impairment, and a platelet dysfunction with prolonged bleeding. Appell discussed her experiences in advancing clinical research through the Hermansky-Pudlak Syndrome Network and other advocacy work. Barriers to researching HPS include the fact that diagnosis takes 7 years on average and experts on the disease are spread out across the world. The blindness usually experienced by patients makes participation difficult. Also, many of those living with HPS reside in Puerto Rico, where language, cultural, and religious barriers also impede participation. Appell has spent time in Puerto Rico educating patients about the disease and research opportunities. She shared her experience in "flipping" how research is done by inviting researchers to her organization's conference. Five academic medical centers received IRB approval to attend and the organization helped 38 patients participate in research during the conference.

Steven Hall explained that, in addition to living with cystic fibrosis, he works full time as a financial planner, coaches youth sports teams, and serves on the board of two non-profit organizations. Advocating for and participating in research is not his only priority. "I am a human first and a CF patient second," he said. Like many patients, he wants clinical trials to work with his life and deliver value. He has found being too healthy to be a barrier to participation and wonders why researchers do not broaden inclusion criteria given the small number of cystic fibrosis patients. "It's a little hard to hear that you are too healthy when you have two hours of treatments to do each day."

Jamil Rivers is a patient advocate living with metastatic breast cancer. She explained that, despite living in a city she described as a "research mecca," she has had to serve as her own advocate to find and access clinical trials. The barriers for metastatic patients are numerous and inclusion/exclusion criteria for breast cancer trials often leave metastatic patients out. Sponsors too often have pre-conceived notions that metastatic patients are in hospice and uninterested in participation. For younger patients who are working and raising families, time is a barrier and

too often clinical trials keep "banker's hours." For patients with significant disabilities who are not working, travel can also be difficult. Rivers has advocated directly with sponsors to add metastatic arms to studies.

Case Examples

Two presenters, Nancy Roach from Fight Colorectal Cancer and Ronnie Tepp from NIH's *All of Us* Research Program, offered case studies and suggested approaches on how to better overcome barriers to enhance awareness of and access to clinical trials. Roach discussed the efforts of Tom Marsilje, a research scientist diagnosed with stage 4 colon cancer who created a process to curate clinical trials for fellow colorectal cancer patients and provided opportunities through a variety of online communities. Marsilje faced his own barriers to trial opportunities, but up until his death worked tirelessly for others.

Ideas from this case study to explore included:

- Opportunities for trial participation were enhanced when "super advocates" created a curation process which took into consideration the potential impact of studies on patients' lives and carefully evaluated eligibility criteria and whether the study was designed for actual rather than theoretical patients.
- This curation process was coupled with online communities where participants could connect with each other to discuss and evaluate opportunities.

Tepp discussed the work of NIH's *All of Us* program – a historic effort to gather data from more than one million people living in the United States to accelerate research and improve health. *All of Us* has a stated goal that 75% of its participants will be minority groups who are under-represented in research. To achieve this goal, the project is working with communities across the U.S. to raise awareness about clinical research and the opportunity to participate in *All of Us*.

Ideas from this case study to explore included:

- The program is not confined by traditional stakeholders and thinks creatively about partnerships. It relies on a national network for organizations including patient advocacy groups, community-based organizations, minority serving groups, faith-based organizations, provider trade associations and professional societies.
- The *All of Us* program understands the need for partners to have the space to define value for themselves.
- The program understands that to communicate value, careful thought is needed about the right messenger and the right tools for messaging. It uses a variety of engagement models.

Best Practices

Richardae Araojo from the FDA's Office of Minority Health and Health Equity, Luther T. Clark of the Office of the Chief Patient Officer from Merck, and Fabian Sandoval from the Emerson Clinical Research Institute joined previous speakers for a panel discussion about how to lower the barriers to participation and encourage greater opportunities for patients.

