DIA

Considerations Guide

to Implementing Patient-Centric Initiatives in Health Care Product Development

TABLE OF CONTENTS

Executive Summary

Involving patients in health care product development is not only an exercise in good corporate citizenship but also an innovative and transformational approach to identifying and responding to the unmet needs of patients worldwide. To get the full benefit from the insights only patients can provide, pharmaceutical companies need to build and commit to processes, structures, and strategic priorities that put patient involvement at the core of its business.

Developed as part of DIA's Study of Patient-Centric Initiatives in Drug Development, conducted in collaboration with the Tufts Center for the Study of Drug Development, this document was designed as a practical resource for pharmaceutical companies as you launch or advance patient-centered initiatives that support health care product research and development.

Whether your goal is to fundamentally change how you do business or simply to revise a single process by integrating patient input, this document will guide you through developing a patient-centric approach. The European Patient Academy for Therapeutic Innovation (EUPATI) captures objectives in their Framework for Patient Involvement in Regulatory Processes[1] that can be applied to initiatives designed for industry. Patient-centricity has the potential to do the following:

- Support your organization in accessing the "real-life patient experiences with disease management and to obtain information on the current use of treatments[1]"
- "Ensure that patients, consumers, and their representative organizations are listened to and consulted and where appropriate involved[1]" in the development of treatments
- Enhance the understanding by patients and patient groups of the mandate and role of industry within the context of the development, evaluation, monitoring, and provision of treatment information[1]
- Optimize communication tools (for content and delivery) to manage the distribution of information to patients and their representative organizations to support their role in the safe and rational use of treatments[1]
- "Facilitate the participation of patients in benefit-risk evaluation and related activities, to capture patients' values and preferences and obtain information on the current use of medicines and their therapeutic environment, all along the life cycle of medicines development, from early development throughout evaluation and postmarketing surveillance[1]"

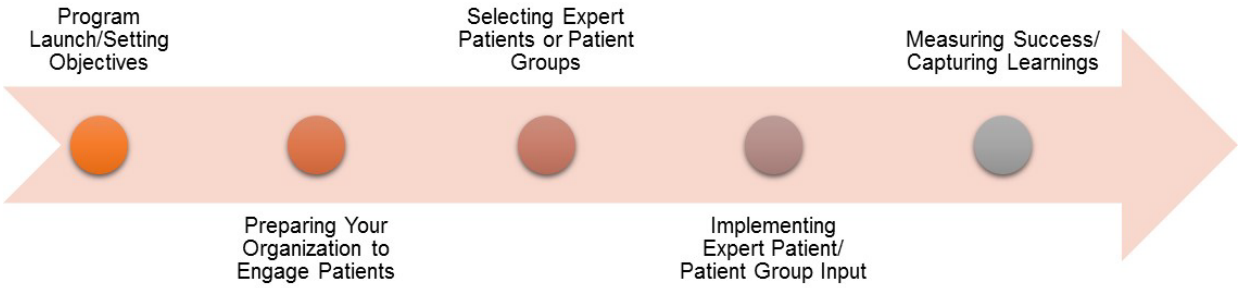
Ultimately, you can build transparency and trust with patients and the wider stakeholder community as well as improve patient access to effective treatments that either extend or improve quality of life.

How this Document is Organized

This document is divided into two sections: *Section I* is a description of the objectives of each process stage relative to building or advancing patient-centricity in your organization, while Section *II* provides questions to guide decision-making and resources to consult as your organization designs and implements a specific patient-centric program or larger initiative.

Within both Section I and II, the content is divided into the following categories:

- Program Launch/Setting Objectives
- Preparing Your Organization to Engage Expert Patients and/or Patient Groups
- Selecting Expert Patients/Patient Groups
- Implementing Expert Patient/Patient Group Input
- Measuring Success/Capturing Learnings



As you develop your approach to patient-centricity, refer to existing regulations on pharmaceutical industry interaction with the broader public and with patients specifically to ensure compliance. Current published guidance documents referenced in this document are listed in the Resources section in the Appendix. Always consult your organization's internal procedures to ensure adherence and/or to identify opportunities to harmonize those procedures with new patient-centric objectives.

A Note About Terminology

A predictable finding of the research project was that definitions for 'patient engagement' and related terms vary widely. Therefore, in this document we define patient engagement as follows:

> *Meaningful engagement of patients in the development of therapeutic products refers to direct and constructive interaction with patients in various important roles, over the entire medicines life cycle (from preclinical laboratory-based studies to launch, and beyond launch for as long as that medicine is available to patients), enabling the implementation of practices and actions that are based on patient perspectives and that result in measurable outcomes that meet patient needs as well as industry needs.*

We further found the terms 'advocate' or 'advocacy' in relation to patients not only vary in meaning but also have the potential to carry negative connotations. For some, 'patient advocates' are individuals or groups who are adversarial in their interactions with industry or regulators. To avoid misunderstanding, this document will use 'expert patient' and 'patient groups' to describe individuals and organizations who are working to advance treatment development.

Finally, 'program' is used in this document as a generic term to cover the full range of possible patient-centricity efforts your organization may undertake.

Section I – Process Overview

Program Launch and Setting Objectives

The work of this initial stage is to define the scope and objectives of your program and the purpose for involving patients* (e.g., IND application, protocol design, patient recruitment, regulatory submission). Be very clear at the outset about what you expect to achieve and what metrics – both quantitative and qualitative – you will use to measure progress against and achievement of both overall program goals and specific patient-centricity goals.

The scope of your program directly affects what preparations you will need to make. For example, if your program will be conducted in multiple countries under various conditions, consider that "variations in cultures, physical environments, infrastructure, research experience, health policies, and national laws can introduce inequalities[2]" between you and your patient stakeholders. This will directly impact how effective your program will be if you do not make the right preparations now or the right corrections once the program is launched. Indeed, "an effective stakeholder engagement plan will help research teams design and implement research that is effective and locally acceptable, and also lays the foundation for a supportive environment for research that extends beyond the lifespan of a specific [*sic*] trial.[3]"

While a stakeholder engagement plan is externally focused, key preparations include internal focus as well. "[E]ngagement must meet the goal of active incorporation of perspectives beyond those of the researchers, to inform decisions about research questions, study design, measures used.[4]" Beyond just buy-in, the degree to which your program leadership and members believe that patient involvement is integral to health care product innovation correlates to the likelihood your program will be successful. If your organization does not currently have guiding principles around patient involvement, develop them.

While some might argue that an expert patient or patient group can provide valuable input at this early stage, you may not have such a relationship already established. Indeed, if this is your first foray into patient-centricity, your organization can build competence in this area by beginning at the lower end of the engagement continuum – Outreach or Consult (see "Community Engagement Continuum" chart below). Over time, as trust and capability builds, you can move to Collaboration and then Shared Leadership. While the model below comes from the *Principles of Community Engagement 2nd Edition*[5], which focuses on a broader definition of stakeholders beyond individuals currently dealing with disease, the definition of engagement at various stages is relevant here.

> "Fostering and establishing long-term relationships is the best approach which deliver benefits for all parties and is to be encouraged…….[*sic*] However it is recognized that relationship building may start with ad hoc interactions or meet short-term needs.[6]"
> European Patient Academy for Therapeutic Innovation (EUPATI)

* It is important here to clarify that 'patient input' here means involving expert patients and/or representatives from patient groups in the *design and development* of processes that improve health care product research and development and not feedback from lay patients.

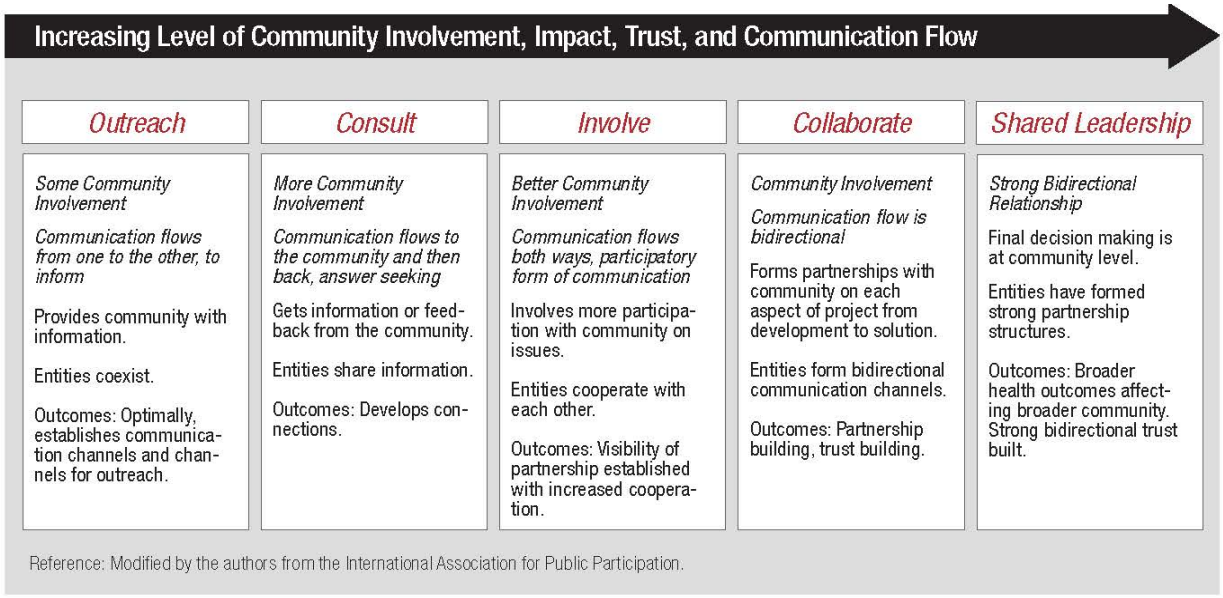


Figure 1.1. Community Engagement Continuum

Principles of Community Engagement, 2nd Edition[5]

When introducing new processes and procedures that support patient-centricity, it is critical to have the right organizational support. The research project found that support for patient-centricity must come from organizational leadership to be successful. A C-suite or executive leadership champion can provide concrete resources (human, financial, procedural) and can help break down barriers resulting from deeply engrained processes, mind-sets, and corporate culture. The support, however, must be more than just verbal backing as many organizational layers and silos need to be aligned and bridged to ensure success.

