MDIC Report:
Maximizing Patient Input in the Design and Development of Medical Device Clinical Trials

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1 The 21 CFR part 812 which was updated in April 2018 uses the term clinical investigations since not all studies that are submitted as valid scientific evidence is a trial. For purposes of the MDIC project we use “clinical trials.”
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Executive Summary

There are key distinctions between device trials and drug trials that present unique opportunities, challenges and resource needs for engaging patient insights in the device field. In developing this report, an MDIC Working Group evaluated a series of characteristics of device trials (level of invasiveness; outcomes assessment; trial enrollment; and trial design) and prioritized them based upon their relevance for patient engagement.

A key step for sponsors seeking to pursue this work is to assess the reasons for doing it, when to do it and how the input will be used. The report delves into the opportunities that exist for patient input to help define unmet need, clarify patient preferences, develop endpoints that measure what matters to patients, assist in reducing burdensome study protocol requirements to enhance recruitment and retention and establishing information that can be used in the regulatory process and for post-marketing activities.

Once the reasons for this work are clearly defined, the report provides information and resources that can be used to assist in evaluating and building needed organizational capacity to successfully pursue patient engagement in clinical development. This includes ensuring that this effort has appropriate internal leadership backing and sufficient resourcing (including training and appropriate legal/compliance input) to support the effort.

Patient engagement in clinical research is best viewed as a continuum that occurs in different ways, for different purposes, across the lifecycle of the product development path. A good rule of thumb to guide this work is ‘engage early and engage often.’ Although the details of each engagement plan (with whom, when, how etc.) will be tailored to the specific development and clinical research program, there are multiple baseline tactics that should be evaluated along the way. The report reviews a set of elements that should be incorporated into a sponsor’s patient engagement plan.

The report underscores that, when done correctly, patient engagement in medical product development is neither superficial nor episodic. The most successful efforts to leverage patient insights are those that recognize the value of this work and have embedded it into the corporate culture. Ideally, this commitment to patient engagement is held by company leaders and incentivized throughout the workforce.

Knowing which type of patient voice is most relevant to a development program can be challenging and is certainly not an “exact science.” Product developers seeking patient input should be aware of the variations in patient experience and related input and should aim to evaluate the extent to which the insights they receive are representative for the population under study. The report provides a series of resources to help identify the most appropriate people to provide the “patient voice.”

Successful engagement with patients within clinical development requires a clear definition of what the patient’s role will be, from providing them a proactive, governance-type of “seat at
the table” with the study team, to engaging them as advisors, to offering a more reactive role. The report addresses this topic and provides resources for sponsors to help define what is the most appropriate role.

The report emphasizes that sponsors should take the time and make the effort to build relationships with patient groups and individual patients that are based on shared commitment to the effort, clear expectations, regular communications and a common language about the project. Avoiding the perception that engagement activities are tokenism and are just being done to “check a box” by ensuring that all parties feel respected and able to contribute within the process is a key component of making this process meaningful. The report offers resources to help sponsors with building the kind of trusting relationships needed to succeed. Included in this section are implementing a contracting and compliance process that is workable, providing appropriate compensation based on Fair Market Value, and ensuring there is transparency and regular communication about the conduct of the study and how patients’ input is being incorporated into the program.

It is hoped that this report provides a concise set of considerations for medical device developers to evaluate as they pursue patient engagement in their clinical trials and product development activities. Recognizing that this work is complex and made increasingly so by the heterogeneity of the device development landscape, and understanding that no single compilation of information can provide everything a sponsor would need, the resources presented within this report are offered as a foundation from which sponsors can advance their efforts to generate and incorporate patient input into trial design and conduct.

As the field of patient engagement in clinical studies for devices evolves and expands, additional efforts could be undertaken to support sponsors, including:

- Development of device company trainings
- Development of case-studies of successful activities in device trials
- Pursuit of projects to capture learnings and measure impact for the field
- Conduct of a re-survey of device manufacturers to compare to baseline results from the 2018 survey.
Background & Objectives

Developing patient-centered medical product trials has the potential to improve the patient experience in clinical trials, accelerate accrual, improve retention, improve data quality, and assure that the trials themselves are focused on outcomes that matter most to patients. All of this facilitates the development of innovative medical products that will make a direct and meaningful impact on the lives of patients.

The art and science of patient engagement in medical product development has evolved and expanded in recent years, in large part due to leadership from the Food and Drug Administration (FDA), sophisticated patient advocacy organizations, and the work of organizations like Clinical Trials Transformation Initiative (CTTI), Patient-Centered Outcomes Research Institute (PCORI), DIA, and the National Health Council (NHC).

FDA’s work in this area has spanned 30 years, beginning with its efforts to engage patient input during the HIV/AIDS crisis in the late 1980’s. Today, FDA’s Centers, Offices and Divisions have many complementary programs designed to incorporate patient insights into its regulatory activities.

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The Center for Devices and Radiological Health (CDRH) has prioritized patient engagement through multiple activities, including establishment of its Patient Engagement Advisory Committee (PEAC) and issuance of a new draft Guidance on this topic. FDA leadership has encouraged medical device companies to include patient perspectives across the medical device lifecycle, writing in 2017 that “[A]dvancements in the science of patient input are needed to help ensure that clinical trials are designed to assess what matters most to patients and to facilitate patient enrollment in studies.”

As device manufacturers pursue patient engagement activities, they still need more specific information on how best to engage patients to collect and employ patient perspectives across the medical device lifecycle.

**MDIC Framework Initiative**

In response to this need and building upon its pioneering work to advance the use of patient preference information in device development, the Medical Device Innovation Consortium

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MDIC is developing a Framework for Patient Input in Medical Device Clinical Trials (Framework). With an emphasis on evidence-based tools for engaging with patients, this project is focused on: describing methods to integrate patient input into the design of clinical trials, advancing a transformative method for integrating patient preferences into the statistical design of clinical trials, and synthesizing practical considerations for reducing the patient burden of participation in clinical trials.

MDIC’s approach in developing its Framework has been to research, examine, highlight and synthesize existing work in these areas. Where possible, this effort has focused on tailoring existing resources for the specific needs of medical device clinical trials. Where there are gaps in existing resources, this initiative has refined existing approaches. The Framework provides a compilation of learnings from the overall medical product development field (including drugs, biologics and devices), practical suggestions for undertaking patient engagement in clinical development, and considerations for determining when it is most important to engage patient insights.

