ENHANCING USE OF PATIENT-CENTERED DATA IN REGULATORY DECISION-MAKING

Supported by:

Table of Contents

ENHANCING USE OF PATIENT-CENTERED DATA IN REGULATORY DECISION-MAKING

About Friends of Cancer Research

Friends of Cancer Research (*Friends*) is our country's leading voice in advocating for policies and solutions that will get treatments to patients in the safest and quickest way possible.

Friends develops groundbreaking partnerships and creates a more open dialogue among both public and private sectors and tears down the barriers that stand in the way of conquering cancer. By collaborating with premier academic research centers, professional societies, and other advocacy organizations, *Friends* is able to accelerate innovation.

Friends works closely with government agencies and congressional leadership to create educational, policy, and scientific approaches to improve health outcomes and cancer care. As a respected independent think tank and advocacy organization, *Friends* is able to cut through bureaucratic red tape, put aside partisan politics, and engage all stakeholders, producing real results.

About The Burroughs Wellcome Fund

This document was made possible by the generous support of Burroughs Wellcome Fund and its Regulatory Science Initiative. The Burroughs Wellcome Fund is a private foundation located in Research Triangle Park, N.C. Its mission is to advance biomedical science by supporting research and education in the United States and Canada.

ENHANCING USE OF PATIENT-CENTERED DATA IN REGULATORY DECISION-MAKING

A Friends of Cancer Research Whitepaper Report

Executive Summary

The incorporation of the patient perspective into medical product development and regulation has been increasingly recognized by many stakeholders as vital to ensure that truly transformational new therapies are advanced. Indeed, this is an explicit goal of the 21st Century Cures Initiative,[1] launched in April 2014 by the House Energy and Commerce Committee Chairman Fred Upton (R-MI), along with committee member Rep. Diana DeGette (D-CO), intended to accelerate the pace of cures and medical breakthroughs in the United States. Patients are uniquely equipped to identify critical gaps and unmet needs in their disease areas, and to advocate for solutions to meet those needs. Patient advocacy is vital for disease-specific research fundraising and for lobbying Congress to enact policies that can accelerate research and development. Patients can also play a direct role in research by helping to set priorities, aiding in the design of clinical trials that measure outcomes that matter, and helping to define benefits that are clinically meaningful as well as risks that may or may not be acceptable in the treatment of their disease.[2]

In order to expand and improve the incorporation of patient input into research and regulatory decision-making, mechanisms to engage with patients are needed. Also needed are methods to identify and systematically measure patient-centric outcomes. These methods must go beyond the scope of traditional clinical trials, which historically opted for controlled experiences in homogenous patient populations and thus may not fully reflect the experience of "real-world" patients with an intervention. This "real-world" data collection may involve patient registries and large research networks that generate data from electronic medical records. Inclusion of the patient voice with these efforts is critical, to ensure that the resources being put into these efforts lead to answers to the questions that matter most to patients. Finally, in order to truly achieve patient-centered care, improved methods to communicate information about what is known about the relative benefits and risks of a potential treatment are needed so patients and their physicians can make informed decisions.

To discuss strategies to further integrate and enhance patient input, Friends of Cancer Research (*Friends*) convened a roundtable meeting in Washington, DC in May of 2015. The roundtable brought together leaders from advocacy, federal health agencies, clinical practice, academic research, and the pharmaceutical industry, and was observed by leading science-policy journalists. The meeting also served as an opportunity to welcome Dr. Robert Califf to his new role as the Deputy Commissioner for Medical Products and Tobacco at the U.S. Food and Drug Administration (FDA).

The dialogue throughout the day was framed around three main topics:

- Development And Utilization Of Patient Experience Data
- Application Of "Real-World" Data In Drug Development
- Communication Of Benefit-Risk And Regulatory Uncertainty

The key objectives of this meeting were to identify current challenges; to generate recommendations surrounding the use of patient experience data in regulatory decision-making and drug development; and to work toward consensus on how to operationalize and integrate proposals related to patient input that are currently under consideration in several venues, including Congress.