Finally, this initial phase challenges your organization to frame the program as a step in a larger, on-going effort to involve patients systemically in health care product development. Identifying the metrics you will use to capture program and patient-centricity success will enable you to demonstrate value to the rest of the organization. By planning now, you can ensure learnings will be adopted more widely within your organization at the conclusion of the program.

In Section II, Program Launch and Setting Objectives contains considerations organized in the following categories:

- Organizational Readiness
- Program Support
- Guiding Principles for Patient-Centricity
- Program Scope Definition
- Engagement Plan/Stakeholder Education Plan
- Environmental Scan
- Measuring Program Success
- Measuring Patient-Centricity Success

Preparing Your Organization for Engaging Expert Patients/Patient Groups

Once you've obtained leadership support and defined the scope and objectives for your program, begin to prepare your organization so you can engage expert patients/patient groups effectively. This includes determining the home of the program (what department, function, or therapeutic area), defining the roles and responsibilities to support it, and identifying the right people with the right skills to participate in this program.

It is important that program team members genuinely value patient perspectives, so be selective. "Research team members participating in PCOR must also value the patient perspective in research and believe there are benefits, whether ethical or practical or both, to capturing and using the patient perspective in research."[7] If there is not support within the program team to embrace patient-centricity, the program will fail to meet its first goal: to model patient-centricity for the rest of the organization.

Although you may not have selected the expert patients or patient groups (EP/PGs) yet, outlining *their* roles and responsibilities at this stage helps to define your needs. Keep in mind that EP/PG roles may vary at different phases of the program or may evolve in response to new requirements. Once selected, discuss the roles with your EP/PGs to clarify what they can contribute based on their unique expertise and experience and to avoid misunderstandings at the outset, e.g., if they're expecting to have a partnership role but you've designed a reactor role (see Types of Patient Roles chart below).

Rubric for Patients as Partners[8]

Patient Role	Examples	Engagement Level
Partnership role	• Patients provide *a priori* and continuous consultation on outcomes of importance, study design, etc. • Patients are paid investigators or consultants • Patients have a governance role —"a seat at the table"	High
Advisor role	• Patients serve as advisory committee members or provide *a priori* consultation on outcomes of importance and study design, but have no leadership role or governance authority	Moderate
Reactor role	• Patient input is collected distally through surveys, focus groups, or interviews, but patients are not consulted directly or *a priori* on such things as study design and outcomes of importance • Patients are asked to react to what has been put before them rather than being the origin of the concepts of interest	Low
Trial or study participant	• Patients are recruited or enrolled as study participant, but are not asked for input, consultation, or reaction	None

Finally, consider the benefits to the EP/PGs – and possibly to their larger patient community – of their involvement with this program. A successful collaboration benefits all participants.

In preparing to select an EP/PG collaborator, formalize the working relationship with a written agreement or Memorandum of Understanding, referred to as a MOU. Documenting the terms of work and the contributions from each party also helps prevent misunderstandings and ensures transparency with the wider community and public. More sophisticated and experienced patient representatives will have areas such as data privacy, conflicts of interest, intellectual property, value of assets already defined, but less experienced EP/PGs will be unfamiliar and will need support and guidance.

Note that the terms of such agreements will vary by country and will depend on local contract law as well as regulatory requirements. Involve legal expertise to prevent your organization from violating these requirements.

> "Industry should have robust operating procedures in place to enable both long-term and punctual interactions with patients and patient representatives which are as effective and inclusive as possible[9]."

In Section II, Preparing Your Organization for Engaging Expert Patients/Patients Groups contains considerations organized in the following categories:

- Organization Roles and Responsibilities
- Expert Patient/Patient Group Roles and Responsibilities
- Communications Plan
- Terms of Interaction/Written Agreement/Contracting
- Questions to Expect from Your Legal Department
- Compensation
- Transparency

Selecting Expert Patients/Patient Groups

Once your organization has committed to and defined a patient-centric program, the next step involves selecting the expert patient and/or patient group (EP/PG) with whom you will collaborate. Finding EP/PGs that meet all the criteria provided in Section II may be difficult, especially for a rare disease population. Furthermore, your program may not need all these qualifications to meet your program objectives, so prioritize the criteria according to the needs of your program before applying them to prospective patient collaborators. In this way, you can identify specific patient group expertise and assets to match the needs of your program, including unique needs that may arise at different stages or phases of your program.[10]

While there are some patient groups that are very sophisticated, expertise, experience, and qualifications vary widely. Rather than using the questions in Section II as elimination criteria, use them to identify where you may need to help bridge gaps or provide support when an EP/PG may otherwise bring significant value to the collaboration. Gaps can be addressed through training, engaging a complementary patient group or expert, or assigning the right patient liaison from within your organization to provide support. The following table, adapted from model developed by Dr. Jane Perlmutter, illustrates the advantages and disadvantages of different types of patients or patient representatives.

Types of Patient Representatives[11]

	ADVANTAGES	DISADVANTAGES
Independent patient experts	• Can maintain independence • Can work with multiple patient organizations • Can work in multiple areas	• May have strong personal biases/blinders • May not have external validation or accountability • May not be well connected to patient community • May not be representative of the larger patient community
Patient groups	• Have access to varied patient communities and populations • May have significant resources and assets (e.g., patient registry, tissue banks) • Have collective knowledge of the disease • May be able to support research financially	• Mission may limit ability to collaborate • Must fundraise • May have COIs with other organizations • May have limited financial resources • May not work well with related/ competing organizations
Cross-disease organizations	• Possess cross-disease data and perspective (e.g., PatientsLikeMe, Genetic Alliance, National Health Council)	• May have weaker connection to the patient community of a specific disease
Consulting organizations or other vendors	• Have processes in place to source and screen patients for a particular need • May be able to source for any disease	• If the program objective is to develop relationships directly with patients, the consultant may be an unnecessary middle man • May not possess detailed knowledge of the disease
Lay patients (may include caregivers or those at risk for the disease)	• More representative of your typical patient or clinical trial participant • Less likely to be biased for or against a particular message or mission	• May lack expertise in the clinical trial process or current technologies • May not be as articulate or organized in speaking to issues of interest to industry • May not understand the difference between research and standard of care

This Considerations Guide assumes that your organization will collaborate with an expert patient and/or patient group because the right ones bring direct experience with the disease, connection to the diversity of patients who suffer with the disease, and expertise in how they can impact health care product development.

In Section II, Selecting Expert Patients/Patient Groups contains considerations organized in the following categories:

- Patient Group Mission
- Patient Community Representation
- Health and Research Literacy/Other Capabilities
- Patient Registry
- Natural History
- Benefit-Risk Assessment
- Collaboration Experience
- Readiness to Collaborate
- Accountability
- Funding
- Communication Mechanisms and Processes
- Communication and Interpersonal Skills
- Disclosure and Transparency

Implementing Expert Patient/Patient Group Input

This program phase identifies ways that your expert patient and/or patient group can best contribute to and support the clinical trial process from discovery to regulatory review and approval. The activities here represent the basis of any patient-centric initiative – integrating the unique expertise of expert patients and/or patient groups to improve each stage of the health care product development process:

- Discovery
- Preclinical
- Phases 1 - 3
- Regulatory Review and Approval

Communications precedes all product development life cycle phases as it applies across the life cycle. This is *not* communication between your organization and the expert patient as part of your patient-centric initiative. This is the plan – *developed with expert patient/patient group input* – for how to communicate effectively with trial participants and other members of the lay patient community who may be impacted by the program.

With the right expert patient/patient group representative(s), you can define the unique unmet medical needs over the progression of a disease or for different populations affected by that disease. You can design a patient reported outcomes collection instrument tailored to patients in cultural or linguistic subgroups. EP/PGs can identify inclusion criteria and study endpoint that ensure a meaningful patient population can participate in a trial and minimize protocol amendments. They can increase trial recruitment and retention by identifying barriers (logistical, social, linguistic, cultural, financial, etc.) unique to the disease or to a particular patient subgroup. The expertise that EP/PGs bring not only provides the data missing in treatment development, but also stimulates a new way of approaching treatment research and the very questions that are asked at the beginning of the process.