The MDIC Framework effort comprises three sub-projects:

1. Guidelines to integrate patient preferences into the statistical design of clinical trials
2. Methodologies to maximize patient participation in clinical trials
3. A report summarizing the evidence base for the methodologies, guidelines, and framework developed under this project

This report is focused on **Sub-Project 2: Methodologies to maximize patient participation in medical device clinical trials**, whose deliverables include:

1. Literature review on existing efforts to reduce patient burden of participating in clinical trials.\(^{13}\)
2. Patient survey to elicit patients’ perspectives on the barriers to participation in clinical trials.
3. Industry, advocacy organization, and health care provider survey to elicit perspectives on the barriers stakeholders face in partnering with patients for the purpose of eliciting patient perspectives on medical device clinical trial design and other operational aspects related to patient participation.\(^{14}\)

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\(^{13}\) Medical Device Innovation Consortium (MDIC) Patient Engagement Literature Review. [https://mdic.org/resource/literature-review-patient-engagement/](https://mdic.org/resource/literature-review-patient-engagement/)

4. Review of successful practices developed by other organizations and assessment of their applicability to device trials (addressed in this report).

5. Summary of services and tools that have successfully reduced patient burden in clinical trials (addressed in this report).

6. Guideline document that synthesizes the findings of this project with actionable recommendations and a toolkit for maximizing patient participation (addressed in this report).

Report Scope and Context

Medical devices fall into multiple categories – ranging from routine items like bandages to MRI machines, diagnostics and therapeutics, as well as highly specialized, implantable items like a heart valve or stent.

While low risk products (Class I) are generally exempt from pre-market regulatory review and most moderate-risk devices (Class II) require demonstration of substantial equivalence to a marketed product for regulatory clearance (although some 510(k)s for Class II devices require clinical data), higher risk devices (Class III) are subject to the approval of a Premarket Approval Application (PMA). All new devices are automatically considered to be Class III if there is no predicate. A novel device may come in through a de novo submission process for classification if there is perception that it should not be considered Class III. These processes require valid scientific evidence.15

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15 According to 21 CFR § 860.7(c)(2): “[V]alid scientific evidence is evidence from well-controlled investigations, partially controlled studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.” https://www.fda.gov/media/90419/download
This report focuses on devices that must undergo clinical testing through trials to provide safety and effectiveness data for regulatory review and decision-making. For such devices, sponsor companies (both in the US and globally) are increasingly seeking to include patient perspectives in the design and assessment, of new medical technologies. Sponsors and regulators increasingly recognize the importance of leveraging patient insights in the conduct of device clinical trials, both in selecting outcomes that matter to patients and designing trial protocols that patients will join and can complete.

To inform development of this report, MDIC undertook two important projects: 1) a broad landscape review of existing materials, literature and resources focused on generating patient insights for clinical trials and 2) surveys of device patients and industry stakeholders to assess potential benefit for and use of patient engagement strategies for clinical trials.16 17

**Literature Review**

The literature review reflects a broad scan of publicly available information about relevant organizations, initiatives, materials and publications, as of March 2019. The summary provides

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a representative snapshot of activities and resources within the highly active and evolving field of patient engagement in clinical research.

Survey

For the survey, which was conducted in two parts during 2018, MDIC received feedback from 53 device and diagnostic industry stakeholders and 123 individuals identifying as patients. The goal of the complementary surveys was to inform efforts to develop guidelines for industry on how to involve patients in the design of clinical trials.

Key findings from the survey indicated a significant opportunity to expand awareness among device and diagnostic companies of the benefits and importance of patient input and, given the perceived barriers highlighted in the industry survey, the need to produce resources for device companies about how to go about gathering and employing patient input in trials. The survey found that:

• More than half of industry respondents to the question “In your estimation how often does your organization gain feedback directly from patients prior to finalizing a study protocol?” reported their organizations never gain patient input to protocol development, while nearly a third estimated their organizations gain input less than 25% of the time.

• Once protocols were finalized, more than 80% of industry respondents said they either never sought patient input on operational study design or did so less than 25% of the time.

• There are disconnects in the perspectives of industry respondents and patients relating to the reasons patients might decide to enroll in a clinical trial, particularly around the importance of doctor recommendations. For example, 92% of industry respondents rated a physician recommendation as Important or Very Important in a patient’s decision to participate in a clinical trial. In contrast, of patient respondents who had been invited to participate in a clinical trial, 32% heard about the trial from their physician or healthcare provider. Of those who agreed to participate, only 9% of respondents marked Doctor Recommendation as their reason for deciding to participate in the trial. As a possible explanation for this discrepancy, 73% of the patient respondents belonged to patient organizations; they may represent a sampling of well-informed patients who do not need to rely solely on recommendation from their own healthcare provider.

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18 20% of respondents were 45-54 years old, 37% were 55-64, and 32% were 65-74. 60% were female. 73% belong to patient groups, though only 38% said they were invited to participate in a trial by a patient support or advocacy group.
Unique Device Trial Aspects

As medical device developers consider opportunities and approaches for engaging patients in their clinical trials, there are many lessons that can be learned from their drug and biologic development counterparts, for whom the patient engagement experience is more robust. Wherever possible, the device industry should assess best practices from across the medical product spectrum, with the recognition that there are multiple unique aspects of medical device clinical trials that make it more difficult to leverage some of these principles from the drug development arena.

However, there are key distinctions between device trials and drug trials that present unique opportunities, challenges and resource needs for engaging patient insights in the device field.

To identify and highlight those aspects for the Framework project, an MDIC Working Group evaluated a series of characteristics of device trials and prioritized them based upon their relevance for patient engagement. The Working Group focused on four categories of device aspects: 1) Level of invasiveness; 2) Outcomes assessment; 3) Trial enrollment; and 4) Trial design. In each category, there were several important aspects identified, as well as the priority patient engagement objectives and opportunities associated with them.

<table>
<thead>
<tr>
<th>Category</th>
<th>Illustrative Patient Engagement Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elements of “Level of Invasiveness:”</td>
<td>Understanding how device trial patient participants evaluate the benefits and risks of undergoing an invasive procedure associated with use of a device (as compared with other potential therapy options).</td>
</tr>
<tr>
<td>- Implantable device</td>
<td></td>
</tr>
<tr>
<td>- External device/impact on daily life</td>
<td>Understanding how patients might evaluate various procedures related to implantation and/or use of the device, in order to 1) best explain these elements to patients, 2) consider ways to mitigate concern re: invasiveness/mode of administration of the device (where possible).</td>
</tr>
<tr>
<td>- Reversibility</td>
<td></td>
</tr>
<tr>
<td>- Impact relative to disease state (early disease vs. later stage disease)</td>
<td></td>
</tr>
</tbody>
</table>

19 While it is also the case that surgery may sometimes be an alternative option to device use (as distinct from the cases in which surgery is central to the use of the device through implantation), for the purpose of this report and the following table comparisons are made between devices (including those that require surgery for implantation) and drugs.

