

FROM MOLECULES TO MEDICINE: HOW PATIENTS CAN SHARE THEIR VOICES THROUGHOUT THE DRUG DEVELOPMENT PROCESS



Introduction

The world of drug development is rapidly changing, and one of the most fundamental changes is the increased participation of patients, their families, and their caregivers throughout the process. Historically, pharmaceutical companies and regulatory agencies included participation from patients at limited points during drug development, most often when a drug was nearing approval. Patients' and caregivers' knowledge was not routinely included at key points such as targeting early research, assessing the benefits and risks of new therapies, developing regulatory guidelines, or designing clinical trials. This is changing and in this Toolkit, which is part of a series on drug development, we will offer information and case studies that highlight how the patients are using their voices to drive conversations, research and drug development to yield significant advances for their disease communities. For more information about drug development in general or to learn in depth about clinical research, visit **From Molecules to Medicine: How Are New Drugs & Therapies Made and From Molecules to Medicine: Clinical Research.**



SECTION 1: PATIENT ENGAGEMENT: DRIVING DRUG DEVELOPMENT

Rare disease patients and their communities have harnessed the power of increasingly accessible medical information and begun to participate proactively not only in their medical decisions, but also in the research toward developing new or improved therapies. Researchers and biotechnology and pharmaceutical companies are recognizing more and more the benefits of engaging with patients early and often to work together on drug development. The Food and Drug Administration and Safety Act of 2012 (FDASIA) required that the FDA enhance patient engagement, which has led to efforts to include patient experiences and insights from the very first stages of drug development. Patient groups can participate in and shape basic research, preclinical research, clinical research, drug development regulations, and post-marketing decisions and access to therapeutics (See Chart). Patient participation is vital at all stages of this process. Patients and their families can think about what is needed to advance therapeutics for their rare diseases and what they are passionate about and choose from many types of important activities that can shape progress toward the development of treatments and cures.

“Patient groups can develop a strong patient community, support or fund research, encourage data sharing, provide data, participate in clinical trials, support research, help provide patient perspectives to the FDA, advocate for regulatory changes, or work to ensure access to therapeutics. None of them are wrong. All of them are good and contribute to a whole. If we all did the same thing, it wouldn’t be useful.” – Pat Furlong, Founding President and CEO, Parent Project Muscular Dystrophy, describing the wide range of missions that patient organizations may engage in at the 2015 Global Genes Patient Advocacy Summit

The goal of this Toolkit is to enable patient communities to identify where and how they can share their voices during drug development. The information relating to interacting with regulatory agencies will focus on the U.S. Food and Drug Administration (FDA). However, the information relating to collaborations with researchers and companies is relevant to organizations worldwide. Each topic includes one or more case studies of patients or patient groups who have engaged in the drug development process.

SECTION 1: PATIENT ENGAGEMENT: DRIVING DRUG DEVELOPMENT

WHERE PATIENTS CAN PARTICIPATE				
Types of Participation	Basic Research	Preclinical Research	Clinical Research	Post-Marketing
Forming Patient Communities	✓	✓	✓	✓
Encouraging research	✓	✓	✓	✓
Funding research	✓	✓	✓	
Encouraging data sharing	✓	✓	✓	
Providing data	✓	✓	✓	✓
Participating in clinical trials	✓	✓	✓	
Participating in advisory committees	✓	✓	✓	✓
Advocate for regulatory changes	✓	✓	✓	✓
Ensuring access				✓

SECTION 2: FORMING PATIENT COMMUNITIES



A critical first step for patients to participate in the drug development process is to create or join a strong, well-organized patient community. Patient communities often are structured, nonprofit patient advocacy organizations and are usually disease-specific. However, patient organizations can also form collaborations with other patient groups, disease organizations, or think tanks to focus on specific policy or regulatory issues where they have overlapping interests. Patient communities can be active at any point during the drug development process—from basic research through post-approval and marketing of therapies.

“The more organized a patient group is, the more they know and can share with researchers and companies. For example, a patient group can provide a better understanding of whether there are unmet medical needs and how many patients there are in the U.S. and in other countries. This information can be very valuable and compelling to researchers when considering an experimental compound for further development.” —Alan Gilstrap, Executive Director, Advocacy and Policy, Akcea Therapeutics

Patient communities provide a way to gather many voices together, emphasizing to researchers, pharmaceutical and biotechnology companies, and regulators that

there is broad importance to patients of issues relating to new therapies, marketed therapies, or regulations for drug development. Having an organized patient community makes it easier for researchers and companies to enroll patients in clinical trials and research studies. They can also serve as a key means to gather well-organized data on patient needs and outcomes that can be used by researchers, companies, and regulators in developing and approving therapies. Patients and their families can work with researchers and companies and provide insights to regulators individually. But, an organization that is able to provide information from many patients and an infrastructure for many patients to engage with other stakeholders is extremely useful. It strengthens collaborations and results in greater influence within the drug development process. Information about setting up a nonprofit organization is available through Global Genes Toolkits [Starting a Nonprofit](#) and [So You Think You Want to Start a Nonprofit](#). There are also great examples of individuals affected by a rare disease who decide to join up with or add a program to an existing nonprofit organization instead of creating a separate nonprofit. Patients and caregivers interested in setting up a nonprofit should consider where there are gaps in the efforts of current organizations. Where there is overlap in interests and missions, patients and caregivers may want to seek out partnerships and collaborations with existing nonprofits. Existing nonprofits should also encourage participation from new partners who want to get involved in achieving the organization’s mission. This helps to prevent redundancies and inefficiencies that can come from having multiple foundations for the same disease. Connecting with other patients who share your rare disease journey can be done by reaching out to existing patient organizations or through online communities such as [RareConnect.org](#).

