



## Tackling Representativeness: A Roadmap and Rubric



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## Introduction

As stakeholders across the health care ecosystem embrace patient centeredness and integrate the patient voice into their processes, decisions, and organizations, meaningful patient engagement has become increasingly important during drug development, regulatory product review, and value assessment. In practical terms, this means that patients, including caregivers, advocates, and advocacy organizations, are active, respected, and full partners in the endeavor, and their views are incorporated into all processes.

To achieve this full engagement, partnering with patients who are *representative*<sup>1</sup> of the target patient community is important. However, the questions of how to define patient “representativeness” and what constitutes a representative sample are integral to successfully achieving the goals of patient engagement. This can often be neglected by those engaging patients, as a standard definition of “patient representativeness” in patient engagement remains elusive.

Aiming to address this issue and assist stakeholders in achieving patient representativeness in their engagements, the National Health Council (NHC) convened a half-day Roundtable on May 8, 2017, with key stakeholders, including representatives from patient groups, life science companies, value-assessment framework developers, payers, research organizations, and the Food and Drug Administration (FDA). The Roundtable focused on the following goals:

- Build consensus around a common understanding of “representativeness” and how it can be applied to patient engagement in: (1) drug development, (2) regulatory decision-making, and (3) value assessment.
- Develop a set of recommendations on good practices to address the challenges of ensuring patient representativeness in patient engagement.

The Roundtable began with a diverse, multi-stakeholder panel discussing how their organizations define patient representativeness and why it is important to them, followed by a series of two breakout sessions in which small groups discussed a specific topic, and came back together as a full group to discuss their thoughts and recommendations. The two breakout sessions focused on: (1) key concepts and characteristics of representativeness and (2) defining what “good” representativeness looks like.

This white paper captures insights from the Roundtable discussion, providing stakeholders with a set of consensus-based recommendations and considerations on characteristics of “good” patient representativeness and identifies gaps and barriers to be addressed in the future. This white paper is not a technical or methodological guidance on patient representativeness in study sampling, nor is it a checklist for organizations looking to say they achieved good representativeness. Instead, it describes key principles with guiding recommendations.

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<sup>1</sup> Importantly, this white paper focuses exclusively on addressing questions of patient representativeness and purposefully excludes the numerous (very important, but distinct from representativeness) considerations relevant to ensuring the broader goal of meaningful patient engagement. Patient representativeness clearly falls within the considerations for ensuring meaningful patient engagement, but it is only one of many factors that contribute to creating a meaningful engagement effort (and developing a patient-centered approach). For example, the NHC’s 2016 Patient-Centered Value Model Rubric identifies best practices associated with six domains of patient engagement in value assessment, including: (1) the importance of patient partnership, (2) transparency to patients, (3) inclusiveness of patients, (4) diversity of patients/populations, (5) the use of outcomes that patients care about, and (6) the use of patient-centered data sources. Patient representativeness is primarily linked to one of these value domains, diversity of patient/populations, but contributes to all domains in the overall goal of meaningful patient engagement in value assessment.

In addition, the Appendix of this white paper includes a roadmap and rubric to help guide stakeholders to plan for and assess achievement of representativeness for their patient-engagement efforts. The roadmap and rubric are meant to serve as a barometer by which stakeholders, including those engaging patients and the patient communities themselves, can evaluate the representativeness of a given patient engagement activity in order to improve current and future activities. The Appendix also includes a hypothetical case study of a patient engagement activity that would follow the roadmap in order to strive for good representativeness.

## Defining Representativeness in Patient Engagement

The following consensus definition of representativeness in patient engagement emerged from the Roundtable discussion:

**“Representativeness” means 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.**

Representativeness in patient engagement exemplifies, in desired characteristics and proportion, who and how many individuals from the patient community are needed to take part in one or more engagement activities with the goal of capturing patient-provided information as part of a specific patient-centered effort. It articulates the benchmark characteristics desired to engage the right individuals to capture the range of input needed.