### Elements of “Outcomes Assessment:”
- Selection of primary and secondary endpoints
- Selection of performance goals
- Required follow up
- Reporting of side effects/symptoms by patients

Understand what outcomes are most relevant to the patient population and incorporate those as endpoints (where possible).

Understanding patients’ views on risk-benefit priorities.

Identifying measurement and data capture approaches that are most acceptable to device trial patient participants to maximize successful adherence to trial protocol elements.

Leveraging patient input to reduce/eliminate burdens on trial participants (including appropriate stratification of patients and effective use of mobile technology (e.g. elderly, rural populations) and other means for tracking progress on trial e.g. measurement of symptoms, side-effects, PRO’s, overall outcomes etc.) while allowing patients to remain connected to the study and the sponsor over time.

### Category

### Illustrative Patient Engagement Objectives

**Elements of “Trial Enrollment:”**
- Study population (including participation by under-represented populations)
- Size of enrollment
- Patient screening/inclusion & exclusion criteria
- Education needs of patients (for successful participation in the trial)

Understanding patient desires for enrolling in the trial, seeking opportunities to adjust inclusion/exclusion criteria and make it easier to accrue patients (where possible) to enhance opportunities for broader access among the target study population.

Understanding what information is most relevant for device trial patient participants in deciding to enroll in, remaining on and being compliant participants within a trial.

Evaluating best approaches for most successfully communicating this information to patients in order to develop and convey the most relevant messaging and materials.

Determining patient interest in receiving real-time (where possible) and follow up communication/information about their own data and the overall success/failure of the trial (data sharing/feedback loop).

### Category

### Illustrative Patient Engagement Objectives

**Elements of “Trial Design:”**
- Placebo/sham procedure
- Crossover option
- Single arm studies
- Unblinded studies
- Adaptive design
- Device modifications during the trial
- Use of Real-World Evidence

Understanding how device trial patient participants feel about a variety of trial design aspects (including use of placebo/sham, lack of control group, unmasked study arms, adaptive design, and potential to modify the device during the trial) to 1) adjust the design if possible/where necessary to facilitate success and/or 2) position patient-facing messaging/materials to speak to/address patients questions/concerns.

Understanding patient perspectives on best ways to reduce/eliminate burdensome study protocol requirements including by leveraging RWE and other innovations in clinical trial conduct.
Key Topics Overview:

Invasive procedures
A key distinction for certain categories of device trials (when compared to most drug studies) is the requirement for patients to undergo an invasive procedure(s). There are myriad considerations for a patient in deciding whether to participate in these types of studies, including evaluating risks associated with the procedure (and post-procedure complications), trusting that the clinician is a trained specialist who can successfully conduct the procedure and understanding the potential impact an implanted device may have on quality of life. By engaging with patients in the trial design, sponsors can develop appropriate messaging and steps in the trial enrollment process that can help to address these and other considerations for potential trial participants.

Reversibility
Unlike most drugs under study that are metabolized and cleared from the body after a defined period, devices that are implanted have a more permanent impact on the patient. Even those devices that are implanted via minimally invasive procedures have a permanent place within the patient’s body, while removal of such devices also can have significant impact (as the associated procedures are often invasive and life-changing). An example of this can be a transcatheter coronary artery valve that must be removed via invasive, open-heart bypass surgery. This lack of routine reversibility for an experimental device may be an issue of concern to patients considering enrollment in a trial. Understanding patients’ perspectives on this topic can help sponsors develop messaging – including providing a level of assurance about what will happen to the patient if the study does not support approval or clearance of the device for marketing in the US -- and communication approaches to address this potential barrier to accrual. Transparency regarding this topic is important to ensure patients understand the potential permanence of a device.

Reporting of side effects & symptoms
In some cases, device patients may see their participation in the study as directly connected to the procedure and related complications. Once that period has ended, patients may be less frequently engaged with ongoing in-person monitoring than occurs in drug trials, especially when the patient does not require specific medical follow up (e.g. ongoing infusions) to continue to “use” the device. Once a device is implanted, for example, patients may not feel the need to stay connected to the study and trial sponsor. This may result in inconsistent reporting of side effects, symptoms or adverse events relevant to the study. The loss of the patient to follow up could impact the effectiveness assessment too, limiting the ability to see a true success even when it is present. Patient insights can help the sponsor evaluate the best way to continue to monitor the patient’s progress (e.g. use of mobile digital health technology, stratification of monitoring based on special needs of certain populations). This is a particular concern with investigational devices used for elective procedures, such as breast implants.
While not all are implanted as elective procedures, most are, and follow-up and post-market vigilance on the safety and effectiveness of these devices has been poor, to date.

**Placebo/Sham procedure**

A significant issue with all clinical trials relates to the need for control arms to fully evaluate the impact of the novel product. In drug trials, the prospective, double-blind\(^{21}\), randomized-controlled clinical trial remains the gold standard, even as innovative trial designs are gaining popularity (e.g. adaptive randomization, crossover arms). A frequent concern expressed by patients who refuse to participate in clinical studies is that they will receive placebo rather than an experimental therapy if they enroll in a trial. The use of the term “placebo” when discussing trial design with patients should be clearly defined early in the process of presenting a trial to patients to demonstrate clearly how it is operationalized in the study.

Additionally, given the variation in delivery modes for certain therapies (infusion vs. oral), it can be difficult to preserve a blinded study, making it more difficult to keep patients assigned to the control arm from dropping out. To address this concern, in some cases, sponsors have provided patients in the control arm the opportunity to “crossover” into the experimental arm if their condition progresses while on study.

In certain device trials, where a procedure is required to implant a device, there are additional issues – practical and ethical – involved with designing a trial that will accurately measure the impact of the novel intervention. Patients who are randomized to control may either have no procedure and would thereby know they were on control or might undergo some type of “sham” procedure to maintain blinding (patients may be highly resistant to this possibility). Patient input can be very helpful as sponsors consider the best approach to addressing these topics.