Ideas for best practices that emerged from the discussion included:

- Trust is critical and partnerships should not be transactional. Researchers looking to build partnerships with trusted organizations need to build and invest in long-term relationships even when there is not an immediate need or "ask."
- Researchers need to go where patients are rather than relying on patients finding them. Panelists offered examples of providing information about clinical trials in consulates where people are waiting for visas, on radio programs reaching rural populations, and at community centers, ministries, and events.
- Community organizations working with patients need more funding. As companies merge and change, relationships may start and stop. Community organizations fill that gap but are chronically under-funded.
- Value is paramount for patients and researchers. Time is a major barrier for many patients – either because they are busy living their lives or because they do not have much time left to wait for a new treatment. Patients want to understand what value a study is going to bring to them and to their community.
- Clinical trial opportunities listed on clinicaltrials.gov or elsewhere need to be curated and accompanied by a solid patient community to help people find trials that bring value.

SESSION II: DESIGN AND CONDUCT OF PATIENT-CENTRIC TRIALS

In the second session, panelists discussed the importance of designing patient-centric clinical studies and the need for greater inclusion of patients and caregivers in study design.

Barriers and Challenges

Patient advocates discussed the barriers they face when studies are not designed with patients' needs in mind. Pat Furlong of Parent Project Muscular Dystrophy moderated the session, which began with three patient perspectives from Melissa Beasley, Eosinophilic Esophagitis Patient Advocate; Len Schwartz, Parkinson's Foundation; and Theresa Strong, Foundation for Prader-Willi Research.

Beasley, who lives with Eosinophilic Esophagitis, a chronic, allergic inflammatory disease of the esophagus, explained that her condition makes eating food extremely painful. She participated in a trial that required her to stop taking her usual medication for 28 weeks and to document her pain symptoms daily using a diary. The requirement for the diary caused significant emotional distress and, in the end, provided poor data. The diary showed improved symptoms, but only because Beasley stopped eating to avoid writing about her painful symptoms. In the end, she had to leave the trial because it became too stressful and difficult. "Patients need the flexibility to communicate our needs," she said.

Schwartz, a Parkinson's patient advocate, has participated in many trials. The nature of his condition means that he experiences cognitive impairment, anxiety, and medication that does not always work. It can be very difficult to predict when he will be well enough to travel to a study visit. Clinical studies need to be flexible enough to understand the constraints and needs of people living with Parkinson's and include their caregivers in decision-making.

Strong is the mother of a son with Prader-Willi syndrome, a genetic disorder that causes the sensation of constant hunger, among other symptoms. The only way to prevent morbid obesity is to tightly control access to food. Because there are so few studies for this syndrome, participation generally involves travel, and airports are a very difficult place to control food intake. Strong said that it is important for researchers to understand the specifics of the disorder and engage families based on their lived experiences.

Case Examples

Case examples of how to better include patients in the design and conduct of trials were offered by Mary Elmer from the TransCelerate BioPharma Patient Experience Initiative and Joseph Kim from Eli Lilly.

Elmer discussed the work of TransCelerate, a non-profit organization working across the biopharmaceutical research and development community to develop a patient experience toolkit. The toolkit will offer best practices for engagement, a resource guide, and a participant feedback questionnaire. The toolkit is expected to be publicly available in July of 2019.

Ideas from this case study to explore included:

- Improving the patient and site experience in clinical research requires collaboration across the global biopharmaceutical R&D community.
- Throughout the process of developing patient experience toolkits, TransCelerate has relied on a patient advisory board to help create and test materials.

Kim talked about his experiences working with patients to co-design studies at Eli Lilly. Thanks to the work of patient advisory groups, his company was able to think more carefully about

appropriate study endpoints, be more judicious about required procedures, change the appearance of a study drug when patients told them how similar it looked to other pills, and make more convincing arguments to IRBs about the use of wearables in studies after getting patient feedback.

Ideas from this case study to explore included:

- Include patient advisors to help researchers think through clinical trial endpoints. While standard endpoints might be focused on evidentiary disease progression and modification, patients may be more interested in measurement of symptomatic relief.
- Through patient and site collaborations, Eli Lilly is often able to uncover scenarios in which the timing and volume of procedures in a study is out of synch with the practical realities of the health care system and patients' lives.
- Eli Lilly is able to build and share evidence on patients' preferences for studies with IRBs.

Best Practices

Susan McCune from the FDA's Office of Pediatric Therapeutics and Karlin Schroeder from the Parkinson's Foundation joined previous speakers in this session for a panel discussion about overcoming these larger challenges and finding potential solutions.