In Section II, Leveraging Expert Patient/Patient Group Input contains considerations organized in the following categories:

- Communicating with Patients Throughout the Clinical Trial Continuum
- Discovery Phase
  - Disease State and Stage
  - Patient Group Assets
  - Unmet Medical Needs/Therapeutic Burden

  - Research Priorities
- Preclinical Phase
  - Data Safety Monitoring
  - Safety Event Reporting
  - Patient Reported Outcomes
  - Patient Recruitment
  - Patient Retention and Compliance
  - Clinical Trial Site Selection
  - Patient Compensation
- Phases 1 - 3
  - Clinical Trial Design
  - Study Protocols/Eligibility Criteria
  - Study Endpoints
  - Benefit-Risk Assessment and Patient Preferences
  - Consent
  - Patient Privacy
- Regulatory Review/Approval
  - Patient Data/Trial Results
  - Trial Closure Plan
  - End of Phase Review
  - Access to Trial Medicines
  - PR/External Awareness

Measuring Success and Capturing Learnings

Whether this program is a pilot or an expansion of patient-centric programs within your organization, a look back allows you to do the following:

- Capture successes that can be shared across the organization and built upon
- Demonstrate value to the organization by sharing quantitative and qualitative measures
- Incorporate learnings to support the next program
- Solidify processes so they take hold across the organization.

In Section II, Measuring Success and Capturing and Communicating Outcomes contains considerations organized in the following categories:

- Engagement Plan Review
- Environmental Scan Review
- Measuring Program Success
- Measuring Patient-Centricity Success
- Sharing Program Deliverables

Section II – Considerations and Resources

Considerations for Program Launch and Setting Objectives

Recommended Contributors:

- C-suite champion
- Program leader(s)
- Program participants
- Key program stakeholders as appropriate

Organizational Readiness

- Does your organization have the capacity (time, intention, skill sets) to engage patients effectively?
- Does your organization "value the patient perspective in research and believe that there are benefits, whether ethical or practical or both, to capturing and using patient perspective in research"?[11]
- Does your organization perceive involving patients in identifying health issues and developing programs as important?
- Does your organization recognize the importance of partnering and collaborating with patients?
- What does your organization want to accomplish through patient engagement?
- Is your organization already working with expert patients/patient groups on specific programs or issues? How? Are there existing collaborations within your organization?
- Do your program leaders and team members perceive involving patients in identifying health issues and developing programs as important?

Program Support

- Who in your organizational leadership will support this program? Do they report directly to the CEO? If not, do they have the CEO's support?
- What is his/her directive from the CEO as it relates to this program's objectives?
- If there is no C-level support, who in the organization will champion the effort?
- Will this program sit in the leader's organization or represent a collaboration across departments/functions/therapeutic areas?
- What experience or expertise related to patient-centricity do they bring to the program?
- What resources (financial, human, organizational, or other) do they bring to the program?
- How do they see this program impacting long-term goals for the organization?
- How will this person or group overcome organizational barriers or resistance?
- What other forms of resistance might your champion/program leaders need to address?
- How will they deal with regulatory and/or legal department resistance?
- Who else in the organization will the Program Leader need to engage for the program to be successful?

Guiding Principles for Patient-centricity

- What are your organization's guiding principles for patient-centricity? What *should* the guiding principles be for this program? How do they align with your corporate mission and vision?

- What are the strategies and mechanisms for building relationships and constructively engaging with lay patient communities, expert patients, or patient groups involved in or impacted by this program?
- In what ways can your organization ensure that your collaboration will be mutually beneficial to ensure the success of the program?

Engagement Plan

- What is your organization's strategic plans related to patient-centricity? How does patient-centricity support or fulfill the organization's mission and vision?
- What is the purpose of the patient-centricity program?
  - Treatment research
  - Disease prevention
  - Improved health through behavior change
- Are there any other objectives or rationale for the program?
- How does this program fit into an overall strategy for your organization to become patient-centric?
- Who are the key stakeholders? What patient populations or sub-populations do you want to engage? Where and how will they be engaged?
- What insights are required and what gaps need addressing?
- What are the key milestones and the timeline of deliverables?
- What is the best way(s) to engage patients? (This may vary depending on the objectives of the program.)
- What is the earliest that patient groups can be engaged in the program?
- What should be included in the Clinical Trial/Study Report (CTR/CSR) related to patient-centricity?
- How will you build trust amount the patient community and among diverse groups (as defined by culture, language, race, age, gender, literacy, etc.) contained within that community?
- How will you overcome mistrust of communities with a history of mistreatment, discrimination, neglect, or exploitation?
- If there will be differences (language, education, race/ethnicity, socio-economic status, etc.) between researchers and the patient community, how will you build trust and establish a productive and mutually beneficial working relationship?
- How will you overcome power imbalances between you and the patient community?
- How will you maintain connection with the patient representative(s) after the conclusion of the program?
- What does your organization offer to the patient group? Why would they want to collaborate with your organization?
- How will you demonstrate to the patient group that your organization is committed to a meaningful collaboration?

<u>Additional Resources (see APPENDIX AND RESOURCES)</u>:

Guidance for Biomedical HIV Prevention Trials, 2011 (UAIDS), p. 35-38: "Stakeholder Engagement Plan."

Recommendations for Community Involvement in National Institute of Allergy and Infectious Diseases, p. 7: "Principles of Community Engagement."

Principles of Community Engagement 2nd Edition, p. 45-53: "Principles of Community Engagement. "Principles of Community Engagement 2nd Edition, p. 109-148: "Challenges in Improving Community Engagement in Research."

Environmental Scan

- What is the current political, social, economic, religious, or other environment related to this disease and/or to its treatment?
- Who are the high-profile people or organizations influencing perceptions of this disease and/or its treatment – good or bad?
- Is there misinformation about the disease that needs to be addressed? Is the misinformation due to lack of accurate information, poorly communicated information, or deliberate manipulation of messaging? Are there interests perpetuating the misinformation?
- What (mis)perceptions are there about your organization as a whole and your organization's motivations behind this program? How will you address the misperceptions?
- Who are the stakeholders* with an interest in helping people with the disease and/or in getting them treatment (e.g., NGOs, Patient Groups, religious groups)?[14]

  *Stakeholders may include a wider group depending on the disease and the scope of the study:
  - Trial participants (including prospective trial participants), their family members, and/or caregivers
  - Others living with the disease but are not trial participants
  - Caregivers/family members
  - Expert health care providers
  - Clinic, hospital, or health system representatives
  - Treatment (and prevention) advocates
  - NGOs
  - Community-based organizations, community groups, religious leaders, or opinion leaders
  - Trial funders, trial sponsors, or trial implementers
  - Regulators
  - Academic experts
  - Policy makers or political decision-makers
  - Payers
  - Journalists/media[14]
- What materials (e.g., FDA patient meeting reports as part of the Patient-focused Drug Development initiative or EMA equivalents) are available related to the particular disease area?
- What benefit-risk or patient preference data has your organization already gathered that might influence what treatments will go through clinical trial? How might this data influence the program?

Program Scope Definition

- How well do you understand the disease state and how it manifests over time?
- What are the unmet needs of patients with this disease?
- Where in the continuum from proof of concept/pre-clinical development to product approval does this program fall?
- What is the scope of this patient-centric program? What will this program *not* include?
- Who is the intended audience for the results derived from this program (e.g., sponsor study team, protocol writer, regulatory agency, prescribers, others)?
- What is the intended use of patient input (e.g., IND application, protocol design, investigator training, study recruitment and conduct, regulatory submission, publication, other)?

- How will the recommendations resulting from this program improve and support patient-centricity and ensure its implementation and wider adoption within your organization?

Program Budget

- What is the budget for the program? If there is no separate budget, in whose budget will this program be included?
- What does the budget cover?
- Who approves or monitors the budget?

Measuring Program Success

- What is being measured in this program? How is the data going to be collected?
- How do you define success of the program related to how patient input improved the program outcome, such as the following:
  - Reduction in protocol amendments
  - Reduction in recruitment times
  - Increased retention rates
  - Shorter cycle times
  - Patient burden reduction
  - Patient satisfaction with protocol
  - Others (e.g., validation of endpoints, patient-reported outcomes)
- What qualitative measures will be gathered?
- Are patient-reported outcomes to be included? How will they be collected?

Measuring Patient-Centricity Success

- What is the intended and expected value of this patient-centric program – both quantitative and qualitative – to your organization?
- How will the effectiveness of this specific patient-centric program be measured (e.g., how program learnings are incorporated into other parts of the organization or the next initiative)?
- How do you define the success of the program as it relates to the collaboration with expert patients/patient groups?
- What qualitative measures will be gathered?
- How will you use the feedback to improve the process next time? How will recommendations be incorporated into future processes at your organization?
- How will you evaluate the effectiveness of the program[13]?
  - Formative to guide program improvement
  - Process to determine whether the program was delivered as originally intended
  - Summative to judge whether the program worked
  - Outcome to evaluate observable conditions and the program's impact on those conditions
  - Impact to identify whether long-term goals were achieved
- When developing evaluation criteria, have you incorporated various standards such as proprietary standards, utility standards, feasibility standards, and accuracy standards?[14]
- What is your process for evaluating patient-centricity success at each stage of the program? How will you involve expert patients/patient groups in the evaluation process?

Additional Resources (see APPENDIX AND RESOURCES):

Principles of Community Engagement 2nd Edition p. 163-179: "Program Evaluation and Evaluating Community Engagement."