**Considerations for Device Developers**

In this section we review the following key considerations for device developers seeking to pursue patient engagement:

I. Defining Patient Engagement Objectives  
II. Building Organizational Capacity  
III. Engagement Planning  
IV. Tactics

**Defining Patient Engagement Objectives:**

There is strong impetus to encourage device developers to engage patients and patient input in their development activities, and specifically in their approach to designing and executing

\(^{21}\) The terms “blind” or “blinded” are often interchangeably used with “masked.” When a trial is “masked” so that participants do not know if they are in the investigational arm or the control arm, regulators will often ask sponsors to test the “mask” to ensure that it is effective.
clinical trials/investigations. In its 2019 draft Guidance on Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations\textsuperscript{22}, FDA noted that effective engagement of Patient input in the development of clinical trials could result in several important outcomes, including:

\begin{itemize}
\item Faster study/research participant recruitment, enrollment, and study completion;
\item Greater study/research participant commitment, resulting in decreased loss to follow-up;
\item Greater study/research participant compliance resulting in fewer protocol deviations/violations;
\item Fewer protocol revisions;
\item Streamlined data collection resulting in better quality data; and
\item More relevant data on outcomes that matter to patients.
\end{itemize}

Previously, in its 2016 Guidance on Patient Preference Information, the FDA wrote: “Patients’ input regarding their experiences and perspectives on their disease or condition and its management may be useful throughout the total product lifecycle for certain devices, by improving understanding of the disease or condition, defining design inputs to meet needs of the patient end user, assessing outcomes most important to patients, and more.” \textsuperscript{23}

A useful definition for patient engagement in medical product development proposed in 2017 by DIA states:\textsuperscript{24}

\begin{quote}
\textit{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 lifecycle (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.}
\end{quote}

In its 2019 draft Guidance on Patient Engagement in Medical Device Clinical Investigations, FDA defined patient engagement as “intentional, meaningful interactions with patients that provide opportunities for mutual learning, and effective collaborations.”\textsuperscript{25}

\begin{itemize}
\item 23 US Food and Drug Administration (FDA) Patient Preference Information Guidance for Industry. \url{https://www.fda.gov/media/92593/download}
\item 24 Drug Information Agency (DIA) Patient Engagement Resources. \url{https://www.diaglobal.org/en/resources/areas-of-interest/patient-engagement}
\end{itemize}
A 2016 article in *Patient Preference and Adherence*\(^{26}\) outlined a useful set of activities that could involve patient input leading into, through and after a clinical study:

![Image of diagram showing phases of a clinical study: Before the study, During the study, After the study, with activities such as Identifying research priorities, Adequate information about the study, Disseminating and applying research findings, Improving access to clinical trials, Informing participants about study results, Assessing patients' experiences, Leading and designing research, Training and information about research objectives, The expert patient.]

Figure 1

How to engage patients in clinical research?

As device trial sponsors rise to this challenge a first critical step is to determine and clearly define the specific objectives for this effort: Why is the company interested in engaging patient input? How will this input be used? At what timepoint in the development program should patients be engaged?

There are multiple answers to these questions that inform compelling reasons to proactively engage patients in the clinical development process for devices, including:

1. **Ensuring device meets unmet need**
2. **Reflecting patient preferences**
3. **Selecting device trial endpoints that matter**
4. **Addressing barriers to trial accrual and retention**
5. **Generating input for regulatory use**
6. **Leveraging insights for post-approval activities**

Ensuring device meets unmet need

The concept of “unmet medical need” (“unmet need”) is an important consideration for medical product developers and regulators. While there is no single definition of this term, it is generally understood to mean a circumstance where there is a lack of effective options to treat certain conditions or groups of patients. In its 2017 report “Unmet Medical Device Needs for Patients with Rare Diseases,” the National Center for Accelerating Translational Sciences (NCATS) and FDA stated that unmet need exists when “there are no approved devices for the treatment or diagnosis of a disease or condition, or when a novel device could provide a clinically meaningful advantage over existing approved devices." FDA regulators have designed a variety of accelerated review processes to evaluate medical products aimed at addressing areas of significant unmet need.

Traditionally, medical professionals have been consulted by medical product developers and regulators to describe unmet need for a specific condition or among a certain patient population. More recently sponsors and regulators have sought to engage patients directly in describing their own needs. Patients can provide detailed and nuanced feedback about ways in which their medical needs are not being met by existing treatment or device options. Engaging directly with patients to understand their condition, disease and symptom burden, as well as the extent to which existing technologies are insufficient or could be improved, can provide important insights to guide the development path for a new device. This is often a foundational objective for patient engagement during product development.

Reflecting patient preferences

One of the most important questions regulators ask in reviewing a medical product is whether its clinical benefit outweighs its risk. Patients can provide valuable input into how they would be willing to make tradeoffs between the potential benefits and risks of a medical device, as well as provide insight into how they would value potential benefits that can impact the design and development of new technology. Patients and their families have a deep and personal understanding of what it is like to live with a disease, and they often have valuable insights on

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how a device could affect their quality of life. Ultimately it is the patients who take the risks to realize the benefits of medical therapies.

The collection and analysis of patient preference information to inform clinical development plans has emerged as an important element of the medical products landscape. Understanding how patients evaluate the potential benefits and risks of new medical products has become a central aspect of regulatory review for new innovations. While the scientific approach to developing patient-preference evidence is generally a scientific (research) pursuit, patient engagement is important for the identification and inclusion of study attributes that matter most to patients.

In 2015 MDIC completed its Framework Report on Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology, providing a review of the potential use and value of this information in medical technology development and regulatory assessments and considerations for those seeking to undertake these studies and leverage their results. In late 2016 the FDA issued a Final Guidance on Factors to Consider Regarding Benefit-Risk in Medical device Product Availability, Compliance and Enforcement Decisions. Additionally, in 2016 the Biotechnology Innovation Organization (BIO) published “Key Considerations in Developing and Integrating Patient Perspectives in Drug Development,” which presented a series of practical considerations for sponsors seeking to decide if, when and how to generate patient preference information as part of their development programs. Although this report was focused on drug development, much of its specific content is relevant across the medical products spectrum.

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In addition to its use in understanding the benefit/risk trade-offs patients may be willing to make, patient preference information developed with the input from active patient engagement can also be used within a product label and to inform effective patient education materials. Importantly, patient preference information is increasingly being used to select clinical trial endpoints that are most relevant to patients and define effect size needed to demonstrate meaningful benefit for a device under study.  

**Case Study Example:**

As described by the FDA, the regulatory review and approval of the obesity device was the first time the agency had relied on quantifiable data relating to patients' views of acceptable benefits and risks associated with use of a device. These data, demonstrating how patients would make the benefit-risk tradeoff, were derived from a study that estimated the maximum mortality risk patients were willing to accept for a certain amount of weight loss, and the minimum amount of weight loss sufficient to undergo the risks of a weight loss device.

The obesity preference study allowed for systemic quantification of tradeoffs patients would be willing to make among benefits, harms, and other features of weight-loss devices. While the study was designed to provide scientific data on patient preferences to inform clinical trial design for obesity devices and it ultimately resulted in data used to inform FDA's regulatory decision-making.


An oft-cited case example of this was the Enteromedics case in 2015 when the FDA used information from a study on patients' preferences while making its regulatory decision to approve a device to treat obesity.

**III. Selecting device trial endpoints that matter**

Patient input during the trial design process can help sponsors better define the outcomes they are seeking to deliver with their novel products. By understanding what outcomes are most important to patients as they set up their studies, sponsors can ultimately develop data that will demonstrate impact that matters for the target population and will be meaningful during regulatory review. While informing endpoint selection is an important potential objective for patient engagement in device trials, sponsors should also ensure that endpoints can be directly impacted by the device during the trial period, clinically significant and statistically significant.