Ideas for best practices that emerged from the discussion include:

- When patients sit down in the same room with researchers, researchers are able to truly hear what patients are saying and better understand the urgency of needs.
- Do not ask one patient to speak for all patients when co-designing studies. Instead, invite a diverse group of 8-12 patients from different backgrounds and with varying stages of disease.
- When researchers communicate objectives to patients, patients will often provide more meaningful suggestions of how best to measure outcomes against that objective.
- Education is needed among research professionals to understand that patients can be involved in all phases of study design, including the parts that may seem too technical, like data analysis. Patients do not leave their skills and experiences behind after a diagnosis and often have the training needed to meaningfully participate at different levels.
- Ideas for pushing the frontiers of patient co-design include embedding patients within sponsor companies and including patients in the site selection process.
- Consider the special needs of children and adolescents in co-designing trials, especially when considering use of technology in a trial. Do not underestimate how much this population wants to help others.

- Collaborate across disease areas to ensure cross-learning, especially in neurology where there might be potential to apply findings from one disease to another. Give patients a say in prioritizing the research agenda.

SESSION III: POST-TRIAL COMMUNICATION AND ENGAGEMENT

In the final session, speakers discussed the importance of communicating with participants after trials and returning both aggregate and individual results to all study participants.

Barriers and Challenges

Bray Patrick-Lake from the Duke Clinical Research Institute moderated a session with two patient advocates: Carly Medosch, Chronic Illness Patient Advocate, and Linnea Olson, Lung Cancer Patient Advocate, who discussed their own experiences with trials and the lack of communication they experienced post-trial.

Medosch, who was diagnosed with Crohn's Disease as a teenager, said her participation in trials often felt like extra homework with diaries and forms to complete. Yet, she was never thanked for her participation or offered information about the results of the trials in which she participated. She was usually told whether she was on a placebo or investigational drug, but that was the extent of the information she was provided. She recounted how a fellow patient was trying to find information about a trial in which he participated. By searching the internet, he found a press release about results sent to shareholders of the sponsor company. "Who is valued?" Medosch asked. "Who has skin in the game? Using your body to test a company's drug is the most skin you can have."

Olson, who has lung cancer, has been participating in trials for 9 of the last 14 years. Participation has been both her privilege and her burden, she said, as trials have extended her life. At the same time, she also often feels that her participation is "feeding a big data collection machine" at the expense of her own health. She described how she has had well over 100 different imaging scans that were not clinically necessary for her variant of cancer. The demand for data did not take her individual situation into consideration and, as each trial is a discrete event, no one kept track of her scans. Because of the repeated testing, she has gadolinium deposits in her brain from excessive scanning. Despite this sacrifice to give sponsor companies extra data, in her 9 years of participation, she has never received information about trial results.

Case Examples

David Leventhal of Pfizer and Jessica Scott from Takeda discussed their organizations' efforts to better return results to patients. Scott began by explaining her first-hand knowledge of the

burden of trial participation, recounting her family's experiences in finding trials for her sister, who had osteosarcoma as a child. She said her sister was treated as a disease —not a person. Her family's experiences motivated her to do more to address the needs of "whole people" who are experiencing diseases.

Leventhal discussed his father's experiences as a clinical trial participant and his difficulty in finding trials to join. When his father did find a trial, he had a positive response. However, the drug was not ultimately approved because of low enrollment and statistical significance. His father still wonders why he was not genotyped and why there is no information about why the drug worked for him but not others. Data needs to be returned to patients, Leventhal said, so that these sorts of questions can be explored, because otherwise, it becomes a story that is not fully told.

Leventhal and Scott said that return of results is an evolving landscape in which companies are working in multi-stakeholder consortia to seek progress internally and externally. Companies are working to meet new EU regulations mandating plain language summaries.