Engaging the right individuals also requires acknowledging that diversity exists not only among patients, but also among different patient groups representing the same condition. These patient groups may offer varying perspectives based on the make of their individual members. It should be the goal of efforts to achieve patient representativeness to acknowledge and balance perspectives.

Importantly, an effort to meet “representativeness” targets for an engagement is distinct from statistical sampling in that it focuses more on identifying individuals with the desired characteristics (and considering any limitations to doing that), rather than meeting a known statistical threshold for the number of patient participants. For example, in sampling, a researcher might identify the need to have a 50 percent female sample to exactly mirror the percentage of women in the broader patient community. In contrast, trying to meet a target for representativeness might require that instead of representing the whole patient community, the engagement needs 50 percent of an advisory committee to be patient community representatives that includes people with early disease, late-stage disease, and their caregivers.

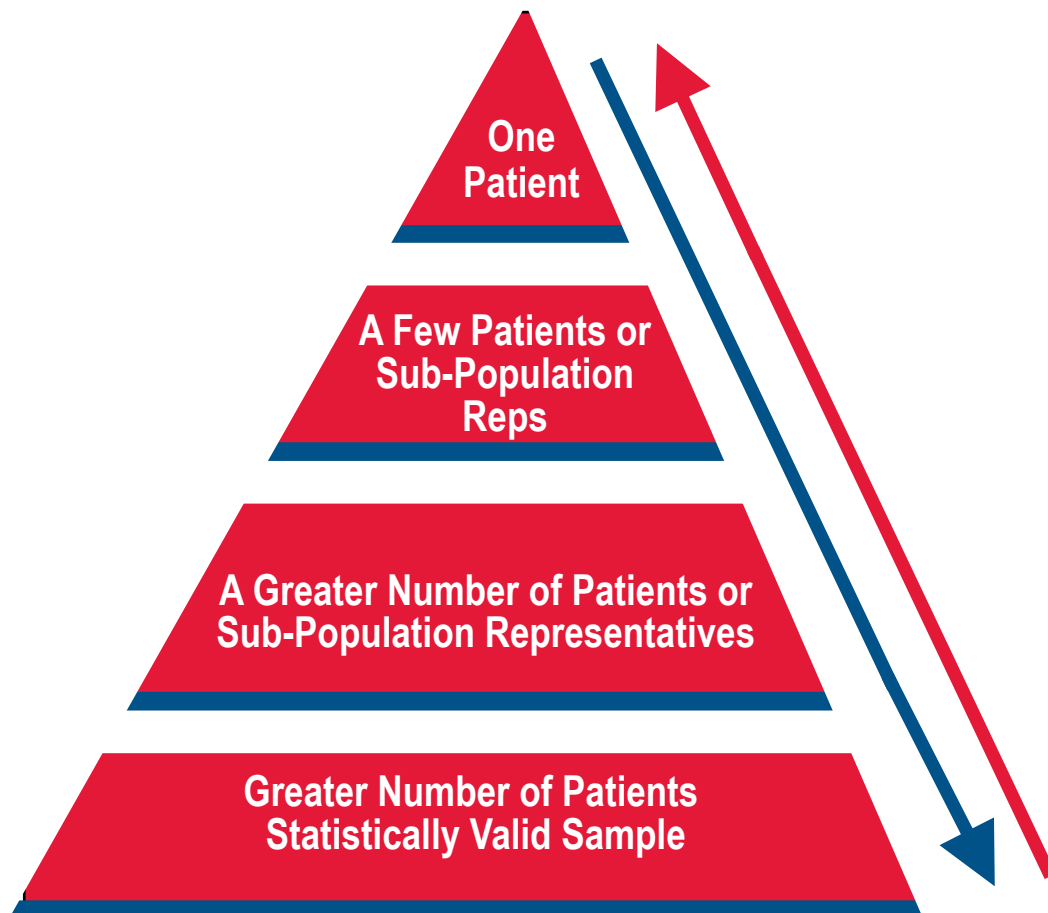
## Context Matters in Achieving Representativeness