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In addition to endpoints that are measured and reported by investigators conducting clinical investigations, the FDA has also encouraged the use of Patient-Reported Outcomes (PROs) as primary and secondary endpoints in medical device studies as part of its commitment to increasing its use and transparency of patient input as evidence in its decision-making. This area of regulatory science and product development remains dynamic and continues to evolve. It can be useful to engage patients in assessing the relevance and ease-of-use of existing PRO instruments, which may not always capture the outcomes of most importance to patients.

**Case Study Example:**

In a study of a nipple reconstruction device in post-mastectomy patients, the primary endpoint was maintenance of nipple projection length over time, likely chosen to facilitate comparison with other similar devices that have reported that metric. As a secondary endpoint, patient satisfaction questionnaires were collected.

The endpoints are listed in the clinicaltrials.gov entry:


Ultimately, the study failed its projection length endpoint (maintaining 50% of its initial length over the course of 12 months). However, the patient satisfaction showed 93% were Pleased or Very Pleased with the outcome and 98% would recommend the procedure to other women.

The publication of the study results de-emphasizes the former result, does not distinguish between primary and secondary endpoints, and only mentions the 50% goal briefly in the discussion section. However, the authors note that (aside from safety) patient satisfaction should be the most important outcome in such a procedure. If they had sought patient input during the design phase of the clinical trial, perhaps they would have learned which endpoints were of most concern and discussed those possible endpoints with the FDA prior to conducting the study.


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34 [https://www.fda.gov/media/109626/download](https://www.fda.gov/media/109626/download)
37 Basu-Roy, U. et.al. Learning from Patients: Reflections on Use of Patient Reported Outcomes in Lung Cancer Clinical Trials. *Journal of Thoracic Oncology*. 2018. [https://static1.squarespace.com/static/54f375dce4b09ea9b4b1b047/t/5bd65f43b208fc08df428750/1540775747843/PRO+Article.pdf](https://static1.squarespace.com/static/54f375dce4b09ea9b4b1b047/t/5bd65f43b208fc08df428750/1540775747843/PRO+Article.pdf)
IV. Addressing barriers to device trial accrual and retention

Device trials in the United States face significant challenges in enrolling the patients needed to complete evaluation of the new products. The FDA’s Patient Engagement Advisory Committee (PEAC) meeting in 2017 considered data indicating that nearly half of all US device trials do not meet their enrollment targets. There are multiple reasons for this problem, many of which are related to the design of the study. Given the many areas of unmet need for patients with a range of medical conditions, diseases and disabilities as well as the financial costs to sponsors caused by delays in product development, there is urgency to improve in this area. Engaging and implementing patient feedback on the design of clinical studies can help sponsors maximize opportunities for successful trial recruitment and accrual.

There could be a variety of reasons why a patient will be interested in participating in a clinical trial, among them availability of effective standard of care therapy, recommendation from their physician, and understanding of how clinical trials work. Unfortunately, even once a patient has demonstrated willingness to enroll in a trial, there are significant barriers that impact ultimate entry into the trial, participating in data collection activities and staying in the trial to completion. Sponsors can understand and may be able to mitigate these barriers if they understand their impact on patients and are willing to consider refinements to their trial plans.

Included among the most commonly cited barriers are:

I. Restrictive Eligibility Criteria
II. Complex Informed Consent
III. Burdensome Protocols

Restrictive Eligibility Criteria:

One often-cited reason for problems in accrual is overly restrictive inclusion/exclusion criteria in clinical studies. This topic has received much recent attention in the drug development arena, with a series of publications and recent FDA draft guidance in oncology. Device developers may be able to engage more patients in clinical studies by including patients in a discussion about the applicability of exclusion criteria, which,

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38 US Food and Drug Administration (FDA) Patient Engagement Advisory Committee Executive Summary for Patient Engagement in Medical Device Clinical Trials Meeting. https://www.fda.gov/media/108162/download
while potentially necessary to remove potential confounders to the impact of the intervention, may be unnecessarily restricting access to trials by patients who otherwise are willing to participate. Device trial sponsors can leverage patient input in evaluating routine or templated exclusions in device trials that may be outdated or irrelevant to studies of novel technology. In addition to facilitating trial recruitment, this effort can also have the benefit of producing data from the trial that are more applicable to a broader population of patients.  

**Complex Informed Consent Procedures**

The process for meeting regulatory and ethical requirements for gaining consent from research study participants has become a cumbersome and daunting one for sponsors, investigators and patients. While borne of noble intentions, the complexity of this component of clinical research has become a barrier to trial recruitment and has also been blamed for frequent confusion among patients about the true risks associated with study participation. Engaging patients to review informed consent materials and approaches for conducting the consent process (e.g. using plain language, translated materials, e-consent tools and multi-media platforms) can provide sponsors with valuable insights about how best to present the specific elements and potential risks of their studies.  

**Burdensome Protocols**

Similarly, trial protocols, would benefit from review and feedback from patients. Increasingly clinical study protocols rely on significant patient monitoring, which can place extensive demands on patients, in terms of time, travel, physical demands, or ability to communicate about their condition. Better understanding of the impact of these demands and the extent to which they create undue burden on study participants (and thereby pose a disincentive to enrollment or retention within the trial) could help sponsors identify ways to refine their protocols without compromising the integrity of the trial. Asking patients to review draft study documents, including the protocol, can highlight areas where adjustment can and should be made. This effort is often described as patient-centric trial design and can be especially impactful in studies involving patients with rare medical conditions, significant issues with mobility or stamina, or other hard-to-engage populations.  

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41 US Food and Drug Administration (FDA) Patient Engagement Advisory Committee Executive Summary for Patient Engagement in Medical Device Clinical Trials Meeting. https://www.fda.gov/media/108162/download  
V. Generating input for regulatory use

Regulators at the FDA have clearly stated their interest in incorporating patient input into their review process for evaluating devices, providing Guidance to industry and other stakeholders and continuing to evolve Agency efforts to encourage the field to advance this work. In addition to patient preference data relating to how patients might make trade-offs between potential benefits of a new technology and potential risks, sponsors can leverage patient insights throughout their clinical development programs to develop information about their patient population’s views on unmet need, burden of living with the specific medical condition, and level of satisfaction with current medical product options/standard of care. This information can all be used to bolster regulatory submissions and other regulatory engagement.