SECTION 2: FORMING PATIENT COMMUNITIES

Case study

Castleman Disease Collaborative Network

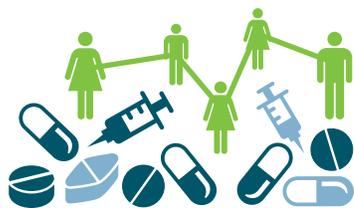
In 2012, Dr. David Fajgenbaum, a physician-researcher and a Castleman Disease (CD) patient himself, and Dr. Frits van Rhee of the University of Arkansas for Medical Sciences, created the Castleman Disease Collaborative Network (CDCN) with the goal of accelerating research and development of treatments for CD. As part of its mission, the CDCN provides information, resources, and ways for CD patients to participate in research. CDCN has partnered with RareConnect.org to moderate an online patient forum allowing patients to share information about diagnosis and treatments with other patients, researchers, and physicians. CDCN also provides physician referrals and disease information for patients. CDCN holds an annual Patients & Loved Ones Summit, which helps CD patients to connect with one another, learn about up-to-date research, and discuss ways to advance treatments and research. CDCN is also developing a natural history study and registry and a biobank to collect data and tissue samples allowing patients to provide critical information and data to researchers. But the critical aspect of the CDCN is that it provides an organized way for patients, researchers, and clinicians to work together. Without the CDCN, Dr. Fajgenbaum points out that it would be much harder for CD patients to participate in research, “it is really difficult to be involved if there is no infrastructure in place,” he says. “If the Collaborative Network was not available, it would be very hard to get involved in research. Instead, patients register themselves on CDCN.org and are updated about the latest research studies. It is crucial to have an entity that can serve as a platform for collaboration. As a result, we’ve been able to launch studies that would never have been possible at one institution because CD is rare.”

Resources

RareConnect.org:
<https://www.rareconnect.org/en>

SECTION 3:

ENCOURAGING RESEARCH THROUGH PERSONAL CONNECTIONS



No one understands the needs of patients like the patients themselves and their caregivers. Similarly, no one can make the case for the need for research and the direction of research like patients and caregivers. Patients can share their perspectives with researchers at academic institutions and at companies, which can provide both new directions on research

approaches and personal connections that connect and motivate researchers. Often patients are focused on encouraging basic research or preclinical research to learn more about the disease or develop animal models or tools to help in drug development. But patients may also be interested in encouraging research to develop more effective therapies even after there are available treatments on the market.

The first step in reaching out to researchers is finding them. A valuable resource is PubMed, an online database maintained by the National Institutes of Health, at pubmed.org. It contains more than 25 million citations from biomedical research publications. These publications are written by academic researchers and by scientists at pharmaceutical and biotechnology companies. The database can be searched by several terms, such as key words or clinical study categories. The search results include the article title, journal title, and a link to the abstract (See Box to the left).

[Policy Issues in the Development and Adoption of Biomarkers for Molecularly Targeted Cancer Therapies: Workshop Summary](#)
 1. [Targeted Cancer Therapies: Workshop Summary](#)
 National Cancer Policy Forum, Board on Health Care Services, Institute of Medicine.
 Washington (DC): National Academies Press (US); 2015.
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 2. Bencivenga F, Cucini R, Capotondi F, Battistoni A, Mincigrucci R, Gianrisostomi E, Gessini A, Manfreda M, Nikolov IP, Pedersoli E, Principi E, Svetina C, Parisse P, Casolari F, Danailov MB, Kiskinova M, Masciovecchio C.
 Nature. 2015 Apr 9;520(7546):205-8. doi: 10.1038/nature14341.
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[Molecular imaging of angiogenesis after myocardial infarction by \(111\)In-DTPA-cNGR and \(99m\)Tc-sestamibi dual-isotope myocardial SPECT](#)
 3. Hendrikx G, De Saint-Hubert M, Dijkgraaf I, Bauwens M, Douma K, Wlerts R, Pooters I, Van den Akker NM, Hackeng TM, Post MJ, Mottaghy FM.
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Personal contact begins with a concise, clear email or phone call requesting a chance to talk about your experience with your disease and ways patients and patient advocacy groups can help researchers advance the research efforts. Patient groups should recognize that researchers are very busy and may not respond immediately. It may take some follow-up requests (spaced a few to several weeks apart).