Considerations for Preparing Your Organization to Engage Expert Patients or Patient Groups

Recommended Contributors:

- C-suite champion
- Program leader(s)
- Program team members
- Key internal stakeholders
- Expert Patients (individuals or members of a Patient Group) with existing relationships with your organization
- Lay patients as applicable

Organization Roles and Responsibilities

- Who among the leadership of your organization will sponsor and support the program to ensure success and remove barriers (see Program Launch/Setting Objectives above)?
  - Is this a formal position (e.g., Chief Patient Engagement Officer) or a temporary role?
  - What are the responsibilities of this role?
- Where will the roles reside within your organization? Will this program be run from a single department/function/therapeutic area or will it represent a collaboration across departments/functions?
- Are there other departments/functions/therapeutic areas where patient-centric initiatives have been implemented? If so, what resources (toolkits, templates, deliverables, etc.) are available and what learnings can be shared? Is there a central repository where this information is stored?
- Who in your organization will perform a liaison role or dedicated patient engagement role? Will this person also be the single point of contact for your organization when working with the expert patient/patient group? What organizational guidelines must they follow, if any?
- How many patient liaisons will there be compared with the number of expert patients or representatives from patient groups? (Note: being outnumbered can create an uncomfortable power dynamic for the patient representatives.) What are the roles and responsibilities of those positions?
- What are the roles and responsibilities of others involved in the program who may be interacting with the expert patients/patient group representatives, even if not on a full-time basis?
- What resources (human, financial, other) will be committed, data shared, and objectives set?
- What are the capabilities needed to be an effective collaborator with expert patients/patient groups for this project? Some recommendations are included below:
  - Communication: ability to translate medical/technical terms into laymen's terms; ability to recognize terms that may have different connotations and select terms that improve receptivity.
  - Cultural sensitivity: understanding explicit differences across various cultures but also more subtle differences among social groups, patient populations, those underrepresented or discriminated against.
  - Training skills: ability to transfer knowledge effectively to various audiences.
  - Listening skills: ability to discern meaning from spoken and unspoken communications from a person or group of people.
  - Technical skills: deep understanding of the drug development process.

  - Emotional intelligence
- What training might be needed for sponsors, researchers, research staff, investigators, or others working with expert patients and study subjects?
  - Understanding the nature of expert patients/patient groups and how they operate
  - Dispelling preconceived notions about them (their abilities, their knowledge of drug development, and their motives or intentions)
  - Patient testimonials regarding their experience of participating in clinical trials or even disease treatment
  - Examples of patient group/industry collaborations (case studies)
  - Basic disease knowledge
  - Standard knowledge of the clinical development and HTA process

Additional Resources (see APPENDIX AND RESOURCES):

Recommendations for Community Involvement in National Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trials Research, p. 8-28: "Part I: Recommended Roles and Responsibilities."

Expert Patient/Patient Group Roles and Responsibilities

- What value do you want them to bring to the program? What value do you think the program will offer them?
- What are the advantages of working with an individual expert patient (e.g., EUPATI-trained patient fellow or other independent consultant) versus representatives from a patient group?
- What are the advantages of working with vendors who have access to networks of patients who can be tapped for surveys/questionnaires?
- Should you engage more than one expert patient/patient group in this program? Would different groups bring different expertise that could be helpful?
- What are the desired characteristics of an expert patient/patient group your organization will want to engage? What is the profile of an expert patient? (See section on Selecting Expert Patients/Patient Groups.)
- What level of engagement is your organization willing to commit to? How/when will this be communicated to the expert patient/patient group?
  - Feedback provider, advisor, expert consultant, collaborator, partner
- What are the specific roles and responsibilities of expert patients/patient groups in this program and how do these roles support the level of engagement desired for your program?
  - Patient recruiter, DSMB for the trial, FDA advisory committee member, research partner designer, communicator, trainer
- What input can the expert patient/patient group provide regarding their role in the program?
- What recommendations can the expert patient/patient group offer regarding the patient liaison roles *within* your organization?
- What benefits with the expert patient/patient group experience from their collaboration with your organization?
- What training might be needed for the expert patients/patient groups?
  - Good Clinical Practice (GCP)
  - Clinical development and HTA process
  - Reading and interpreting research results

Additional Resources (see APPENDIX AND RESOURCES):

Assessing Meaningful Patient Engagement in Drug Development: A Definition, Framework, and Rubric, p. 1-5: "A Proposed Rubric - How do we know the patient has been engaged in drug development?"

Communications Plan

- Who are the point people on both sides to ensure smooth communications and what are their responsibilities? (See Roles and Responsibilities above.)
- What formal and informal communication mechanisms will be in place to support the following?
  - Relationship management
  - Program management
  - Issues management
  - When input will be used/not used and why
  - Updates/changes to the program including redirections to research priorities
  - Start up and conclusion of the program
  - Important dates and events
  - Day-to-day interactions among program members
- How frequently will you communicate, particularly in formal settings such as meetings or conference calls?
- How and when will the expert patients/patient groups involved be informed of program outcomes?
- How can expert patients/patient groups provide feedback or ask questions throughout the program?
- How will you encourage and capture feedback from expert patients/patient groups on their experience with your organization?

Additional Resources (see APPENDIX AND RESOURCES):

Communications Handbook for Clinical Trials; Strategies, tips, and tools to manage controversy, convey your message, and disseminate results, 2011 (USAID).

Guidance for Biomedical HIV Prevention Trials, 2011 (UNAIDS), p. 39-41: "Communications Plan."

Guidance for Biomedical HIV Prevention Trials, 2011 (UNAIDS), p. 41-42: "Issues Management Plan."

Terms of Interaction/Written Agreement/Contracting

- Who from your organization will be involved in developing the agreement? Who from the patient group?
- What are the specific details of your collaboration including scope of work, types of interaction, resource requirements, and timelines?
- What are the common areas of interest in order to establish an agreed-upon, structured, and well-defined interaction, providing all involved with appropriate and necessary protection?[15]
- What are the tools and methods of interaction (e.g., frequency of meetings, ground rules, and conflict resolution)?
- How will activity outputs be used?
- How will you formally engage and contract with expert patients/patient groups?
- What intellectual property considerations might there be for both sides?
- What are the specific issues to consider related to access to data, confidentiality, and patient privacy?

- How will you monitor compliance and what enforcement actions can be taken if a breach of confidentiality/NDA occurs on either side?

  Recommendation: Interaction may only proceed on the basis of a written agreement that spells out the basic elements of the collaboration, such as the following:

  - A description of the interaction
  - Consent
  - Release
  - Confidentiality, Non-Disclosure Agreement (NDA)
  - Compensation to individual patients, patient advocates, or patient advocacy organizations
  - Data privacy
  - Intellectual property
  - Revenue sharing
  - Declaration of conflict of interest
    - Previous, current, or planning working relationships with regulators, especially if that work was paid
    - (see below under Compensation)

Questions to Expect from Your Legal Department

- What type of model will be used to define the role of the expert patient/patient group?
  - Service provider to your organization
  - Recipient of charitable giving
  - Non-compensated collaborator[16]
- How do you plan to recruit patients? (Include methods used to reach out/who reaches out.)
- How will you obtain consent from patients?
- What is the health care professional contract/consultancy agreement (i.e., for simulations)?
- How will the HIPPA Compliance/Data Storage/Handling of PII/PHI be managed?
- Will the research be single or double blinded?
- What insurance does the vendor have to protect the sponsor?
- What is the participant compensation (fair market value)?
- What is the privacy policy for online surveys?
- How is patient data accessed and stored? Is it all in the US or within each country? If different countries, you will need to explain.
- Where does the patient database reside?
- What SOPs are in place to support patient engagement?
- How many personal data records are your company likely to collect, use, access, disclose, or retain? (i.e., information associated with 1 HCP, 1 employee or 1 patient would count as a single personal data record.)
- What personal data will your company collect, use, access, disclose, or retain on behalf of the sponsor? (Some examples of the types of personal data could be: patient test results and other health information, names, contact details, identification numbers/logon IDs, transaction purchase details, pay, and other benefits.)
- Does your company have an established compliance program for assessing and managing data privacy risks?

- Do you have appropriate legal measures in place to allow for international transfers of Personal Data (e.g. intra-group agreements/safe harbor certification/model clauses)?
- How will personally identifiable information (PII), or Sensitive Personal Information (SPI), like patient name, address, and other personal information be de-identified before sharing with the sponsor?

Compensation

- How will the expert patient/patient group be compensated? How will you determine the appropriate compensation for their participation?
  - Compensation should reflect fair market value of the knowledge and experience of the person
  - Internal policies and guidelines on interacting with expert patients/patient groups
- What other payments from a company, HTA body, regulatory agency, ethics committee to individual patients, patient representatives, or patient organizations might there be?
- How will these payments be detailed in the written agreement?
- How will these payment be reported? What are the local laws and regulations regarding this (e.g., Sunshine Legislation as part of the ACA in the U.S.)?

Transparency

- What mechanisms will be in place to ensure transparency of your organization's priorities, goals, and processes?
- What mechanisms will be in place to ensure transparency of patient involvement?
- How will your company and the Expert Patient/Patient Group publicly disclose your activities? How frequently?
- Should any of the input provided by Expert Patient/Patient Group be reported to regulatory agencies and how? What guidelines already exist about this?

Considerations for Selecting Expert Patients/Patient Groups

Recommended Contributors:

- Program leader
- Program Participants
- Other program stakeholders

Patient Group Mission

- What is the mission of the Patient Group? How does that mission support or align with this program or with your organization's patient-centricity goals or strategic objectives?
- Does the organization have clear strategic priorities and are their activities consistent with those priorities?
- Is the organization part of a patient-led research network?
- How does their mission differ or align with organizations that support the same disease (if they exist)?

Patient Community

- How many patients and/or patient caregivers are part of their network?
- What percentage do they represent of the total population (approximated)?
- If the patient population is primarily children, what percentage of their community is parents or caregivers?