The action steps and recommendations presented in this paper were distilled from the dialogue throughout the day at the *Friends'* Roundtable and are not directly attributed to any one individual nor have they been endorsed by the participants or the organizations which they represent.

[1] The 21st Century Cures Act of 2015, H.R. 6, 114th Congress.

[2] Chakradhar, Shraddha. Training on trials: Patients taught the language of drug development. Nature Medicine. 2015; 21:209-210.

I. DEVELOPMENT AND UTILIZATION OF PATIENT EXPERIENCE DATA

In oncology, the traditional approach to understanding the safety and efficacy of new drugs has been to rely on objective measures of disease, such as tumor response and overall survival. However, these measures provide little information about the patient experience during treatment. Questions about treatment tolerability, ability to function, and symptom burden have been left largely unanswered; while some efforts exist to collect information about toxicity, it is often filtered through physician assessment, which research has shown to contain significant under-reporting.[3] Patient-reported outcomes (PROs), defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else," [4] would address this gap by helping establish a more complete benefit-risk profile of a new drug and help clinicians and payers arrive at a clearer understanding of its value.[5]

Meeting participants discussed several existing initiatives aimed at identifying which patient-centered outcomes are most important to measure and how to measure these outcomes. The Patient-Focused Drug Development Initiative,[6] the Patient Representative Program, [7] and the Patient Preferences Initiative[8] are leading FDA's efforts to engage patients during the regulatory review processes. The National Cancer Institute (NCI) has developed the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE),[9] as part of its commitment to develop quantifiable data about the patient experience. Despite these efforts, numerous challenges continue to impede progress in this area.

- **Patient diversity:** Unique experiences inform attitudes about benefits, risks and treatment goals. Additionally, perspectives may differ prior to, during, and following treatment and depending on experience with different therapies. Moreover, the experiences of patients who have experienced harm as a result of treatment are rarely shared beyond standard adverse event reporting.
- **Drug development and regulatory processes may hinder engagement:** Despite significant interest from patients to provide input, lack of familiarity with clinical trials, the policies and process of drug regulation, and access to and awareness of available opportunities for engagement may be significant barriers. Few mechanisms currently exist for systematic engagement of patients in the drug development continuum.

Action Steps

The most robust approach to ensure that patient experiences are captured is to develop mechanisms to standardize, optimize, and operationalize patient-reported data in clinical trials. Consistent use of standardized PRO tools, such as the PRO-CTCAE, across publicly and privately funded trials would enable standardization and interpretation of the data obtained using such a tool. Development of a core "advanced cancer symptom score," a method of measuring key symptoms across multiple disease types, should be pursued in order to facilitate standardized data capture and reporting of cancer symptoms.

---

[3] Di Maio M, Gallo C, Leighl N, et al. Symptomatic Toxicities Experienced During Anticancer Treatment: Agreement Between Patient and Physician Reporting in Three Randomized Trials. J Clin Oncol. 2015; 33(8):910-5.
[4] *Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling* Claims. 2009.
[5] Basch, E. Toward Patient-Centered Drug Development in Oncology. N Engl J Med. 2013; 369:397-400.
[6] Klein, R. FDA Voice Blog. FDA's Latest Efforts in Patient-Focused Drug Development Now in Full Swing. 2013. http://blogs.fda.gov/fdavoice/index.php/2013/06/fdas-latest-efforts-in-patient-focused-drug-development-now-in-full-swing/ . Accessed July 2015
[7] Patient Representative Program. http://www.fda.gov/ForPatients/About/ucm412709.htm . Accessed July 2015.
[8] McMurray-Heath. FDA Voice Blog. FDA Brings Patients into the Process. 2013. http://blogs.fda.gov/fdavoice/index.php/2013/09/fda-brings-patients-into-the-process/ Accessed July 2015.
[9] PRO-CTCAE, NCI. http://healthcaredelivery.cancer.gov/pro-ctcae/ . Accessed July 2015

As we continue to improve the use of patient experience data, the following robust engagement and education activities can substantially bolster these efforts.