PubMed Journal Citation Search Results (from <http://www.ncbi.nlm.nih.gov/books/NBK3827/#pubmedhelp>.
[How_do_I_search_PubMed](http://www.ncbi.nlm.nih.gov/books/NBK3827/#pubmedhelp))

SECTION 3: ENCOURAGING RESEARCH THROUGH PERSONAL CONNECTIONS

Patients can also encourage research by helping to develop connections between researchers. Patients may be able to introduce researchers who are working independently in order to encourage collaborations. If resources are available, patients may be able to bring several researchers together at a meeting or symposium to discuss gaps in current knowledge or therapies and the next steps needed to close those gaps. Patient groups should also consider asking these researchers to serve as advisors or to serve on an advisory board to provide guidance on research topics.

Case Studies

Castleman Disease Collaborative Network

One of the first tasks of the CDCN was to identify all the researchers or physicians who had done any work on CD, because the CDCN wanted to connect the community for collaboration and prioritization of research. The researchers and physicians were identified through searches on PubMed and were contacted by email. Then, the CDCN held an in-person and virtual meeting of researchers

working on CD. The CDCN scheduled the in-person meeting to overlap with an international hematology conference, where many of the researchers would already be attending, which made it easier for researchers to come to the CDCN meeting. After the meeting, the CDCN invited select meeting participants to serve on the CDCN's Scientific Advisory Board (SAB). The SAB set out to determine what research studies should be done first. The CDCN did not turn down any researchers or physicians who expressed interest in joining the SAB, and two patients, who happened to have medical backgrounds, were appointed to serve on the SAB. Now the SAB provides strategic guidance to identify gaps in CD knowledge and approach researchers or offer research grants to try to fill in those gaps.

Bridge the Gap - SYNGAP

In 2012, Monica Weldon's son, Beckett, was diagnosed with a rare autosomal dominant disorder, SYNGAP-1. This genetic condition causes intellectual disability and developmental delays. Following her son's diagnosis, she co-founded Bridge the Gap—SYNGAP, a patient organization dedicated to uniting stakeholders in research on SYNGAP disorders. In beginning the patient organization, Monica began searching for researchers working on her son's disorder. She found one paper published on the condition and sent an email to the researcher. After about six months, the researcher responded by inviting her to his lab to discuss her and her son's experience with the condition. Monica shared her knowledge of some recent patient experiences, including that some patients had experienced improvements in cognition and verbal skills with seizure medications. The researcher, who had not been aware of these experiences, quickly searched about the seizure medicine and noted that it was a glutamate inhibitor, which put him on an

author information link

Curr Treat Options Neurol, 2016 Jan; 18(1):2. doi: 10.1007/s11940-015-0387-9

Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic.

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Abstract

OPINION STATEMENT: Neuromyelitis optica spectrum disorder (NMO) is a rare, autoimmune disease of the central nervous system that primarily attacks the optic nerves and spinal cord leading to blindness and paralysis. The spectrum of the disease has expanded based on the specificity of the autoimmune response to the aquaporin-4 water channel on astrocytes. With wider recognition of NMO, a standard of care for treatment of this condition has been developed based on a growing series of retrospective and prospective studies. This review covers the present state of the field in the treatment of acute relapses, preventive approaches, and therapies for symptoms of NMO.

KEYWORDS: Azathioprine; Eculizumab; Immunosuppression; Mycophenolate; Neuromyelitis optica spectrum disorder; Rituximab

PMID: 26705758 [PubMed]

Abstract page showing author information (from a search for “rare diseases” on pubmed.org)

SECTION 3: ENCOURAGING RESEARCH THROUGH PERSONAL CONNECTIONS

entirely different track in his research about the causes and mechanisms of the condition. The researcher also asked Monica and another parent of a SYNGAP child what would be the one thing they would want to change for their children. Both parents immediately said they would want their children to have the ability to speak. The researcher had been focused on the intellectual disabilities, but this desire expressed by the parents led him to think about different aspects of the disease. The researcher had noted that mice models of the disease also involved paralysis of facial muscles, which could be a primary cause of the limitations in speech of SYNGAP patients. Again, this put the researchers on a different focus of their investigations.

After the visit with the researcher, the families continued to accelerate the process by making available the information needed to narrow down the types of seizure medications their children take. On a voluntary basis, parents of our SYNGAP children consented to providing formal letters to the researcher explaining the different types of seizure medications that provided a benefit and ones that created negative side effects. This gave the researcher a better perspective of the observations seen in real time. This may help him pinpoint the types of drugs to focus investigation on. Providing the other non-seizure related medications gave the researcher an idea of different drug combinations that worked and didn't work. This was the best way families could provide information until they had a patient registry up to officially provide the needed information for researchers to continue to accelerate the process. Another benefit the letters provided was the needed evidence to support current research grants that the researcher was applying for.

What began as a short meeting led to parents providing their perspectives and understanding of the daily life of the condition, which resulted in the researchers considering new avenues in their research approach.

Resources

PubMed: <http://www.pubmed.org>

SECTION 4: FUNDING RESEARCH



Research and clinical trials require funding. When patient groups provide that funding, they can make sure that research relevant to their rare disease proceeds. Funding for research may be needed at all stages of the drug development process. Patients can help identify specific research questions needed to continue building the foundation toward drug development, such as biochemical research, animal models, biomarker development, outcomes research, or genomics. They can identify promising treatments that may need additional research to support or begin clinical trials. They can also help identify and conduct research on repurposing already approved therapeutics that may be effective as treatments for rare diseases.