- Is their patient community regional, national, or international? How well do they collaborate with other chapters or the national/international mother organization?
- How effectively does the organization represent the concerns of their patient community?
- How well do the concerns/priorities of the Patient Group align with those of their patient community?
- Does the Patient Group represent the entire patient population with the disease or do they advocate for a particular subtype of the disease or subgroup (e.g., under-served populations) or a specific priority?
- How attuned is the Patient Group to disparities their patient community experiences with respect to access to treatment or information, treatment outcomes, or inclusion in trials?
- How attuned is the Patient Group to cultural differences in understanding and coping with the condition (including getting treatment and participating in trials)?
- How much access will the Patient Group allow you to their patient community?
- Under what circumstances has the Patient Group coordinated or collaborated with other Patient Groups for the same disease?
- How effectively does the Patient Group reach out to those who are living with the disease but not associated with a Patient Group?
- How effectively does the Patient Group mobilize members of their community?
- What insights can the expert patient/patient group provide regarding the role of the patient generally beyond "study subject"?

Health and Research Literacy/Other Capacities

- How much knowledge of the drug/biologic/device development process will they need to possess for this program?
- How technologically savvy do they need to be?
- Do they have a sufficient understanding of the scientific process including defining research questions, developing appropriate trial designs, and analyzing data to ensure valid results?
- Do they know what clinical research is, particularly in the context of drug research and development? Is clinical research an organizational priority for the patient group?
- If there are gaps in knowledge, how will those gaps be filled? What training or support will be offered?
- Have any of their members participated in a trial before? Are those members willing to share their experience and/or participate again?
- What other characteristics should the expert patient/patient group representative possess?
  - "Knowledgeable about the medical and social aspects of [the disease] and willing to expand and maintain their knowledge base[17]"
  - "Familiar with, or eager to learn about, clinical trials that are being conducted and the types of research questions relevant to the communities that are being targeted by their network or site[17]"
  - "Culturally sensitive to populations traditionally underrepresented in ….[*sic*] clinical trials generally and specific to the disease in question[17]"
  - "Self-motivated and committed to independently pursuing knowledge and information about trends in the treatment (and/or prevention) [17]" of [the disease]
  - Skilled at communicating and translating complex medical/scientific information to a lay audience through different media

- What additional education or training might the expert patients or patient group representatives need in order to be ready to collaborate?
  - Definitions of terms
  - Clinical trial process
  - Roles of various individuals and teams involved in clinical trial process
  - Technology being used during the program

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, 2011 (UNAIDS), p. 37-38: "Stakeholder education plan."

Principles of Community Engagement 2nd Edition, p. 102-108: "Appendix 4.1 Structural Capacity Tables."'

Patient Registry

- Does the Patient Group have a patient registry?
- If so, how does the Patient Group define "patient registry"?
- What kind of registry is it?
  - Patient-powered registry (PPR)
  - Patient-powered research network (PPRN)
  - Researcher-generated registry
- What is the purpose(s) of the registry for the Patient Group?
  - Recruit patients for clinical trials
  - Learn about population behavior patterns
  - Monitor outcomes or disease progression
  - Pursue a specific, focused research agenda
  - Collect data to answer existing and emerging questions
  - Collect tissue or blood samples
- Is the registry part of a larger network of registries or other service (e.g., PatientsLikeMe)?
- How was their registry developed?
- Does the Patient Group own the data?
- Are there competing registries that might limit the value of their registry?
- What data is collected and by whom?
- How much of the registry are they willing to share?
- What patient confidentiality issues might there be related to sharing registry data?
- What is the participation rate?
- What information might be missing from the registry? How can that missing information be obtained?
- How is the data maintained and by whom?
- What are the standards for collecting data? Are they scientifically sound? Is there a scientific advisor who oversees the process?
- Have their patients consented to the use of the data and possibly to use of tissue or blood samples?
- Does the Patient Group have a biobank or repository to collect tissue or blood samples? Who stores them? What consent have the patients given for use of those samples?

- How might their registry encourage physicians or patients to make more educated treatment decisions, if at all?

Additional Resources (see APPENDIX AND RESOURCES):
US Department of Health & Human Services, Agency for Healthcare Research and Quality. "Engaging Patients in Information Sharing and Data Collection: The Role of Patient-Powered Registries and Research Networks". September 2013.

Natural History

- What natural history studies has the Patient Group led or participated in?
- Did the natural history data reveal specific genotypic or phenotypic subpopulations with the disease?
- If the Patient Group has not conducted a natural history study, what information has the Patient Group collected about the natural history of the disease? How has the information been collected and stored?
- Has the Patient Group collected information on how various interventions impact the natural history?
- Has the Patient Group used their knowledge of the disease's natural history to educate HCP, researchers, the FDA, or others?
- Has the Patient Group ever used its natural history data to aid in clinical trial design or identify study end points?

Assets

- Beyond a patient registry or natural history data, what other assets does the Patient Group have to offer (e.g., tissue or biobanks)?
- Can the patient group demonstrate impact on trial metrics (e.g., reduced trial cycle times and length, reduced number of protocol amendments, study volunteer recruitment, or retention) as a result of their involvement?
- What financial assets are available to fund research?

Benefit-Risk Assessment

- What benefit-risk data has the Patient Group gathered from their patient community, if any?
- What method was used to gather benefit-risk data?
  - Stated-preferences
  - Best-worst scaling (BWS)
  - ISPOR conjoint analysis
  - Discrete choice
- Did the basic demographic data screen for high risk-taking personality traits (e.g., as assessed by the Jackson Personality Inventory)?
- What stakeholders participated in developing the B-R tool (e.g., patients, patient/disease advocates, caregivers, drug developers, clinicians, others)?
- Were under-served populations or patient subgroups included?
- What qualitative data was gathered to complement the benefit-risk analysis and how?
- How were the results shared with the patient community?

Collaboration Experience

- What is their experience in collaborate on health care product development?
- Were their collaborations successful? How did they define success? If they were not successful, what prevented the collaboration from being successful?
- What was their contribution to the collaboration?
- What is their experience in the following innovative approaches:
  - Medicine co-development partnerships
  - Designing apps for clinical data collections
  - Adaptive trial designs and/or adaptive licensing
  - Open trial design or crowdsourcing
  - Telemedicine
  - Direct-to-patient clinical trials
  - Real-world, practice-based clinical trials
  - Human factor testing/simulations
- What experience do they have with accompanying sponsors to meetings with regulators to advocate for a study (e.g., pre-IND with FDA)?
- What is their experience collaborating with the NIH or other similar organizations, academia or other research institutions, industry, or regulators?
- What types of sponsors have they worked with on clinical trials?
  - Pharma, biopharma, biotech, medical device
  - Government agencies (e.g., NIH, DOD, VA, European agencies)
  - Individual researchers
  - Academic medical centers

Readiness to Collaborate

- Do they have pre-defined expectations, guidelines, or templates around the following:
  - Memoranda of Understanding/SOPs
  - Working with other Patient Groups
  - Working with your competitors
  - Intellectual property
  - Clear definition of their assets (data, bio samples, cell and animal models, natural history database, patient community)
  - Confidentiality
  - Data-sharing parameters
  - Working with regulators (do they advocate for specific treatments/approvals or for general principles?)
  - Compensation for consulting
  - Revenue sharing expectations
  - Expanded or continued access to research treatments
  - Ethical treatment of research subjects
  - Policy on use of social media

Accountability

- Do they respect the scientific process?
- Will their input into the research process be fair and constructive?
- Will they act in the best interests of the patient stakeholders as a whole, even if some are represented by a different Expert Patient/Patient Group?
- If their input is not used and organization explains why, will they be okay with that?

Funding

Note: This may apply more for small biotech and research organizations, and may be more common for rare disease organizations.

- What is the Patient Groups' funding priorities (e.g., identifying target molecules)?
- What is their experience funding research?
- Does their experience include funding basic research and/or 'bench-to-bedside' translational research?
- Do they have funding available to cover their own expenses, to support patient costs for the trial, or for trial operations?
- Are they willing to fundraise for trial operations support?
- How much funding is available?
- What limitations are there on using those funds?
- Is there money for training programs / fellowships?
- Do the sources of their funding matter to your organization?
- What is their process and criteria for awarding grants?

Communication Mechanisms and Processes (for Patient Group)

- What are the goals of its communications efforts (e.g., for external vs. internal audiences)?
- How effective are their various communications mechanisms in engaging its patient community?
- What is the quality and reach of the Patient Group's social media presence?
- Who moderates their social media forums? How effectively do they moderate? What are the guidelines they use for moderating?
- Have they had any issues (e.g., misinformation shared)? How have they addressed them?

Communication and Interpersonal Skills (for Individual Expert Patient)

- How well are they able to understand and translate medical, technical, and legal terms into laymen's terms?
- How effectively can they identify terms that may have different connotations and recommend alternatives that improve receptivity?
- How influential are they with their patient community in terms of getting responses and buy-in?

Disclosure and Transparency

- What policies do the Patient Group have in place that support full disclosure, conflict of interest, transparency, and accountability?
- How do they disclose activities with industry, regulators, researchers (clinical or academic), etc.?
- Do their agreements list indirect benefit in kind (such as services provided free of charge) or any other non-financial benefits in kind (such as training sessions, agency services, setting up of web site) when these benefits are significant?

- What are the agreed upon decision-making processes? (e.g., is the Expert Patient/Patient Group clear on when their input will be adopted and when it won't and why?)

Additional Resources (see APPENDIX AND RESOURCES):

CTTI Recommendations: Effective Engagement with Patient Groups Around Clinical Trials, p. 16-20.