46 “The U.S. Food and Drug Administration (FDA or the Agency) values the experience and perspectives of patients. The Agency understands that patients and care-partners who live with a disease or condition on a daily basis and utilize devices in their care may have developed their own insights into and perspectives on the benefits and risks of devices reviewed under the premarket approval, humanitarian device exemption (HDE), or de novo classification pathway. FDA believes that patients can and should bring their own experiences to bear in helping the Agency evaluate the benefit-risk profile of certain devices. This kind of input can be important to consider during FDA’s decision making for these devices. . . FDA aims to provide a systematic way to ensure that patients are represented, and patient perspectives are considered in the decision-making process.” https://www.fda.gov/media/92593/download
VI. **Leveraging insights for post-approval activities**

Once a new medical product has been approved for commercial use, sponsors continue to need to understand the views of the relevant patient population. While marketing designed to enhance awareness of the new product and promote its use can be developed using post development market-research, these efforts can be informed and enhanced by leveraging patient insights gleaned during the clinical research phase. Additionally, patient input can help define opportunities for best ways to communicate the impact of the new product, while explaining its potential benefits and risks. Finally, patient insights can be extremely useful in activities aimed at educating payors about the value of the new product to the patient population\(^\text{47}\).

**Building Organizational Capacity:**

Once a sponsor has clearly defined objectives for gaining patient insights, it is critical to evaluate and, where necessary, build the organization’s capacity and readiness to successfully engage and implement patient input for the device development program.

Among the important elements to think about are:

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I. Securing internal support

Done correctly, patient engagement in medical product development is neither superficial nor episodic. Rather, the most successful efforts to leverage patient insights are those that recognize the value of this work and have embedded it into the corporate culture. Ideally, this commitment to patient engagement is held by company leaders and incentivized throughout the workforce. Securing this type of leadership support, may require concentrated effort to demonstrate the importance of patient engagement activities, pointing to FDA’s clear recommendation for patient input and increasing examples of return on investment in the form of streamlined clinical development programs that offer fewer study protocol amendments, enhanced accrual timelines and improved retention rates.  

It is also important to have engagement with colleagues from a variety of disciplines within the company, to support a successful outreach strategy that will yield useful patient input. Increasingly, companies are staffing a patient advocacy or patient engagement function within their ranks, identifying point people to lead these efforts. Working with clinical development study teams, patient advocacy colleagues can help to identify appropriate partners within patient advocacy organizations and among the patient community. Additionally, medical affairs, commercial and policy colleagues can also play important roles in and benefit from these activities.

II. Accessing needed resources (expert support, funding)

Just as any prioritized activity must be appropriately resourced, successful patient engagement requires planning and appropriate budget support. Although this work is generally not costly when compared to other aspects of a medical product development program, there are costs associated with developing appropriate patient advocacy relationships, identifying and accessing expert patients/patient advisors and hiring


outside expertise (as needed) to help plan and execute events designed to bring patients together to engage their input.  

III. Conducting training

Although gathering patient input into medical product development is becoming much more common, it is still a relatively new concept and many people who work in device companies may not have the needed skills to accomplish this work effectively. Working directly with patients and patient advocacy organizations requires a level of understanding and expertise that must be learned. There are myriad resources – some that can be borrowed from the drug development arena – as well as external consultants that can be used to ensure that all colleagues involved in these activities are appropriately trained.  

IV. Engaging legal and compliance

Conduct of clinical trials is subject to a host of legal, regulatory and ethical guidelines. It is crucial to ensure that any patient engagement activities are compliant with these elements, as well as and additional company policies. It is advisable to begin this work by developing principles for patient engagement in clinical research for the company. Prior to finalizing any plans, communications, materials or outreach activities, it is critical to consult legal and compliance experts within the company to ensure understanding of how engagement efforts impact upon those requirements.  

Engagement Planning:

In addition to ensuring that all foundational elements for an engagement program are in place, it is important to develop a detailed clinical trial patient engagement plan. There are multiple approaches for engaging patient input that have been successfully employed by product developers. While much of the experience with these activities has occurred in the drug development arena, there are opportunities for leverage in the device space.  

Sponsors seeking to pursue this work should take the time to develop an engagement strategy designed for success. This strategy should clearly lay out the objectives of each effort, a detailed budget, realistic timelines, specific tactical steps, including identification and  

engagement of collaborators where appropriate (e.g. patient advocacy organizations),
measurement of critical success factors, a pragmatic assessment of risks associated with this
activity, and a workable plan for implementation.

In its 2017 Considerations Guide\textsuperscript{\textdegree}, DIA provided the following useful summary graphic to
visualize these key elements of an engagement strategy:

Another useful framework for planning patient engagement in clinical studies was developed in
2015 by M-CERSI at the University of Maryland\textsuperscript{\textdegree}:

\textsuperscript{\textdegree}Drug Information Agency (DIA) Patient Engagement Resources.
https://www.diaglobal.org/en/resources/areas-of-interest/patient-engagement. Figure used here with
permission.

https://www.pharmacy.umaryland.edu/centers/cersievents/patient-focused-drug-development/deliverables.html. Figure used here with permission from the author.
Tactics:

Patient engagement in clinical research is best viewed as a continuum that occurs in different ways, for different purposes, across the lifecycle of the product development path. A good rule of thumb to guide this work is ‘engage early and engage often.’ Although the details of each engagement plan (with whom, when, how etc.) will be tailored to the specific development and clinical research program, there are multiple baseline tactics that should be evaluated along the way.

Among the most important tactics to consider are:

I. Identifying representative patients
   1. Working with advocacy organizations

II. Defining patient role

III. Building trust relationships

IV. Evaluating multiple types of activities

V. Contracting and compliance

VI. Compensation

VII. Transparency/Communication

VIII. Implementing patient input

Identifying representative patients

Finding the right patients to provide input to a medical product development program is critical to ensuring that the patient voice provided is relevant to the population that will access the product once it is approved.

A key stakeholder community in today’s medical product innovation landscape is the patient advocacy organization (sometimes referred to as a patient group or other similar terms). These typically non-profit organizations have a variety of missions to serve their constituencies. Some are disease (or even sub-type of disease) focused, while others have defined their areas of interest by different categories (e.g. therapeutic approach, prevention vs. research vs. public policy, rare diseases, pediatrics etc.). In general, within a disease area, there may be one or several patient advocacy organizations that lead the space and it is important for sponsors to assess the landscape in determining which groups would make the most appropriate partners based on the engagement objectives for the development program. A proposed framework for evaluating patient group expertise and assets was developed by CTTI and is shown here as an example:

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Patient groups generally understand the needs and interests of their communities, often with significant direct connections with large numbers of patients and caregivers, and they frequently have highly sophisticated key opinion leader (clinician) networks. Patient advocacy organization leaders can directly assist sponsors in thinking through issues relating to their clinical development program, as well as help identify, engage and even train patients to provide input to the sponsor through the process.