Patient groups can provide funding to researchers at academic institutions or to start-up companies. Funding can take the forms of research grants, angel investing, or venture philanthropy. In any instance, a Scientific Advisory Board is very helpful in selecting the recipient of the research funding.

Research grants can be made to researchers at academic institutions or to companies. The size of a research grant can be very large such as a multi-million dollar grant, but much can be accomplished with smaller grants such as \$25,000-\$50,000 or even microgrants such as \$3,500-\$5,000. A research grant often involves no stake in any future development of intellectual property or future revenues. Patient groups can hold open research grant solicitations (often called “Request for Applications” (RFA) or “Request for Proposals”

(RFP)), where applicants submit an application for funding. Patient groups may also identify a research project needed to fill gaps in understanding of a rare disease and directly approach a leading researcher in the field to offer funding for that project. Research grants may, and clinical trials definitely will, require review by institutional committees, such as the Institutional Review Board. If data or specimens are being provided to the researcher, additional agreements beyond the research grant may be required, such as Material Transfer Agreements.

Another means of providing funding to start-up companies is through angel investing or venture philanthropy. This typically requires a fairly large investment, often in the millions of dollars. It also often involves the patient group receiving a stake in the company or royalty rights for a therapy.

For all research funding, it is important to be sure that the researchers or companies have the needed skills to complete the research or clinical trial. Again, this is where a Scientific Advisory Board can provide valuable insights. To ensure progress is continuing on research, patient groups should consider developing a reporting process for research grants, such as requiring quarterly progress reports or structuring the grants so the researchers receive additional funding upon the completion of specific achievements. For clinical trials, the FDA is also willing to meet with patient groups funding clinical trials to review the planning and design of clinical trials.

Along with finding an expert in the disease to serve as a principal investigator for a clinical trial, patient advocates should ensure that clinical trials they are involved in funding are run by researchers with knowledge of clinical trial regulations and of the FDA. Patient advocates should consider the “regulatory merit” as well as the scientific merit of a

SECTION 4: FUNDING RESEARCH

clinical trial they may fund. Adhering to clinical trial regulations allows the FDA to be confident in the reliability of the data they are reviewing. If regulations are not followed, the FDA may not consider the data to be reliable and usable. – Summarized from a presentation at the 2015 Global Genes Rare Patient Advocacy Summit by Dr. Gayatri Gao, Director of the Office of Orphan Products Development at the FDA, on Mapping Drug Development

Case Studies

Castleman Disease Collaborative Network

One of the principal programs of the Castleman Disease Collaborative Network (CDCN) is providing research grants to further the understanding of CD. They have two approaches: investigator-initiated grants where interested researchers can apply in response to a Request for Proposal (RFP) and strategically-directed research grants where the CDCN directly seeks out labs to perform a particular study that has been identified by the CDCN. They place at least one RFP per year for one to two grants of \$10,000 to \$20,000. For the strategically directed research grant, the CDCN Scientific Advisory Board recommends to the Board of Directors that there is a study that needs to be done and then discusses who would be best to do the research. The CDCN then contacts the strongest researcher directly, even if it is a researcher who has expertise in a particular method or research approach but is not working on CD. Regardless of how the CDCN funds research, the CDCN always provides assistance with identifying samples for the study and the logistics of getting the study off the ground (such as Institutional Review Board submissions, Data Sharing Agreements, and project management).

Cure SMA

Spinal muscular atrophy (SMA) is a genetic disease that affects the motor nerve cells. Children affected lose the ability to walk, talk, and, eventually, breathe. It is the leading genetic cause of infant deaths. Cure SMA works to support research to develop treatments and ultimately a cure for SMA as well as to support patients and their families in getting the care they need. As part of its mission, Cure SMA provides funding for research on new therapies. However, their funding strategy has shifted over the last several years. Initially, more than 15 years ago, companies were not very interested in pursuing drug development for SMA, so the organization, in collaboration with other patient groups, provided funding for preclinical development of about \$20 million. Now, several companies are actively investigating new therapies, and Cure SMA now provides “seed money” or early-stage funding, to help get projects going where they can then receive government or private funding to continue. Cure SMA funds both basic research and drug development. For basic research, Cure SMA, under the guidance of their Scientific Advisory Board, puts together a Request for Proposals (RFP) for investigator-driven projects. The award recipients provide progress reports every six months, but, beyond that, Cure SMA does not actively manage the project unless there is a significant issue. When funding drug development programs, Cure SMA takes a much more active role. They often use a Joint Steering Committee (JSC) with representatives from Cure SMA and from the company. The JSC is charged with making all project decisions, and all the funding is dependent on meeting specific milestones, such as having an optimized a drug compound for animal testing. Further, Cure SMA retains some rights to intellectual property for compounds they fund research on. Any money that Cure

SECTION 4: FUNDING RESEARCH

SMA receives from this intellectual property is invested back into research or family support programs.