DIA Patient Advocacy Lifecycle Model

Considerations for Implementing Expert Patient/Patient Group Input

Recommended Contributors:

- Program leader
- Patient liaisons
- Sponsor representatives
- Clinical investigators
- Research team
- Trial site staff
- IRB
- Expert patient(s)/Patient Group representatives

Communicating with Patients throughout the Program

- How does the phase of drug/biologic/device development process covered by this program impact communication with patients?
- What translation and/or cultural adaptations will be needed? How can the Expert Patient/Patient Group help identify and prepare for those adaptations?
- What language will be used to communicate with and about the patients?
  - Are research questions and procedures culturally sensitive and appropriate?
  - How will patients be referred to (e.g., "subject" vs. "patient" vs. "participant")?
- What is the communication plan for patients throughout the program?
  - Message content
  - Audience
  - Messenger
  - Delivery mechanisms
  - Timing
  - Feedback mechanisms
- What feedback mechanisms and processes are in place for the patients to comment on sites, investigators, and the study participant experience?
- What role will social media play in the communications?
  - How is social media defined?
  - What restrictions should there be, if any?
  - How can social media be used to advantage (e.g., for trial recruitment, to educate patients)?
  - What limits should be placed on use of social media, if any? Why?
  - How will those limits be communicated and enforced?
- What methods will be used to interact with patients and other stakeholders?
  - Focus groups

  - Interviews
  - Surveys
  - Inclusion on advisory councils
  - Inclusion in meetings with researchers
- What data/information can and will be shared with the patients and when?
  - Aggregate (de-identified)
  - Patient-specific
- What are the restrictions (proprietary and regulatory) constraining the release of data?
- How do we ensure that this information is shared in patient-friendly language? How will that be determined/monitored?

Additional Resources (see APPENDIX AND RESOURCES):

Communications Handbook for Clinical Trials.

Guidance for Biomedical HIV Prevention Trials, p. 37-38: "Stakeholder education plan."

DISCOVERY

Disease State and Stage

- What information regarding the natural history of the disease can the Expert Patient/Patient Group provide that was unknown?
  - Rare, genetic
  - Onset, duration, resolution, co-morbidities, range of manifestations
  - Lifestyle, age, gender, race
  - Religious, ethnic, or other cultural difference within patient subpopulations
  - Other factors which may impact management or progression of condition
- What are patient subpopulations - by severity, onset, comorbidities, phenotype?
- How does the disease impact the patients' daily lives? What impact does this have on caregivers, particularly for pediatric patients?
- How is the disease diagnosed?
- What tests, including early screening (infant screening, genetic testing, etc.), are available to diagnose the disease?

Patient Group Assets

- What assets do Patient Groups have access to that would advance clinical research?
  - Tissue banks
  - Biomarkers

Unmet Medical Needs/Therapeutic Burden/Quality of Life

- What unmet medical needs are there for the disease state and stage?
- What are the therapeutic burdens for the patients?
- What opportunities are there for expanding indications and defining better targets?
- Are there unique needs for patients with this disease?
  - Over the progression of the disease
  - Over the lifetime of the patient
  - For different populations affected by the disease

- What are the intended benefits to patients in their daily lives?
    - Improved survival rates
    - Managing or relieving symptoms
    - Preserving or restoring function
    - Quality of life
- What are meaningful patient reported outcomes?
- What are quality of life objectives for patients with this disease?
- How will you measure quality of life impact of treatments?

Research Priorities

- What input can Expert Patients/Patient Groups provide on research priorities?
- What research question is of interest to the patient community?

PRECLINICAL

NOTE: While these steps are important preparation for a clinical trial, it is important to revisit them during each phase of the trial as circumstances are likely to evolve over the course of the program.

Data Safety Monitoring

- What are the potential risks to study participant safety?
- How will they be communicated?
- How will they be mitigated?
- What criteria should be used to determine whether the study should be modified or discontinued?

Safety Event Reporting

- How will trial-related harms be communicated to participants?
- What treatment or compensation will be offered?
- How will harms be mitigated?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 57-58: "Policies on trial-related harms."

Patient Reported Outcomes (PRO)

- What quantitative PRO data will be collected? How has the PRO objective been incorporated into the overall clinical trial objective?
- Will the PRO instrument collect data on adverse side effects or effectiveness of treatment?
- How will PROs be collected? For what purpose, and how will they be shared?
- How will you leverage expert Patient/Patient Groups input to develop a PRO?
- How can you develop patient interview questions that help them describe their disease and how it impacts daily life and functioning?
- Will the PRO be measured in absolute terms or a change/progression of the disease or symptom?
- Are there existing PRO tools that have been used in a clinical study?
- For children, are there proxy measurements or will have be limited to using only observable outcomes?
- How will you demonstrate to regulators that your PRO instrument captures the patients' experience across disease severity and population characteristics?
    - The FDA suggests that "an instrument's measurement properties be well established before enrollment begins for confirmatory clinical trials. Therefore, sponsors should begin

instrument development and evaluation early in medical product development, and engage the FDA in a discussion about a new or unique PRO instrument before confirmatory clinical trial protocols are finalized."[18]

- What role with the PRO endpoint play in the clinical trial (primary, key secondary, or exploratory endpoint)?
- What documentation will you provide to demonstrate the reliability, validity, and ability to detect changing responses of your PRO over time?
- How will you ensure the PRO instrument does not create and undue burden on the patient or the survey administrator (e.g., length of questionnaire, readability, patient literacy, patient privacy, any physical limitations in responding)?
- How will the instrument be modified to support issues presented by populations with specific needs or challenges such as children and adolescents, patients with cognitive impairments, and culture or language subgroups?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Industry – Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, 2009.

Patient Recruitment

NOTE: For rare diseases, patient populations will be small and heterogeneous.

- For the purposes of this program, how do we define "patient" or "patient participant"?
- What are the underlying drivers for this patient population(s) to participate in clinical research?
- Under what circumstances would a patient be compensated? What is the appropriate compensation to *recruit* a patient to a clinical trial? Does it vary by phase?
- What is the full spectrum of patients to be represented including hard-to-reach and under-represented populations?
- Who are the under-represented populations?
- When do patients need to have previous clinical trial experience, if at all?
- What considerations are there around country selection?
- What are the unique attributes of the condition (i.e., disease spectrum) that need to be considered?
- What are the special considerations for pediatrics and geriatric populations?
- What are the special considerations for patients who are incapacitated and cannot give consent (i.e., cognitive impairment) or whose input may be unreliable?
- What issues are there related to trial site access for the various patient populations?
- What are the barriers (financial, logistical, emotional, social, physical/medical, language, etc.) for this patient population(s) to participate in clinical research? How can they be overcome?
- How would a trial simulation help identify ways to overcome barriers to participation?
- What type of support or accommodations might patients need to participate?
- What training might industry recruiters need to recruit effectively?
- What is the best approach to sourcing for this particular patient population (e.g., direct appeal, use of Patient Groups, HCPs, community leaders, social media)?
- When are care-givers needed or valuable?
- How many patients will be needed?
- How will recruitment affect site selection?
- How might patient segmentation help with site selection, if at all?

- If the trial is for prevention research, what are the special considerations for recruiting trial participants?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 26-65: "Good participatory practices in biomedical HIV prevention trials."

Patient Retention and Compliance

- What are the underlying drivers for this patient population(s) to complete a clinical trial?
- Under what circumstances would a patient be compensated? What is the appropriate compensation to *retain* a patient in a clinical trial?
- What is the experience of the trial participant? What feedback loop is in place to make modifications to improve retention and protocol compliance?
- What are the issues related to retention for various patient populations or subgroups?
- How might home visits, technology, or concierge services increase retention?
- How can the trial experience be personalized?
- What communication method (particularly related to answering patient questions and concerns) be implemented and better serve this patient population?
- What influence do Patient Groups, HCPs, family, caregivers, community, and society have on patient recruitment? Does it vary by subpopulation?
- How can the Patient Group assist with ensuring patient compliance with the treatment protocol?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 59: "Trial Accrual, Follow-up, and Exit."

Clinical Trial Site Selection

- What is the full spectrum of patients to be represented including hard-to-reach and under-represented populations?
- Can home visits be included as part of the trial?
- How might technology be used to complement trial sites in terms of data collection?
- What are patient preferences regarding frequency and duration of on-site visits?
- Where are these patients currently being treated/not being treated in the health care system?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 43: "Site Selection."

Patient Compensation

- What is the fair market value of the patient participant for this program (other than for trial participation)?
- What reimbursements can trial participants receive that support participation and compliance (e.g., transportation, child care)?
- What other incentives might be appropriate and effective?

PHASES 1~3

Clinical Trial Design

- What conditions would suggest that novel trial designs are appropriate?
- Would an adaptive trial design or adaptive licensing be appropriate here?
- Would open design or crowdsourcing be appropriate?

- When would it be appropriate to reduce exposure to placebo?
- How can you reduce the time off drug between trials?
- How can data from one trial be made available for use in another trial, especially in the case of rare diseases?
- How can clinical trial outcomes measurement be harmonized across trials and sites?
- When is a biomarker appropriate for a single primary outcome measure, for a supportive secondary outcome measure?
- How many invasive procedures are necessary? How can invasive procedures be minimized? How might invasive procedure inadvertently impact the disease itself, quality of life, or patient retention in a trial?
- How many noninvasive procedures are necessary?
- How might the trial impact secondary conditions or complications?
- What ethical considerations are their related to the trial (e.g., inclusion of pediatric patients)?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance Industry Duchenne Muscular Dystrophy Developing Drugs for Treatment over the Spectrum of the Disease

Study Protocols/Eligibility Criteria

NOTE: For rare diseases, patient populations will be small and heterogeneous.