- **Patient training programs:** Improved training and education processes can increase engagement and the robust nature of data collected, ensuring increased understanding of multiple disease experiences. While some programs are underway, comprehensive training programs for both individuals and organizations need to be developed to facilitate patient involvement in clinical trial design and risk-benefit decisions. Outreach and funding are needed to ensure effective participation.
- **Improving outreach to patients who have been adversely impacted by a treatment:** Capturing data not only from patients who have benefited from a treatment, but also from those who did not benefit or who may have been harmed, is vital to understanding the impact of a treatment.
- **Generating and publicizing data:** Methodological FDA guidance may facilitate patient data collection to improve knowledge of populations, diseases, and available therapies.
- **Publication of negative trial results:** Patient advocacy organizations, researchers and clinicians should advocate for the publication of negative trial results to inform our understanding of the full range of patient experiences.

II. APPLICATION OF "REAL-WORLD" DATA IN DRUG DEVELOPMENT

Only about three percent of adult cancer patients participate in clinical trials. Most of what we know about drug safety and effectiveness is gathered from this tiny sample that may offer an inaccurate or incomplete picture of a drug's performance. Ideally, marketing approval would not mark the limit of our understanding of a drug's performance, but instead the first step in an ongoing process to assess a drug's impact in real-world populations. Programs such as the FDA's Sentinel Initiative,[10] have improved the capture of patient outcomes data in real-world clinical practice, allowing for enhanced safety surveillance of new drugs. However, there is still much information on drug outcomes not recorded in a way that can inform regulatory decisions or medical practice. With improved data technology, many efforts are now underway to address this need, though challenges in data collection and management remain.

- **Off-label use:** While off-label drug use is common practice in oncology, particularly for patients who have exhausted all other treatments, or for patients with rare cancer types, very little information about off-label use is collected in any systematic way.
- **Data management**: Existing programs, such as the Sentinel Initiative, CancerLinQ,[11] and PCORnet,[12] intended to capture information about clinical care practices and generate large amounts of data, will require resources to ensure data can be effectively analyzed and disseminated to inform practice. This will require organization, interpretation, sharing, and incorporation into FDA procedures before it has any impact on patients' lives. Designing standards and a framework for sharing data while ensuring interoperability pose significant challenges. Additionally, standards will be needed for incorporating data into regulatory and medical practice, including benchmarks for altering labeling and guidelines for informing providers about changes to safety and efficacy data.

Action Steps

Despite these challenges, there are clear steps to facilitate drug development reflecting real-world scenarios. As more is learned from patients, who commonly receive treatments outside the clinical trial setting through new and existing programs, these lessons can then be applied to future clinical trial development.

[10] http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm
[11] http://www.instituteforquality.org/cancerlinq
[12] http://www.pcornet.org/

- **Alter clinical trial accessibility**: The tendency to reduce the number of variables to facilitate interpretation of trial results is directly at odds with increasing real-world representation in clinical trials. In an effort to move towards a more realistic representation within clinical trials, the following adaptations could facilitate the process:
    - Collect data from patients who do not meet eligibility criteria for clinical trials
    - Minimize exclusion criteria that lack scientific justification to facilitate patient enrollment and our understanding of drug performance in real-world patients
    - Enroll broader patient populations while identifying unique patient subsets on which to perform separate efficacy analyses to maintain scientific rigor
- **Improve the research infrastructure to better serve patients:** Bringing patient input into research requires a robust research infrastructure that encourages institutional collaboration and is designed to yield meaningful results. Reforms that can improve trial efficiency include reducing the number of uninterpretable safety reports for products under investigational new drug (IND) applications.[13] Similarly, reforms to expand the use of central institutional review boards (IRBs) to minimize trial delays and improved incentives to ensure rapid update of these programs are needed.
- **Use real-world data to bolster existing knowledge:** Using existing and future health information technology platforms, conduct randomized trials to the greatest extent possible to maximize the utility of real-world data. In addition, use observational data to identify drug effectiveness in small subpopulations of patients with a particular genetic characteristic.