Resources

Cystic Fibrosis Foundation Venture

Philanthropy Model: <https://www.cff.org/Our-Research/Our-Research-Approach/Venture-Philanthropy/>

FasterCures University Foundation

Relations: <http://www.fastercures.org/programs/university-foundation-relations/>

FasterCures Philanthropy Advisory Service:

<http://pas.fastercures.org/>



SECTION 5: ENCOURAGING SHARING OF DATA

Research projects and clinical trials often depend on data that can sometimes be difficult to collect from many patients, particularly for patients who live with rare diseases. Unfortunately, sometimes when researchers do collect this data they try to keep tight control over it and do not share it broadly. This is partly because researchers must write original journal articles as often as possible to get promoted and to get research grants, so it is useful to be in control of original data. But patient groups should work to be sure this data is shared, which will maximize the chances of learning about how rare diseases work and of speeding development of therapies. Patient groups can encourage sharing of valuable data. When looking for researchers to work with, patient groups can seek out researchers who are willing to share data and collaborate with other researchers. Patient groups can also encourage researchers to share data by talking about the importance of many researchers working on a problem. Another way for patient groups to encourage data sharing is to gather data themselves and then allow open access by researchers (see also the section “Providing Data”). In setting up shareable databases or collections of biological samples, patient groups should be sure to have input from a Scientific Advisory Board or other scientific consultants. Setting up databases or biobanks also requires working with an institution capable of properly storing the data.

Case Study

A-T Children’s Project

Ataxia telangiectasia, or A-T, is a rare genetic disease that becomes apparent in childhood. It causes progressive loss of muscle control, immune system problems, and a high rate of cancer. When two of their three children were diagnosed with A-T, Brad and Vicki Margus founded the A-T Children’s Project to fund research, scientific conferences to share research results and next steps, and a clinical treatment center to discover and develop therapies to improve quality-of-life, and, ultimately, to cure the disease. While speaking to researchers, Brad Margus realized that there was a need for blood, tissue, cell, and spinal fluid samples to advance understanding of the disease. There were two researchers who had been gathering these biospecimens, but, unfortunately, they did not collaborate together and they would not always provide access to researchers working on the disease. So Brad determined that the A-T Children’s Project would develop its own biobank that it could share with any qualified researcher. He reached out to the Coriell Institute for Medical Research to set up the biobank and worked with 100 families to have samples sent. This removed a major barrier to research on A-T. As Brad explained at the 2015 Global Genes Rare Patient Advocacy Summit, “That completely changed the game. I didn’t need to worry about people having to pass through these two researchers.”

The A-T Children’s Project is also trying to collect a large database of clinical data and genetic sequencing. Again, the organization will make this database widely available to qualified researchers. Brad described the goal, “We want to make sure the database isn’t owned by one consortium of researchers who have a private club and you have to get in their club to get access to their data.”

SECTION 6: PROVIDING DATA



Patient groups can play a key role in gathering and sharing many different kinds of data for drug development with researchers, regulators, and companies.

They can encourage patients to participate in registries, biobanks, or other databases developed by researchers or companies. Disease registries may include information such as symptoms, genomic data, treatments, and/or disease progression. A biobank is a collection of biological samples such as tissues, blood, or cells, which can be very useful in research and drug development.

Patient groups can also create and maintain their own registries and biobanks. They can create a contact registry that contains names, contact information, and basic information about their rare disease. This contact registry can then be used as a way for patients and researchers to connect—patients can learn about clinical trials and researchers and companies can seek out patients to participate in clinical trials or surveys or focus groups about their disease. Contact registries can also provide a way to let patients know about opportunities to contact the FDA and provide feedback to advisory committees (see the section on Participating in regulatory agency or industry advisory committees). Patient groups can also create more detailed registries that include clinical data for the patients. Patients and patient groups should keep the “long view” in mind when creating a registry and try to create a database that will allow extended future use, including using standardized language, specifying potential future uses in

the informed consent process, and ensuring the potential for data sharing. Patient groups should also consider the importance of owning the data within the patient registry, which can make it easier to share the data and ensures any financial benefits can be returned to the patient organization.

Patient groups may want to set up a biobank that is controlled by the patient organization, so that the samples can be easily shared with qualified researchers. Biobanks must be stored carefully, requiring a contract with a research organization that can store the samples properly.

Patients can also play a role in facilitating participation of their family members in registries or biobanks. When a rare disease has a genetic cause, it can be very helpful to understand how the patient is different and similar to other family members.

Case Study

Cure SMA

Cure SMA has supported two different types of patient registries—a registry that is maintained by another organization and an internal contact or membership registry. The Cure SMA membership-based registry has information from almost 2,000 newly diagnosed families who have contacted Cure SMA for resources. Families are asked a core set of 20 questions, such as when the child was first diagnosed and how long was the time from noticing symptoms to diagnosis. But, they are thinking of how to expand the internal database and include more clinically oriented information. Still, this contact registry has been enormously helpful to patients’ families and to companies. Patients’ families have learned about clinical trials that are open for enrollment when companies have

SECTION 6: PROVIDING DATA

used the registry for help with recruiting. The registry also contains some data about time to diagnosis for different types of SMA, which can be very helpful for companies when planning their clinical research efforts.