One of the main reasons a standard definition of patient representativeness, applicable across all patient-engagement efforts, does not (yet) exist is that context matters. In other words, what a group initiating the interaction (the “sponsor”) is trying to accomplish affects the definition of patient representativeness for that effort.<sup>2</sup>

For example, what “good” patient representativeness looks like when the desired objective is to learn the patient perspective on how easy or difficult it is to follow a care regimen may vary greatly from what “good” patient representativeness looks like when the goal is to determine how patients with cancer define the value of a therapy. As illustrated by Figure 1 below, for some cases, engagement with only one individual patient may be sufficient to achieve representativeness (top of the pyramid), while other engagements may call for individuals from or representing a specific sub-population or numerous sub-populations, and still others (e.g., population-based questions) can require greater numbers of individual patients to represent an entire community or may require a statistically valid sample (bottom of the pyramid).

<sup>2</sup> Tobias Hainz & Daniel Strech (2014) “Which Public to Involve? More Reflection on Collective Agency and Sufficient Representativeness is Needed,” *The American Journal of Bioethics* 14:6, 31–33.

**Figure 1. Representativeness Pyramid**



## Achieving Patient Representativeness through a Process with Minimum Targets

Given the complexity of defining patient representativeness, using numerical measures (e.g., engaging 10 percent of the target population) alone to assess representativeness is typically not enough. Similarly, addressing patient representativeness is met via a checklist of specific requirements or a list of “dos” and “don’ts” is problematic because of the variability across types of interactions. There is simply no “one-size-fits-all” test for whether one has achieved “patient representativeness.”

Instead, addressing representativeness as a process involving a minimum target (or targets) emerged from the Roundtable discussion as the most viable solution. In this model, establishing “good” patient representativeness requires approaching it as an iterative process, using process measurements to assess how close one has gotten to the target measures.

### Patient Representativeness Roadmap and Rubric



The Patient Representativeness Roadmap and Rubric is intended to guide decision-making on representativeness for a given patient engagement activity. The Roadmap and Rubric consist of six guiding principles with examples of what “good” and “poor” processes look like. The six key principles are:

1. *Define* – Clearly define the objective(s) for each engagement effort.
2. *Understand* – Understand as much as possible about the full population and subpopulations and the challenges to reaching them.
3. *Specify* – Develop a description of the minimum target(s) for representativeness for the engagement activity.
4. *Plan* – Develop a plan to achieve the minimum target(s) defined.
5. *Evaluate* – Develop an evaluation plan to assess progress on achieving target(s) or make adjustments if they need to be adjusted based on new information.
6. *Document* – Record how patient representativeness was defined, targeted, achieved, and assessed.

#### **1. Define – Clearly define the objective(s) for each engagement effort.**

The objective, goal, or research question is critical to defining what “good” patient representativeness means for that engagement. Stakeholders should first clearly define their objective(s) for the engagement. The objective guides the entire endeavor from defining the most appropriate engagement method(s) and target patient population(s), as well as informing how to achieve (and how to measure up to) good patient representativeness. Poorly defined objectives can lead to wasted resources when work must be re-done due to use of the wrong method or target patient population (e.g., chosen too few patients with the wrong characteristics to achieve the objective).

The method(s) used to engage patients (e.g., focus groups, surveys, individual discussions, or patient preference studies) should also be considered when defining patient representativeness and a “representative sample” for that engagement activity. For example, conducting patient preference studies may require a greater number of patients to obtain a statistically valid, representative sample than a focus group can accommodate or requires.

## **2. Understand – Understand as much as possible about the full population and subpopulations and the challenges to reaching them.**

Importantly, prior to the engagement, it is important to understand as much about the total patient population of interest to avoid missing critical details (including inadvertently ignoring relevant smaller subpopulations) that can impact how to define a target population. Stakeholders should educate themselves as much as possible, from a variety of sources, about a patient population of interest and avoid assumptions.