It is advisable to engage with one or more patient advocacy organization early in the device development process to build a productive working relationship and provide the foundation for collaboration in engaging patient input in the clinical trial. Selecting the most appropriate partner(s), developing a trust relationship, and putting in place the right expectations and compliance guardrails are key steps in this process. Sponsors should review and consider the

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2015 CTTI Recommendations for Effective Engagement with Patient Groups around Clinical Trials as they approach these efforts.  

It should be noted that patient advocacy groups are not always the only or even the best source of engagement within a specific disease area, and sponsors should carefully evaluate the landscape within the community to understand any unique considerations. If possible, sponsors can also reach out to find individual “expert patients” that may not be affiliated with a specific patient organization.

There is often significant heterogeneity within patient populations, with distinctions across many domains like demographics, socioeconomic status, disease sub-type, phase of disease/disease severity, and co-morbidities. As a result, there can be many different voices within a disease/medical condition community, and it can be difficult to ensure that the insights derived from the limited number of patients engaged in a clinical development program are representative of the target population. Determining what type of voices are most relevant to a sponsor’s objectives for patient engagement is an important step to ensuring the input received is useful.

A proposed rubric for considering these differing types of patient representatives was proposed by DIA in its 2017 Considerations Guide and is shown here as an example:

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63 Drug Information Agency (DIA) Patient Engagement Resources. [https://www.diaglobal.org/en/resources/areas-of-interest/patient-engagement](https://www.diaglobal.org/en/resources/areas-of-interest/patient-engagement). Figure used here with permission.
In its 2019 draft Guidance on Patient Engagement for designing and conducting medical device clinical investigations, FDA recommended that sponsors identify patient advisors who can undertake a clearly defined role in the planning process for the study.\(^{64}\)

Knowing which type of patient voice is most relevant to a development program can be challenging and is certainly not an “exact science.” Although there is no set formula for how to approach this work, product developers seeking patient input for their clinical studies should be aware of the variations in patient experience and related input, and should aim to evaluate the extent to which the insights they receive are representative for the population under study. This concept of “representativeness” within a patient sample is well-known within the clinical development arena (as clinical trials often seek statistical representativeness).\(^{65}\) However,

\(^{64}\) US Food and Drug Administration (FDA), Patient Engagement in the Design and Conduct of Medical Device Clinical: Draft Guidance for Industry. September 2019. [https://www.fda.gov/media/130917/download](https://www.fda.gov/media/130917/download)

\(^{65}\) A consensus definition of statistical representativeness within a device clinical study states: “A study measuring a sample of adequate size to ensure that the study results can be generalized to the population of interest – may be
there are differing considerations – and unique challenges – associated with seeking “representativeness” for the purpose of engaging patient input in the design of a study, endpoints, or understanding patient priorities when it comes to evaluating benefits and risks.

In 2017, the NHC issued its Roadmap and Rubric for Tackling Representativeness which defined “representativeness” in the context of patient engagement as “a sufficient number of and types of people are included in the engagement activity to ensure that those engaged can speak on behalf of the target population. It refers to “who” and “how many” individuals to include in an interaction in order to, as closely as possible, engage with individuals that represent the broader, target patient population.” The NHC Rubric developed a roadmap for achieving representativeness (including the likely need for training for all stakeholders, and especially individual patients, to ensure that insights gained through the engagement activity reflect as broad a swath of the target patient population (including demographic diversity) as possible).  

Shown here is a useful graphic representation developed by NHC to demonstrate how these concepts can work in practice:

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Multiple organizations, including the Patient Centered Outcomes Research Institute (PCORI) and the National Organization for Rare Disorders (NORD) offer training for study sponsors conducting studies and for patients seeking to engage as “expert patients” or “patient advisors” in clinical research studies.

https://www.pcori.org/research-results/2015/pcor-training-program-rare-disease-patient-advocates

https://rarediseases.org/changing-landscape-rare-disease-research/


Published November 2017. Accessed August 14, 2019. Figure used here with permission.
Defining patient role

Successful engagement with patients (and, where appropriate, caregivers) within a clinical development program requires a clear definition of what the patient’s role will be. There are multiple ways to involve patients, from providing them a proactive, governance-type of “seat at the table” with the study team, to engaging them as advisors, to offering them a more reactive role.

The University of Maryland M-CERSI published a useful rubric\(^68\) for thinking about the type of partnership that would be appropriate for sponsors to pursue with patients within clinical research programs:

<table>
<thead>
<tr>
<th>Patient Role</th>
<th>Examples</th>
<th>Engagement Level</th>
</tr>
</thead>
</table>
| 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             |

FDA has issued draft Guidance on this topic.\(^69\)

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Figure used here with permission from the author.

Building trust relationships

A successful patient engagement effort requires a relationship-based approach. Sponsors should take the time and make the effort to build relationships with patient groups and individual patients that are based on shared commitment to the effort, clear expectations, regular communications and a common language about the project. Avoiding the perception that engagement activities are tokenism and are just being done to “check a box” by ensuring that all parties feel respected and able to contribute within the process is a key component of making this process meaningful.  

There are multiple examples of principles for interaction that can underpin patient engagement. Device trial sponsors are encouraged to review these examples and others to develop their own set of guiding principles for approaching patient engagement within their clinical development programs.

One example, implemented by pharmaceutical company UCB, relies on its “STAR” principles. The STAR approach as published is shown here:

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Pushparajah, DS. Making Patient Engagement a Reality. *Patient*. 2017. doi: 10.1007/s40271-017-0264-6. Figure used here with permission from the author.
Another approach to guiding principles was published by the Duke Clinical Research Institute (DCRI) in 2018\textsuperscript{72}:

![Table 3. DCRI Core Principles for Patient Engagement](image)

A third set of recommendations for good vs. poor practice for sponsors is provided by the National Health Council\textsuperscript{73}:

\textsuperscript{72} Duke Clinical Research Institute (DCRI) Stakeholder Engagement Principles. [https://dcri.org/stakeholder-engagement/](https://dcri.org/stakeholder-engagement/). Figure used here with permission.

Evaluating multiple types of activities

There are multiple types of patient engagement activities that can be employed to generate patient insights within a clinical development program. Depending on the objectives for engagement, sponsors may pursue individual interviews with patient group leaders or expert patients, conduct focus groups with a limited number of patients, or surveys to a larger cohort of patients.

Each of these transactional activities can be supported by a sophisticated use of social media platforms (e.g. posting to closed Facebook groups and discussion boards/chat rooms moderated by patient groups, leveraging Twitter using hashtags/keyword etc.). A more passive approach that is being used increasingly has been termed “social listening,” and envisions the opportunity for sponsors to “listen in” to patient discussions to gain insights that can inform medical product development.  