Ideas from this case study to explore included:

- Improving the patient and site experience in clinical research requires collaboration across the global biopharmaceutical R&D community. Some concepts in research take many sentences to explain in plain language, making documents lengthy. Finding the right balance is crucial.
- EU regulations mandate 10 elements that must be addressed in plain language summaries, but there is no clear guidance yet from the FDA. Any future guidance should be harmonized.
- Guidance is needed from academic journals to ensure that distributing plain language summaries does not jeopardize publication for trial manuscripts.
- There is a risk that return of results could be seen as promotional. Distributional channels for return of results need to be carefully thought out.
- The skills required to write more formal medical documents are not the same as those needed to communicate medical findings to the public. Plain language communication can be difficult.
- If any one company returns results poorly, it could reflect poorly on the entire industry. Cross-industry collaborations are essential to ensuring that lay summaries are all consistently high-quality.
- Individual return of results is more than an opportunity, it's an obligation. It could be of enormous benefit, for example, to a patient who is able to take results to his or her regular clinician.
- A 2017 TransCelerate survey found that returning individual study results could improve recruitment and retention. At the same time, a better understanding is needed of what information patients want to receive.

Best Practices

Suzanne Schrandt from the Arthritis Foundation and Michelle Tarver from the FDA's Center for Devices and Radiological Health joined the previous speakers for a panel discussion. Ideas for best practices that emerged from the discussion include:

- Sharing results with participants is too often seen as something "extra," rather than a requirement. There should be a social contract between sponsors and participants that ensures information is shared.
- Dissemination plans for returning results should not be created as the study closes, but rather as the study begins. Initial discussions should include patient advisory groups who can help identify the types of information that will be most important to participants.
- Plain language summaries should be developed and disseminated in parallel to a clinical study report.
- Panelists discussed the difficulties of returning results when a study is not completed. Patients still need to know why studies were stopped and what was learned.
- Study participants are frustrated when they hear that results are not returned because of regulatory or other hurdles. They want sponsors to remember the tremendous difficulties patients face to participate.

KEY THEMES & LOOKING FORWARD

To wrap up the key insights from the day and discuss potential next steps, Donna Cryer, who delivered the keynote speech, moderated a panel discussion that included:

- Michael Kurilla, National Center for Advancing Translational Sciences, NIH
- Craig Lipset, Pfizer
- Theresa Mullin, Center for Drug Evaluation and Research, FDA
- Peter Saltonstall, National Organization for Rare Disorders
- Pamela Tenaerts, CTTI
- John Wilbanks, Sage Bionetworks

Panelists highlighted the importance of recognizing that people are not for clinical trials—clinical trials are for people. Trials need to be designed for people, recognizing that those who are living with diseases also have numerous responsibilities to their families, their jobs, and their communities. They encouraged attendees to think about supports that move beyond just travel reimbursement to truly address patient needs.

For patients to be engaged, panelists said, communities also need to be engaged to raise awareness and educate about clinical research in general as well as to learn about communities' specific needs and experiences. Likewise, clinicians also need to be engaged so

that a patient finding a trial opportunity is not a matter of luck but, rather, the result of a discussion between physician and patient.

Just as the workshop began with a discussion about bringing value to participants, this concluding panel circled back on the same topic. Participants too often do not feel valued at the end of a study. Return of results is part of the social contract. Sponsors should see thank you messages and return of results as a part of the routine suite of deliverables they create for every study. Patients were encouraged to use their collective power to demand the same rights to information as investors.

Finally, panelists said that the future of research should include engagement of patients from before studies begin to after they have concluded. Engagement with patients should not just be during one discrete opportunity, but rather structured as long-term relationships that include generosity of time, transparency, and accountability.

DISCLAIMER

The views expressed in this meeting summary represent the individual perspectives of the attendees and do not necessarily represent the official views of the FDA or CTTI or of any organization with which the attendees are affiliated.

APPENDIX: PUBLIC COMMENTS

In conjunction with the workshop "Enhancing the Incorporation of Patient Perspectives on Clinical Trials," the FDA also issued a call for public comments regarding the perspectives on challenges and barriers to patients participating in clinical trials, and best practices and key considerations for enhancing the incorporation of patient perspectives on clinical trial access, design, conduct, and post-trial followup. A call for comments was published on February 11, 2019 and the deadline for commenting was May 20. The agency received a total of nine comments. Comments were received from five organizations (representing patient advocacy, the pharmaceutical industry, and health technology) and four individuals.

Comments pertained both to topics addressed during the March 18, 2019 workshop as well as additional relevant topics not addressed during the workshop. All comments are available from the docket page at www.regulations.gov (Docket ID: FDA-2018-N-4731).