III. COMMUNICATION OF BENEFIT-RISK AND REGULATORY UNCERTAINTY

Regulatory decisions need to communicate all information about the safety and effectiveness of a medical product at the time of marketing approval. Patient involvement in the development and approval process will help identify the information most meaningful and informative to patients, particularly with respect to the effect of treatment on specific symptoms or functional status.

Existing efforts, such as the Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making,[14] seek to clarify FDA's regulatory decisions so that patients, caregivers, and other stakeholders can better understand the rationale behind those decisions. Additionally, the FDA has several initiatives to educate health professionals, including CDERLearn, Bad Ad Program and Prescription Drug Promotion,[15] and the Expert Commentary and Interview Series on Medscape.

Roundtable participants discussed a number of ways to better communicate with patients and consumers as well as how existing communication tools, such as drug labels and direct-to-consumer advertising, can be improved so that quality information is conveyed to patients and health professionals.

- **Drug labels:** While the primary tool for communicating information is the label, the extent of drug label use in clinical practice is unclear.
- **Direct-to-consumer (DTC) advertising:** Minimal information about the uses, benefits and harms of a drug are conveyed with these communications. However, an opportunity exists to use DTC as a mechanism to communicate valuable public health messages about a product, such as what is known about a drug's efficacy from clinical trials and the specific populations most likely to benefit.

---

[13] *FDA Guidance for Industry and Investigators: Safety Reporting Requirements for INDs and BA/BE Studies*. December 2012.

[14] Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making Draft PDUFA V Implementation Plan - February 2013 Fiscal Years 2013-2017. Accessed July 2015.

[15] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/DrugMarketingAdvertisingandCommunications/ucm209384.htm . Accessed July 2015.

Action Steps

The following recommendations highlight ways to improve communication of benefit-risk and regulatory uncertainty.

- **Expand FDA-patient advocacy partnerships:** Many patients and their caregivers seek information relating to their treatment options through patient advocacy organizations. Thus, strengthening collaborations and more open communication between FDA and these groups can ensure that the information they provide to patients is accurate. Through patient training programs, such as those discussed in Section I, patients can be introduced to the various opportunities they have to engage with the agency.
- **Improve accuracy and timeliness of label updates:** With new information being gathered – including new data on supplemental indications, a drug's comparative effectiveness, or new safety signals – labels need to be rapidly updated to reflect the new knowledge.
- **Improve usability of Medication Guides:** Medication Guides should be written to ensure they are more clearly understood by patients with a varying base of knowledge and experience.

CONCLUSION

Drug developers, researchers, physicians, and regulators are forming closer collaborations with patients. This development has been critical to identify outcomes and safety signals that are most valuable for informed decision-making prior to drug marketing and during clinical use. Thus, the field has made great strides in understanding the appropriate balance of benefits and risks of new drugs. Even so, significant work is still needed in these critical areas: Finding standardized mechanisms to collect patient experiences, developing new ways to communicate benefits and risks, and capturing more information from real-world clinical experience.

The discussion at the Friends of Cancer Research Roundtable on May 15, 2015, garnered a strong consensus that comprehensive patient education programs are needed to improve patient engagement in health care decisions and the research process. Programs must be made available to guide understanding of the drug development and approval process; to educate medical students and practicing physicians; to simplify drug labels such that they provide direct, succinct and useful information; to use real-world data to enhance understanding of drug performance; and to assimilate the data that is collected from different sources to allow for the full utilization of findings by the greater community. Taken together, these steps will incorporate a strong patient voice throughout the process and will thereby improve the quality of care for millions of individuals.