- What benefit-risk or patient preference data is available that might influence what treatments will go through clinical trial? How might this data influence trial design?
- What are appropriate and meaningful eligibility criteria?
- What are appropriate trial inclusion/exclusion criteria? How can exclusion criteria be minimized?
- What other criteria are there to assess the feasibility of the protocol or the study overall?
- How can the trial design best include patient subgroups and/or under-served populations in order to capture differential effectiveness?
- How can procedures be minimized to only those that are absolutely necessary to achieve the stated goal of the trial?
- Has the protocol design been optimized to minimize the burden on the patient for participation (i.e., limited labs, limited visits, location)?
- Under what circumstances would it be possible to shorten placebo-control phase?
- How can you minimize or prevent amendments to the protocol?
- How can qualitative data be incorporated to get a better picture of the 'patient ecosystem'?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 44-45: "Protocol Development."

Study Endpoints

NOTE: For rare diseases, patient populations will be small and heterogeneous.

- What are meaningful clinical endpoints for the disease/disease stage?
- How does the progression of the disease effect the selection of endpoints?
- How does the selection of endpoints impact the eligibility to participate in clinical trials?
- Under what circumstance can endpoints include novel surrogates and intermediate clinical endpoints, particularly if the drug will be used for serious or life threatening diseases with no current treatment options?

- Can the trial design use a single primary endpoint supported by appropriate secondary endpoints rather than multiple primary endpoints?

Benefit-Risk Assessment and Patient Preferences

- What patient preference and benefit-risk preferences have been or can be defined for the (stage of) disease?
- What treatment benefits matter most to patients?
- What are patients' perspectives on the adequacy of available therapies?
- Who is making treatment decisions – patients, caregivers, others? How might this impact benefit-risk or preferences?
- How might benefit-risk assessment evolve over the progression of the disease or once pediatric patients have reached adulthood?
- How can we quantify this data if it has not been quantified?
- How can we best leverage qualitative data?

Consent

- How can Expert Patients/Patient Groups help with consent design?
- How can EPs/PGs function as peer advocates during consent procedure?
- How can EPs/PGs assess the reading and health literacy level of the trial participants?
- How can EPs/PGs provide training or educational materials to support vulnerable populations during the consent process?
- How can EPs/PGs ensure use of culturally appropriate ways to present consent information? How can they address fears and other barriers to trial participation (e.g., losing access to primary physician)?
- Is consent in patient-friendly language? How is comprehension determined? Should e-ICF be considered?
- What are new or particular issues here not already covered by existing guidance?
- Need for assent (or not) for pediatrics

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 45-48: "Informed Consent Process."

Patient Privacy

- What are the privacy laws already in place for each particular geography (e.g., HIPAA for the U.S.)? How will they impact this program?
- What privacy issues are unique to this program? What country or region-specific privacy legislation do we need to consider (e.g., EU)?
- What privacy concerns might this patient population have?
- What measures will this effort undertake to ensure privacy?
- What are the unique compliance issues for this effort?

REGULATORY REVIEW/APPROVAL

Patient Data/Trial Results

- How will patient data be collected and stored?
- What patient data can be shared with patients? When and how?
- What trial results be shared with patients? When and how?

- Will the patient help present results?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 60-63: "Trial Closure and Results Dissemination."

Trial Closure Plan

- What is the plan to address a range of possible closure scenarios?

End of Study Survey/Phase Review

- What is the best way to survey participants on their experience with the study?
- What other ways are there to collect patient feedback?
- What can study participants or expert patients contribute to the sponsor audit?
- What should be included in a lay summary of clinical trial results?

Access to Trial Medicines/Devices

- What access post-trial will trial participants have to trial products or procedures (this should be addressed early in the process)?
- Will participants have access to treatment after the trial? How can the Expert Patient/Patient Group assist in getting access under managed access programs?

Additional Resources (see APPENDIX AND RESOURCES):

Guidance for Biomedical HIV Prevention Trials, p. 63-65: "Post-trial Access to Trial Products or Procedures."

PR/External Awareness

- How can Expert Patients/Patient Groups support the following:
  - Transparency of clinical trials through awareness of the existence of clinical trials
  - Public confidence in validity of the research process
  - Presentation of trial results
  - Educating patients, families, the community, and policy makers to build research literacy and support for research
  - Advocacy and influence on policy makers for research funding, reimbursement, and patient needs

Considerations for Measuring Success and Capturing Learnings

Recommended Contributors:

- C-suite champion(s)
- Program leader(s)
- Patient liaisons
- Program participants
- Key internal stakeholders
- Expert Patient/Patient Group representatives
- Lay patients as applicable

Engagement Plan Review

- How well did your engagement plan anticipate and address the strategies and mechanisms for building relationships and constructively engaging with patient communities, expert patients, or patient groups involved in or impacted by this program?

- What would you do differently?
- In what ways was your collaboration mutually beneficial?

Environmental Scan Review

- How accurate was your environmental scan? What was missing?
- How helpful was it to assess the current environment?
- In what ways did it help your program be successful?

Measuring Program Success

- Based on the measures you defined at the outset, how successful was your program?
- What qualitative measures were gathered? What did they indicate?
  - Are patient-reported outcomes to be included? How will they be collected?
- What did the metrics show in terms the impact of patient engagement on your organization?

Measuring Patient-Centricity Success

- How well were patient-centric processes followed?
- How effective was this specific patient-centric program?
- How will program learnings be incorporated into other parts of the organization?
- What was the value of this patient-centric program – both quantitative and qualitative – to your organization?
- How will you use the feedback to improve the process next time? How will recommendations be incorporated into future processes?
- What are the mechanisms for incorporating learnings from this effort into future efforts of your organization, including individuals responsible for ensuring that learnings are incorporated into future practices?
- What are the mechanisms for communicating the outcomes of this program (to build awareness and reduce resistance over time)?

Program Deliverables

- What documents can be shared as templates or examples of good practice, such as the following:
  - Master services agreement template
  - Memorandum of understanding
  - Confidentiality agreements
  - Non-disclosure agreements
  - Communication plans
  - Job or role descriptions

Appendix and Resources

Reference List

1. European Patients' Academy for Therapeutic Innovation. *Framework for patient involvement in regulatory processes*. https://www.eupati.eu/advocacy/consultation/; p. 6 Accessed August 29, 2016.
2. AIDS Vaccine Advocacy Coalition (AVAC) and Joint United Nations Programme on HIV/AIDS. *Good Participatory Practice. Guidelines for Biomedical HIV Prevention Trials*, p. 18. June 2011. http://www.avac.org/sites/default/files/resource-files/Good%20Participatory%20Practice%20guidelines_June_2011.pdf Accessed February 26, 2016.
3. Ibid, p. 35.
4. Frank L, Forsythe LP, Ellis L, Schrandt S, Sheridan S, Gerson J, Konopka K, Daugherty S. Conceptual and practical foundations of patient engagement in research at the patient-centered outcomes research institute. *Quality of Life Research*. 2015; 24(5): 1034.
5. Clinical and Translational Science Awards Consortium, Community Engagement Key Function Committee Task Force on the Principles of Community Engagement. *Principles of Community Engagement 2nd Edition, p. 8*. June 2011. https://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf. Accessed February 26, 2016.
6. European Patients' Academy for Therapeutic Innovation. *Framework for patient involvement in industry-led medicines R&D*, p. 6. https://www.eupati.eu/advocacy/consultation/. Accessed August 29, 2016.
7. Frank L, Forsythe LP, Ellis L, Schrandt S, Sheridan S, Gerson J, Konopka K, Daugherty S. Conceptual and practical foundations of patient engagement in research at the patient-centered outcomes research institute. *Quality of Life Research*. 2015; 24(5): 1034.
8. University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI). *Assessing Meaningful Patient Engagement in Drug Development: A Definition, Framework, and Rubric*, p. 1. March 2015. http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/cersievents/pfdd/mcersi-pfdd-proceedings-rubric.pdf. Accessed March 25, 2016.
9. European Patients' Academy for Therapeutic Innovation. *Framework for patient involvement in industry-led medicines R&D*, p. 6. https://www.eupati.eu/advocacy/consultation/. Accessed August 29, 2016.
10. Clinical Trial Transformation Initiative. *CTTI Recommendations: Effective Engagement with Patient Groups around Clinical Trials*, p. 6. 2015. https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/pgctrecs.pdf
11. Perlmutter, Jane. The Power of Individual Advocates on Influencing National Research Issues. Paper presented at: 52st DIA Annual Meeting; June 26, 2016; Philadelphia, PA.
12. AIDS Vaccine Advocacy Coalition (AVAC) and Joint United Nations Programme on HIV/AIDS. *Good Participatory Practice. Guidelines for Biomedical HIV Prevention Trials*, p. 14. June 2011. http://www.avac.org/sites/default/files/resource-files/Good%20Participatory%20Practice%20guidelines_June_2011.pdf Accessed February 26, 2016.

13. Clinical and Translational Science Awards Consortium, Community Engagement Key Function Committee Task Force on the Principles of Community Engagement. *Principles of Community Engagement 2nd Edition, p. 165*. June 2011. https://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf. Accessed February 26, 2016.

14. Ibid, p. 167.

15. European Patients' Academy for Therapeutic Innovation. *Framework for patient involvement in industry-led medicines R&D*, p. 6. https://www.eupati.eu/advocacy/consultation/. Accessed August 29, 2016.