Often, researchers and others refer to the case of “hard to reach” populations when they discuss engaging or recruiting subpopulations based on race, ethnicity, income, or geographic location. Often the challenge is not that these individuals are “hard to reach,” (noting that patients resent being referred to in this way), but that ineffective or inappropriate mechanisms for outreach have been employed, or there were no efforts at all. Still, identifying and reaching diverse and underserved populations are key concerns given that not being able to engage them limits representativeness, particularly when the objective is focused on issues specifically relevant to those populations. In some cases, those seeking to engage patients may not know that certain subpopulations exist. As mentioned above, while it may not be possible to identify and contact some patient populations in a specific effort, acknowledging the limitation and the need to address this gap in the future, is important. Ultimately, new ways to identify and reach more diverse and targeted patients are needed.

## **3. Specify – Develop a description of the minimum target(s) for representativeness for the engagement activity.**

Defining the optimal target population – or the patient population that the desired “representative sample” should represent – is key to achieving patient representativeness. Factors influencing the choice of a target population include:

- The total size of the patient population of interest, and the size of the (sub)population that would be impacted by a decision, involved in a topic, or otherwise be relevant.
- The goals and aspirations of the individuals comprising the patient population of interest.
- Characteristics of the individuals comprising the patient population of interest (e.g., age, gender, socioeconomic status, race, patient or caregiver, health literacy, disease state, genetic marker status, preferences, and goals).
- The degree of heterogeneity across the patient population of interest with regard to characteristic(s) of interest.
- Whether caregivers, parents, or other advocates for patients are included in the patient population of interest.

Those engaging with patients should consider all of the factors above to determine the appropriate target population(s) and define (along with engagement objectives) how many and which (i.e., with what combination of characteristics) patients to engage to achieve patient representativeness. In addition, setting the target population will also serve as a baseline to define “good” patient representativeness and to measure performance. For example, a patient population with a low degree of heterogeneity (i.e., variation in characteristic(s) of interest) may require fewer patient representatives to encompass, understand, and reflect the views and priorities of – and thereby achieve representativeness of – the entire patient population.

An important consideration in determining the target is distinguishing between what an individual patient provides (e.g., their personal experiences with disease and treatment) versus what a patient representative might provide (e.g., a patient advocate with who provides their experience, but also data on a range of patient views), both of which have high value. Again this is related to context and objective. If the engagement activity is early data gathering, individual patient experiences are a vital starting point. As data gathering continues, it will include a growing body of evidence from larger numbers of representative patients that will support and expand the information individuals have provided. (See Figure 1.)

#### **4. Plan – Develop a plan to achieve the minimum target(s) defined.**

For each patient engagement effort, clearly defining and developing a plan for achieving the minimum target(s) should be outlined prior to the engagement and with patient input. Stakeholders need to also consider the following engagement factors when developing a plan for achieving patient representativeness:

- Burden on patients (and ways to minimize that burden);
- How ready patients are to contribute in a meaningful way (i.e., “patient readiness”);
- Whether a single patient can be identified to represent a community;
- Power imbalances that might occur during the engagement (e.g., a committee of 20 physician specialists with one patient member) and ways to mitigate imbalances; and
- Responsibilities of the patient representative(s) as well as the patient’s perception of their responsibilities.<sup>3</sup>

Achieving patient representativeness can often prove difficult given practical limits on time, funds, and other resources, including public information. For example, in situations where little information (or only outdated information) about a patient population is available, including more patient perspectives becomes even more important, though they may be difficult to gather. Furthermore, the feasibility of reaching members of a patient population, and the willingness (or lack thereof) of those patients to engage, impact the ability to access and engage members of the target population, thus effecting the ability to achieve representativeness.