Resources

Global Genes Toolkit: [Understanding Rare Disease Registries](#)

SECTION 7: PARTICIPATING IN CLINICAL TRIALS



New therapies that improve the quality-of-life or even provide a cure for rare disease patients must pass through a series of clinical trials before being made available to everyone. But these clinical trials cannot be completed without patients who are willing to participate. Finding a relevant clinical trial is the first step toward participation. Patients can ask their physicians about available clinical trials. Patients also can seek out potential clinical trials on their own and directly contact the clinical investigators using resources such as clinicaltrials.gov. Patient groups can help with encouraging patients to join clinical trials by providing information about trials that are recruiting for patients and providing information about participation.

The second toolkit in this series, **From Molecules to Medicines: Clinical Research**, provides more detailed information about clinical trials, how to find them, how to join, what patients should ask before joining, and how to find information from completed clinical trials.

Case study

Cure SMA

Cure SMA often is one of the first contacts that newly diagnosed families turn to for resources and guidance. Each family receives a care package that includes information about caring for a person with SMA, research publications, information about Cure SMA events, and a list of clinical trials that are currently recruiting. This provides a valuable resource to SMA families of all the available options for receiving experimental therapeutics, particularly key since there are no treatments available at this time. Companies also value this resource since it provides a way to recruit for clinical trial participants.

Resources

Global Genes Toolkit: From Molecules to Medicine: Clinical Research

Clinical Trials 101 from the Michael J. Fox Foundation for Parkinson's Research:
<https://www.michaeljfox.org/page.html?Clinical-Trials-101>

SECTION 8:

PARTICIPATE IN REGULATORY AGENCY OR INDUSTRY ADVISORY COMMITTEES



During the drug development process, regulatory agencies and companies seek input and advice from many different advisory committees. Patients can provide valuable insights as members of these advisory committees for companies and for the FDA. Patients can also provide valuable perspectives as outside experts providing testimony to help FDA advisory committees in their decision-making.

Pharmaceutical companies may put together advisory committees of patients and their families to understand how rare diseases affect their daily lives. This helps companies develop patient reported outcomes that can demonstrate the effectiveness of new therapies for patients to regulatory agencies. Companies may reach out to patient groups or to online patient communities to search for patients willing to participate. Patients may also reach out directly to companies. Patients can search for companies that are developing therapies for their disease. They can then contact the Patient Advocacy Department to offer to assist the company in understanding their disease.

Patients and their caregivers can also provide input to regulatory agencies in a number of ways. They can provide direct input to advisory committees, serve as a member on an advisory committee, or provide input as a consultant or presenter.

Patients, caregivers, and their families and loved ones can have their voices heard by **directly submitting letters, testimony, or comments to Advisory Committees**. Each Advisory Committee meeting is announced publicly in the Federal Register (www.federalregister.gov) and on the FDA's Advisory Committee website. Interested people can submit written information or can request to present at the Advisory Committee meeting. You must register to be recognized as a speaker through the FDA website or on site before the Advisory Committee meeting. However, if there are many people interested in speaking, the FDA may choose speakers by lottery. Presentations to FDA Advisory Committees also are another place where patients and patient groups may engage with companies to work to be sure patient perspectives are included in the Advisory Committee discussions. Patients can share their stories to advisory committees, even at a very early stage in the drug development process. Patient input can change the status of an experimental therapy from the standard review process to an accelerated review process, which can speed up the developmental timeline.

Through the **Patient Representative Program**, patients and caregivers can serve as voting members on FDA Advisory Committees charged with reviewing new drugs, as consultants for the review divisions to provide perspective on patients' needs and patients' own assessment of benefits and risks of new therapies, and as presenters at FDA workshops on regulatory and health policy or disease-specific topics. The FDA posts application information for patient representatives in specific programs as opportunities occur.

Another forum for providing the patient perspective are **Patient-Focused Drug Development: Disease Area Meetings**.

SECTION 8: PARTICIPATE IN REGULATORY AGENCY OR INDUSTRY ADVISORY COMMITTEES

These meetings are not directly tied to review of an experimental therapeutic. Instead, these meetings are a way for the FDA to gather patient and caregiver perspectives on their disease and on any benefits or limitations of current treatments that will be used to inform future FDA decisions. The meetings involve a panel discussion led by patient advocates followed by a facilitated discussion involving audience members. Information on applying to serve as a panelist presenting comments is available on the registration website. If a meeting is not scheduled to be held for a specific disease, patient groups can contact the FDA and host their own disease area meetings. The results and discussions of these meetings will be heard and treated by the FDA as if they had sponsored the meeting.

When working with the FDA, it is important to remember that the FDA is required to consider the benefits versus the risks of therapeutics. It is not enough to just let the FDA know about the difficulties patients experience while living with a rare disease, getting diagnosed, or receiving therapeutics. The FDA must be able to consider how new therapies improve outcomes in ways that can be measured. When talking about approving a new therapeutic, patients should let the FDA know how it has improved daily life, and let the reviewers know that the improvements are worth the potential side effects. When talking about your disease, let the FDA know how your daily life is affected, the drawbacks of any available therapies, what would be improvements that would help you, and, most importantly, why those improvements would help. Whenever possible, try to include numbers with your descriptions, such as how many more times you can do something or how many fewer times you experience symptoms of your disease. Outcomes of an experimental therapy that are predictable and measurable are extremely useful within the review process.