16. Clinical Trial Transformation Initiative. *CTTI Recommendations: Effective Engagement with Patient Groups around Clinical Trials*, p. 4. 2015. https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/pgctrecs.pdf

17. NIH, National Institute of Allery and Infectious Diseases. *Recommendations for Community Involvement in National Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trials Research*, p. 8-9. February 2009 https://www.niaid.nih.gov/about/organization/daids/Networks/Documents/cabrecommendations.pdf. Accessed March 20, 2016.

18. US FDA. *Guidance for Industry Patient-Reported Outcome Measures: Used in Medical Product Development to Support Labeling Claims*, p. 5. December 2009. http://www.fda.gov/downloads/Drugs/.../Guidances/UCM193282.pdf. Accessed February 26, 2016.

Additional References and Resources

AIDS Vaccine Advocacy Coalition (AVAC) and Joint United Nations Programme on HIV/AIDS. *Good Participatory Practice. Guidelines for Biomedical HIV Prevention Trials*. June 2011. http://www.avac.org/sites/default/files/resource-files/Good%20Participatory%20Practice%20guidelines_June_2011.pdf Accessed February 26, 2016.

Banerjee AK, Okun S, Edwards IR, Wicks P, Smith MY, Mayall SJ, Flamion B, Cleeland C, Basch E, Patient-Reported Outcomes Safety Event Reporting (PROSPER) Consortium. Patient-Reported Outcome Measures in Safety Event Reporting: PROSPER Consortium guidance. *Drug Safety*. 2013; 36(12);1129-49.

Boutin M, Dewulf L, Hoos A, Geissler J, Todaro V, Schneider R, Garzya V, Garvey A, Robinson P, Saffer T, Krug S, Sargeant I. Culture and Process Change as a Priority for Patient Engagement in Medicines Development. *Therapeutic Innovation and Regulatory Science*. 2017; 51(1); 29-38.

Bridges JF, Hauber AB, Marshall D, Lloyd A, Prosser LA, Regier DA, Johnson FR, Mauskopf J. Conjoint Analysis Applications in Health – a Checklist: A Report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value Health 2011;14(4):403-13.*

Brigham Research Institute, Patient-centered Comparative Effectiveness Research Center. Patient Engagement Best Practices Resource Document. http://www.brighamandwomens.org/Research/centers/PCERC/resources.aspx. Accessed August 26, 2016.

Calvert M, Kyte D, Duffy H, Gheorghe A, Bercieca-Bebber R, Ives J, Draper H, Brundage M, Blazeby J, King M. Patient-Reported Outcome Assessment in Clinical Trials: A Systematic Review of Guidance for Trial Protocol Writers. 2014. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110216. Accessed August 1, 2016.

Chassany O, Sagnier P, Marquis P, Fullerton S, Aaronson N. Patient-Reported Outcomes: The Example of Health-Related Quality of Life – A European Guidance Document for the Improved Integration of Health-Related Quality of Life Assessment in the Drug Regulatory Process. *Therapeutic Innovation and Regulatory Science*. 2002; 36(1); 209-238.

Clinical and Translational Science Awards Consortium, Community Engagement Key Function Committee Task Force on the Principles of Community Engagement. *Principles of Community Engagement 2nd Edition*. June 2011. https://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf. Accessed February 26, 2016.

Clinical Trial Transformation Initiative. CTTI Recommendations: Effective Engagement with Patient Groups around Clinical Trials. 2015. https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/pgctrecs.pdf. Accessed February 26, 2016.

DIA. Patient Advocacy Lifecycle Model; June, 2016. http://www.diaglobal.org/en/resources/news#article=ec61d791-47f6-48ad-8ce6-a9ec83049229. Accessed August 1, 2016.

European Medicines Agency. Reflection Paper on the Regulatory Guidance for the Use of Health-related Quality of Life (HRQL) Measures in the Evaluation of Medicinal Products. July 2005. http://www.ispor.org/workpaper/emea-hrql-guidance.pdf. Accessed August 29, 2016.

European Patients' Academy for Therapeutic Innovation. Framework for patient involvement in industry-led medicines R&D. https://www.eupati.eu/advocacy/consultation/. Accessed August 29, 2016.

European Patients' Academy for Therapeutic Innovation. *Framework for patient involvement in regulatory processes (Draft)*. https://www.eupati.eu/advocacy/consultation/; p. 6 Accessed August 29, 2016.

Fleurence RL, Forsythe LP, Lauer M, Rotter J, Ioannidis JPA, Beal A, Frank L, Selby JV. Engaging Patients and Stakeholders in Research Proposal Review. *Annals of Internal Medicine*. 2014; 161(2):122-130.

Forsythe L, Ellis L, Edmundson L, Sabharwal R, Rein A, Konopka K, Frank L. Patient and Stakeholder Engagement in the PCORI Pilot Projects: Description and Lessons Learned. *Journal of General Internal Medicine*. 2016; 31(1):13-21.

Forsythe L, Szydlowski V, Hassan Murad M, Ip S, Wang Z, Elraiyah T, Fleurence R, Hickam D. A Systematic Review of Approaches for Engaging Patients for Research on Rare Diseases. *Journal of General Internal Medicine*. 2014;29(3):788-800.

Frank L, Forsythe LP, Ellis L, Schrandt S, Sheridan S, Gerson J, Konopka K, Daugherty S. Conceptual and practical foundations of patient engagement in research at the patient-centered outcomes research institute. *Quality of Life Research*. 2015; 24(5): 1033-1041.

Gallin E, Bond E, Califf R; Crowley W, Davis P, Galbraith R, Reece EA. Forging Stronger Partnerships between Academic Health Centers and Patient-driven Organizations. *Academic Medicine.* September 2013; 88(9):1220-1224. http://journals.lww.com/academicmedicine/Abstract/2013/09000/Forging_Stronger_Partnerships_Between_Academic.21.aspx.

Hasnain-Wynia R, Beal AC. Role of PCORI in Addressing Disparities and Engaging Patients in Clinical Research. *Clinical Therapeutics*. 2014 July; 36(5):619-23.

ISPOR. Clinical Outcomes Assessment (COA) in Rare Disease Clinical Trials – Emerging Good Practices: Report of the ISPOR Rare Disease Trials COA Measurement Task Force. https://www.ispor.org/TaskForces/ClinicalOutcomesAssessment-RareDisease-ClinicalTrials.asp. Accessed August 29, 2016.

NIH, National Institute of Allery and Infectious Diseases. in National Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trials Research, February 2009 https://www.niaid.nih.gov/about/organization/daids/Networks/Documents/cabrecommendations.pdf. Accessed March 20, 2016.

Parent Project Muscular Dystrophy. Guidance for Industry – Duchene Muscular Dystrophy Developing Drugs for Treatment over the Spectrum of the Disease. http://www.parentprojectmd.org/site/PageServer?pagename=Advocate_fdaguidance. Accessed February 26, 2016.

Peay HL, Hollin I, Fischer R, Bridges JF. A Community-Engaged Approach to Quantifying Caregiver Preferences for the Benefits and Risks of Emerging Therapies for Duchenne Muscular Dystrophy. *Clinical Therapeutics*. 2014 May; 36(5):624-37.

Perlmutter, Jane. The Power of Individual Advocates on Influencing National Research Issues. Paper presented at: 52st DIA Annual Meeting; June 26, 2016; Philadelphia, PA.

Smith SK, Selig W, Harker M, Roberts J, Hesterlee S, Leventhal D, Klein R. Patrick-Lake B, Abernethy AP. Patient Engagement Practices in Clinical Research among Patient Groups, Industry, and Academia in the United States: A Survey. PLOS One. 2015; 10(10); 1-10.

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI). Assessing Meaningful Patient Engagement in Drug Development: A Definition, Framework, and Rubric. March 2015. http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/cersievents/pfdd/mcersi-pfdd-proceedings-rubric.pdf. Accessed March 25, 2016.

US Department of Health & Human Services, Agency for Healthcare Research and Quality. Engaging Patients in Information Sharing and Data Collection: The Role of Patient-Powered Registries and Research Networks. September 2013. https://www.effectivehealthcare.ahrq.gov/ehc/assets/File/Patient-Powered-Registries-white-paper-130911.pdf. Accessed March 20, 2016.

USAID. Communications Handbook for Clinical Trials. July 2011. https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey. Accessed August 23, 2016.

US Department of Health & Human Services, Agency for Healthcare Research and Quality. The AHRQ Informed Consent and Authorization Toolkit for Minimal Risk Research. August 2009. http://www.ahrq.gov/sites/default/files/publications/files/ictoolkit.pdf. Accessed August 29, 2016.

US FDA. Duchene Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment Guidance for Industry. June 2015. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/UCM450229.pdf. Accessed February 26, 2016.

US FDA. Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency, Completed: September 30, 2011. http://www.fda.gov/downloads/AboutFDA/Transparency/TransparencyInitiative/UCM285124.pdf. Accessed February 26, 2016.

US FDA. Guidance for Industry – Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: Developing Drug Products for Treatment. March 2014. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm388568.pdf. Accessed February 26, 2016.

US FDA. Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors – Exception from Informed Consent Requirements for Emergency Research, March 2011. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf. Accessed February 26, 2016.

US FDA. Guidance for Industry Patient-Reported Outcome Measures: Used in Medical Product Development to Support Labeling Claims, December 2009. http://www.fda.gov/downloads/Drugs/.../Guidances/UCM193282.pdf. Accessed February 26, 2016.