For correspondence relating to this report please contact:
Ryan M. Hohman, JD, Managing Director, Policy & Public Affairs, at 202.944.6708 / rhohman@focr.org

PARTICIPANTS IN MAY 2015 ROUNDTABLE MEETING IN WASHINGTON, DC

Jeff Abrams, MD	Associate Director, Cancer Therapy Evaluation Program, National Cancer Institute
Jeffrey S. Akman, PhD, MD	Vice President for Health Affairs, George Washington University
Jeff Allen, PhD	Executive Director, Friends of Cancer Research
Margaret Anderson, MA	Executive Director, FasterCures
Joel W. Beetsch, PhD	Vice President, Patient Advocacy, Celgene
Cynthia Bens	Vice President, Public Policy, Alliance for Aging Research
Robert Califf, MD	Deputy Commissioner for Medical Products and Tobacco, US Food and Drug Administration
Renzo Canetta, MD	Vice President, Oncology Global Clinical Research, Bristol-Myers Squibb
Heather S. Chaney	Director of Programs, Friends of Cancer Research
Toni Clarke	Health Correspondent, Reuters
Allan Coukell, BSc (Pharm)	Senior Director for Health Programs, Pew Charitable Trusts
George Dahlman	Executive Vice President, Federal Affairs & Operations, National Patient Advocate Foundation
Anna Edney	Reporter, Bloomberg
Andrea Ferris, MBA	President and Chairman of the Board, LUNGevity Foundation
Mark Fleury, PhD	Principal, Policy Development, Emerging Science, American Cancer Society Cancer Action Network
Megan Frisk, PhD	Associate Editor, AAAS-Science
Ryan Hohman, JD	Managing Director, Policy & Public Affairs, Friends of Cancer Research
Kay Holcombe	Senior Vice President, Science Policy, BIO
Nina Hunter, PhD	Special Assistant for Medical Policy, Office of Medical Products and Tobacco, US Food and Drug Administration
Karen Jones	Vice President, Global Oncology Regulatory Head, Genentech
Paul Kluetz, MD	Medical Officer, US Food and Drug Administration
Marina Kozak, PhD	Science Policy Analyst, Friends of Cancer Research
Jonathan Leff	Partner, Deerfield Management
Theresa Mullin, PhD	Director, Office of Strategic Programs, US Food and Drug Administration
Richard Pazdur, MD	Director, Office of Hematology and Oncology Products, US Food and Drug Administration
Andy Pope, PhD	Director, Board on Health Sciences Policy, Institute of Medicine
Amrit Ray, MD, MBA	Chief Medical Officer, Janssen Pharmaceuticals
Sara Reardon	Reporter, Nature
Nancy Roach	Founder and Chair, Fight Colorectal Cancer
Samantha A. Roberts, PhD	Science Policy Analyst, Friends of Cancer Research
Deborah Roth	Associate Commissioner of Operations, US Food and Drug Administration
Richard Schilsky, MD, FACP, FASCO	Chief Medical Officer, American Society of Clinical Oncology
Roslyn Schneider, MD, MSc	Global Patient Affairs Lead, Pfizer
Joe Selby, MD, MPH	Executive Director, Patient-Centered Outcomes Research Institute
Michael Shea	Policy Research Analyst, Friends of Cancer Research
Rachel Sherman, MD, MPH, FACP	Principal, Greenleaf Health
Jeff Shuren, MD, JD	Director, Center for Devices and Radiological Health, US Food and Drug Administration
Ellen V. Sigal, PhD	Chair & Founder, Friends of Cancer Research
Pamela Tenaerts, MD	Executive Director, Clinical Trials Transformation Initiative


FRIENDS
of CANCER
RESEARCH