The FDA has resources dedicated to helping patients and medical providers understand how to work with the agency. **The FDA Patient Network** works to communicate with patients and educate patients and healthcare professionals about drug development regulations. The Patient Network also provides resources including patient-specific webpages providing guidance on interacting with the FDA, a twice monthly newsletter, and an annual Patient Network Meeting that provides details on the FDA process. The Center for Drug Evaluation and Research at the FDA also has recently created the Professional Affairs and Stakeholder Engagement (PASE) office. The role of PASE is to be the primary contact for patients, patient groups, and healthcare professionals regarding education and advocacy during drug development and review. Patient groups are encouraged to review online and written materials about how FDA works and develop a clear vision of the outcomes they want from working with the FDA when contacting PASE.

Case Studies

Akcea Therapeutics

Akcea Therapeutics is developing new therapeutics for cardiometabolic lipid disorders, many of which are rare diseases. Alan Gilstrap, Executive Director, Advocacy and Policy, focuses on ensuring that the patient voices are included in drug development to understand how to improve their daily lives. To do this, he turns to patients to speak with them about their experiences living with their rare diseases and how to design clinical trials to test new therapeutics. For example, he recently put together an Advisory Board of patients to inform the company about how their rare disease affects daily living. Because there is not much in the scientific literature on patient experiences with this disease, it is

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critical to speak directly to patients. For this Advisory Board, he reached out to organized support group to invite interested participants. Regulatory authorities are becoming more and more interested in not only how an experimental treatment improves the clinical numbers, but also how an experimental treatment improves the daily lives of people living with the condition. To understand this, researchers must understand the daily impact of the disease. Listening to patients is the best way to understand the daily impact of any disease, particularly in rare diseases where published information is, oftentimes, very limited.

Patient Representative: Ms. Bray Patrick-Lake

Bray Patrick-Lake, Director of Patient Engagement, Duke Clinical and Translational Science Award, has been focused on ensuring patient perspectives are included throughout the drug development process for several years. Her efforts began after she was diagnosed in 2004 with a hole between two chambers of her heart, or patent foramen ovale (PFO), which led to pain, migraines, shortness of breath, and exhaustion. Her condition worsened, and with no treatment options left, she participated in a clinical trial of a device intended to close the hole. The clinical trial was stopped due to low enrollment. Frustratingly, Bray learned of the trial closure not from the company or her physician, but from tracking news of the company. This led her to begin working with patient groups and regulators toward improving the clinical trial system. As part of her efforts, she became a Patient Representative and has served on several FDA Advisory Committees and panels. Bray emphasizes that patients and caregivers serving as Patient Representatives should understand that the FDA must weigh the risks versus the benefits of new therapies in terms of outcomes that can be measured.

Patient Representatives also should know that review packets are large, but they should work their way through the entire packet and be sure that data related to patient perspectives are included. She noted that for one panel she served on, the executive summary for the review packet mentioned a patient-reported outcomes study that was not included because the data were “subjective.” Knowing the importance of including patient perspectives, she spoke with the committee chairperson and raised the importance of the Advisory Committee including that study in their discussions. She recommends that people interested in becoming Patient Representatives consider learning the basics about clinical trial procedures and statistics to better understand the review packet materials through online resources, books, or fellowship programs such as the Patient Advocate Fellowship offered by the Drug Information Association (DIA).

Cure SMA

Cure SMA has been working to gather patient perspectives together through research studies of patient experiences to provide the patient voices of SMA to the FDA. Cure SMA has been a partner with other patient groups and companies developing SMA therapeutics to conduct focus groups and surveys to gather patient perspectives on clinical trials, the diagnostic journey, and what would be meaningful benefits from SMA therapeutics. Publications resulting from these projects, as well as collection of patient stories supporting their findings has been sent to the FDA for their information. Cure SMA and their partner organizations have had several meetings with the FDA to talk about collecting and sharing this data. They are also discussing putting together an industry consortium where they can work on some of these projects together and provide a cohesive voice to the FDA.

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Resources

Announcements of Advisory Committee meetings: <http://www.fda.gov/AdvisoryCommittees/default.htm>

Information regarding how to register as a speaker can be found at <http://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/ucm408555.htm>. Information on how to submit written comments is included in each public meeting announcement.

Patient Representative Program: For a list of current opportunities and details about the application process, see <http://www.fda.gov/ForPatients/About/ucm412709.htm>.

Past and planned meetings, including links to open registration for meetings, are listed at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm>

More details about hosting a Patient-focused Drug Development meeting can be found at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm>.

FDA Patient Network: <http://www.fda.gov/ForPatients/About/default.htm>.