On the other end of the spectrum, Patient Advisory Boards (PABs) made up of expert patients can be convened by sponsors for a one-time engagement or to serve in an ongoing capacity throughout the development program. In 2017, the Center for Information and Study on Clinical Research Participation (CISCRP) published Insights and Best Practices for Planning and

74 Inspire. Social Listening to Understand the Unmet Needs of Patients. https://corp.inspire.com/blog/social-listening/
Implementing Patient Advisory Boards\textsuperscript{75}, noting that “the practice of systematically soliciting input directly from patients on protocol designs and on other clinical research–specific support areas is still a relatively foreign concept to many sponsor organizations.” Some pharmaceutical sponsors have undertaken labor intensive “study simulations” to gauge the extent to which planned study protocols may be acceptable to patients and create the opportunity to modify trial designs before protocols are finalized.\textsuperscript{76}

Noting that the “development and validation of partnership models to engage patients in the design and governance of clinical research programs is still in its infancy, and approaches that can ensure meaningful and effective patient participation in research are needed,” DCRI published a review of various models for patient engagement in clinical research, citing examples of patients as advisory board members, steering committee members or co-investigators.

**Contracting and compliance**

Whether engaging with patient advocacy organizations or individual patients, sponsors should ensure that the aspects of the engagement are clearly outlined and codified through appropriate contracts. It is especially important to spell out roles, responsibilities and expectations for the sponsor and the patient/patient group representative. In its recommendations for trial sponsors, CTTI encouraged establishment of rules of engagement that would define what type of contracts would be needed, including non-disclosure agreements (NDAs) and contractual terms that address issues of privacy, kickbacks, promotion and actual or perceived of conflict of interest.\textsuperscript{77}

Since industry contracts are often dense and complex, thereby creating potential barriers to working with patient organizations and individual patients, the NHC is developing contract templates to support opportunities for patient engagement in clinical development activities.\textsuperscript{78} Additional tools to advance reasonable (and more streamlined) agreements between sponsors and patient advocates (albeit with a European focus) have been created by Patient Focused Medicines Development (PFMD).\textsuperscript{79}


\textsuperscript{76} National Academies of Science (NAS) Advancing the Science of Patient Input in Medical product R&D Workshop. \url{http://www.nationalacademies.org/hmd/Activities/Research/DrugForum/2018-MAY-09.aspx}

\textsuperscript{77} Clinical Trials Transformation Initiative (CTTI) Recommendations on Engaging Patient groups Around Clinical Trials. \url{https://www.ctti-clinicaltrials.org/files/pgctrecs.pdf}


Compensation (Fair Market Value [FMV])

Industry sponsors are generally comfortable engaging expert advice from clinicians throughout their development programs, with a standardized approach to contracting and compensation in consideration of the time and expertise provided. There is less experience within sponsor companies for how to work with patient advocacy organizations and individual patients in similar context. There has been uncertainty and concern about if and how best to compensate groups and individuals for providing patient insights to support clinical development activities. Sponsors need to appropriately value the expertise that patients and advocacy organization representatives are providing in this context and provide a fair market value level of compensation.

To help identify best practice approaches in this category, in 2015 Patient Centered Outcomes Research Institute (PCORI) developed the following compensation rubric based on differing levels of engagement.  

Table 1. Sample Model Addressing Fair Compensation for Engaged Research Partners: Engagement Spectrum with Examples: An Ideal Moving Toward Greater Collaboration

<table>
<thead>
<tr>
<th>Engagement Activity Levels</th>
<th>I. INFORM</th>
<th>Simply informing</th>
<th>Communicating plans to the patient community</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II. CONSULT</td>
<td>Consulting on decision</td>
<td>Offering opinions, advice, feedback</td>
</tr>
<tr>
<td></td>
<td>III. COLLABORATE</td>
<td>Deciding together</td>
<td>Joint decisions solicited</td>
</tr>
<tr>
<td></td>
<td>IV. STAKEHOLDER DIRECTED</td>
<td>Acting together</td>
<td>Taking actions jointly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Encouraging independent initiatives</td>
<td>Leading to patient/caregiver/organization generated research</td>
</tr>
</tbody>
</table>

Additionally, NHC is producing a Fair Market Value (FMV) calculator that can be customized by individual companies to best meet their needs.

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Transparency/Communication

Ensuring plan for transparency, especially communication with patients throughout the development program is an important component of building and maintaining the patient engagement relationship. A seemingly mundane but important set of considerations relates to identifying the most productive format for meeting with/engaging with the patients whose insights are sought (e.g., conducting in person meetings, phone calls, video calls or online/email communication; selecting meeting times that work for patients’ schedules etc.).

A frequent lament by patients who have engaged with clinical trial sponsors (and participated as subjects in trials) is that they rarely see follow up communication from the sponsor about the result of the development process. Sponsors should evaluate and build upon existing data sharing requirements promulgated by ICMJE/WHO and develop proactive communication plans based on appropriate levels of transparency.

Implementing patient input

The process of patient engagement does not end once insights have been gathered and evaluated. Determining where patient input can/should impact sponsor’s development strategies and clinical trial plans is crucial. For example, sponsors should consider how they will address cases where the input received through engagement is not considered relevant or implementable. This may be the case where certain fundamental aspects of the device and related trial requirements cannot be modified. However, in those instances, patient insights can help device trial sponsors refine their patient education materials to best reflect and address patient concerns.

Additionally, it may be necessary to reconcile patient input with involvement from other stakeholders (e.g. clinicians, also FDA), especially if the feedback is not aligned or in conflict. Sponsors should plan for these instances, set expectations up front, and develop plans for addressing such disparities and communicating about their reasoning and decisions in these cases.

Finally, it is crucial for sponsors to understand and leverage opportunities to incorporate patient input in regulatory submissions, including the possibility of including information related to this input in product labeling (e.g. via Patient Reported Outcomes and Patient Preference Information) and post-approval marketing activities.

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82 US Food and Drug Administration (FDA) Patient Preference Information Guidance for Industry [https://www.fda.gov/media/92593/download](https://www.fda.gov/media/92593/download)


Opportunities for Future Work:

As the field of patient engagement in clinical studies for devices evolves and expands, additional efforts could be undertaken to support sponsors, including:

- Development of device company trainings
- Development of case-studies of successful activities in device trials
- Pursuit of projects to capture learnings and measure impact for the field
- Conduct of a re-survey of device manufacturers to compare to baseline results from the 2018 survey.

It is hoped that this report provides a concise set of considerations for medical device developers to evaluate as they pursue patient engagement in their clinical trials and product development activities. Recognizing that this work is complex and made increasingly so by the heterogeneity of the device development landscape, and understanding that no single compilation of information can provide everything a sponsor would need, the resources presented within this report are offered as a foundation from which sponsors can advance their efforts to generate and incorporate patient input into trial design and conduct.