FDA CDER Professional Affairs and Stakeholder Engagement (PASE): <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm385522.htm>

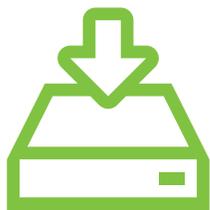
CDER Drug Approval Case Studies: <http://www.fda.gov/Training/ForHealthProfessionals/ucm464124.htm>

DIA Patient Initiatives: <http://www.diaglobal.org/en/get-involved/patients>

Federal Register:
<https://www.federalregister.gov>

An example of Cure SMA's work to gather patient perspectives: Understanding the experiences and needs of individuals with Spinal Muscular Atrophy and their parents: a qualitative study: <http://bmcneurol.biomedcentral.com/articles/10.1186/s12883-015-0473-3>

SECTION 9: ENSURE ACCESS



Patients and their families also can work with companies, government regulators, researchers, and clinicians to ensure that patients have access to newly approved therapeutics as quickly as possible. Patient groups can work with payers on reimbursement and with companies to develop assistance programs to help patients with insurance co-pays if needed. Patient groups also can inform companies if there are any problems with receiving the therapeutic if delivered directly to the patient. For example, if a delivery company is not appropriately storing the therapeutic or is leaving the therapeutic where it might be damaged by heat or cold, patients and companies can work to change the process. Another way to ensure access is to work with state and federal regulatory agencies to perform newborn screening for rare diseases, which often reveal themselves at a very young age. When a therapeutic is available, newborn screening is a diagnostic tool that can ensure patients receive therapeutics and any other treatments quickly. Another way to improve access to therapies is to work with researchers and clinicians to develop centers of excellence. Centers of excellence allow patients to receive coordinated care from several clinical specialties, the most recent advances in clinical care, and access to clinical trials. Visit the Global Genes Toolkit, [Leveraging a Rare Disease Center of Excellence](#) for more information.

Case Study

Cure SMA

For a disease that is the leading genetic cause of infant death, newborn screening could provide numerous benefits including speeding access to therapies or clinical trials and improved early care. It could also greatly shorten the time to diagnosis and allow parents to consider the implications of a diagnosis for family planning. The SMA community, including Cure SMA, has been actively engaged for several years in working with federal and state regulators and researchers to add SMA to Newborn Screening panels in all 50 states. A pilot study of newborn screening for SMA in Colorado and Utah was recently conducted with funding from the National Institute of Child Health and Human Development at the National Institutes of Health. Efforts to include SMA in newborn screening panels continues, but state-level pilot data using a public health lab is a critical step toward gaining approval.

Resources

Many companies, as well as independent organizations, have patient assistance programs for some therapies. Following are examples:

GSK for You <http://www.gskforyou.com/patient-assistance-programs/reimbursement-resource-center.html>

Jazz Pharmaceuticals <http://www.jazzpharma.com/reimbursement-assistance/>

Lilly Patient One
<http://www.lillypatientone.com/>

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NORD Patient Assistance Programs
<http://rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs/>

Patience Assistance Now http://www.patientassistancenow.com/info/programstoaccessmedicines/patientassistanceinformation.jsp?usertrack.filter_applied=true&Novald=2935377031732093801

Patient Services Incorporated (PSi)
<http://www.patientservicesinc.org>

SECTION 10:

ADVOCATE FOR REGULATORY CHANGES



Patient organizations can advocate for regulatory or public policy changes when an aspect of the drug development process is not working well for advancing treatments for their rare disease or there are gaps in the drug development process. Patient groups can advocate for increased basic or clinical research efforts. They may identify a need for guidance from regulatory agencies on developing therapies for their rare disease. Patients may identify changes to the research system or clinical trials to make the process more open and transparent. Patient groups and patients also may find other advocacy organizations or patient groups working on these issues with which to collaborate.

Case Study

Parent Project Muscular Dystrophy (PPMD)

Pat Furlong received the diagnosis that her two boys both had Duchenne's muscular dystrophy when they were four and six. She immediately began to advocate for research and treatment advances for her boys and other muscular dystrophy patients through the organization she founded—the Parent Project Muscular Dystrophy (PPMD). She has continued her fight long after she lost both boys to the disease. PPMD identified the need for regulatory guidance to companies, and also reached out to the FDA to ask the agency to develop guidance to help accelerate drug development and to help advisory committees

review potential therapies. The FDA replied that there were not enough resources for the FDA to develop guidance for rare diseases, but proposed that PPMD develop the guidance. PPMD engaged more than 80 stakeholders in the Duchenne community to participate in developing guidance. The guidance document focused on six areas: determining the community's tolerance for risk or uncertainty of benefits with new therapies; improving the diagnostic process; performing rigorous natural history studies to understand the effects of Duchenne; developing clinical trials that allow participation for all ages and all stages of the disease; collecting muscle biopsies only when necessary; and developing new non-invasive methods to assess disease progression. The FDA accepted and published the guidance in June 2014.

Resources

FasterCures R&D Policy: <http://www.fastercures.org/programs/r-and-d-policy/>

Clinical Trials Transformation Initiative: <http://www.ctti-clinicaltrials.org/briefing-room>

PPMD: http://www.parentprojectmd.org/site/PageServer?pagename=Advocate_fdaguidance

Conclusion

There is room and need for patient voices at all stages of the drug development process. Patients and patient groups can and should work with researchers and companies. They can be the driving force to ensure funding for research, access to data, collection of data, participation in clinical trials, working with regulatory agencies, and ensuring access to new therapies. When needed, patients can

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Speak loudly for changes to the system that will help accelerate research and approval for therapies. The importance of the patient perspective is recognized more and more by researchers, companies, and regulatory agencies as integral to overall success. Patients, patient organizations and caregivers have the ability to make large and small contributions to advance drug development, just as all stakeholders are essential in moving therapeutic advances forward.



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<http://globalgenes.org/toolkits>

March 2016