Given this reality, it is important that limits on feasibility and resources do not cause stakeholders to avoid trying to achieve patient representativeness altogether. Stakeholders should not “let the perfect be the enemy of the good,” but make every reasonable effort to accurately define patient representativeness for their engagement and to come as close as possible to achieving it.

#### **5. Evaluate – Develop an evaluation plan to assess progress on achieving target(s) or make adjustments based on new information.**

Any plan for achieving patient representativeness should include continual assessment and refinement. Such an iterative and evolving process allows for flexibility and integration of new information and learnings. As in the beginning, patients should be involved in the refining of any plans, definitions, or minimum targets throughout the entire engagement, and their input should be integrated into decision-making. Stakeholders should continue to ask questions, listen and learn, and refine plans to get as close to “optimal” patient representativeness as possible for that engagement (i.e., follow where patient input is leading). This is also represented in Figure 1. The arrows beside the pyramid depict bidirectional feedback to refine processes for patient representativeness (e.g., the blue arrow denotes a process begun by talking with one patient to build awareness of a broader patient community that leads to wider engagement).

<sup>3</sup> Kath Maguire & Nicky Britten (2017) “How can anybody be representative for those kind of people?” Forms of patient representation in health research, and why it is always contestable, *Social Science & Medicine* 183: 62-69.

## **6. Document – Record how patient representativeness was defined, targeted, achieved, and assessed.**

It is important that stakeholders document the processes and outcomes of defining a target(s) and creating achievement and assessment plans, recording their processes of defining, achieving, and assessing patient representativeness for each engagement. This will help in articulating their rationale and ensure processes are understandable to others. Documentation should include any limitations, missing data, challenges, or barriers anticipated or experienced (e.g., individuals or sub-groups that the stakeholder cannot reach). Stakeholders should focus on documenting those gaps and learnings that were not initially planned or expected. It is important that patients are engaged in this work and their perspectives are considered. The organization attempting to engage should try to document the challenges encountered, and efforts made to overcome or mitigate them. Stakeholders can utilize this process to not only identify unexpected gaps, but also to understand why they occurred. This does not need to be an overly extensive or onerous effort. It is simply good practice to document actions and rationale.

### ***Need for Training***

The Roundtable participants also discussed one aspect of representativeness where there is an important gap. A need exists for training all stakeholders on patient representativeness – both patients and those who engage them. This includes education to understand what patient representativeness means and how it can be achieved and assessed as a part of patient engagement, and training to provide skill sets needed by different stakeholders in patient engagement. For example, it may be necessary to establish training for patient readiness, including how a single patient can act effectively as a “patient representative” (i.e., representing a broader community versus speaking to their own experiences). In addition, participants identified a need to train people who are engaging with patients, because they need to know effective engagement methods, including the impact of patient representativeness, and how to define, achieve, assess, and document it in a transparent way.

## **Conclusion**

The NHC’s May 8, 2017 Roundtable brought together key stakeholders from across the health care ecosystem to discuss patient representativeness and reach consensus on considerations for defining, achieving, and assessing representativeness as part of patient engagement efforts. The Roundtable participants considered many issues related to patient representativeness, and this white paper captures the key principles from the discussion.

Participants strongly agreed that a single target for patient representativeness cannot fit every patient engagement situation. Instead, context, including the objective of the engagement, must influence how patient representativeness is defined for any engagement activity. Moreover, the variability of patient interactions requires that stakeholders address representativeness as a process with a minimum target, rather than a fixed standard.

This work represents an important first step in advancing the discussion and enhancing stakeholders’ ability to meet a high target of patient representativeness for each patient engagement activity. The NHC, along with other stakeholders, will continue to contribute to this discussion and develop tools to advance the understanding and achievement of patient representativeness in engagements across health care contexts, including in drug development, product review, and value assessment. While greater representativeness improves any engagement effort, the quality of the engagement interaction is often more important. A focus on the quantity and representativeness of patients involved must never detract from the quality of the interaction.



## Appendix A

### Patient Representativeness Roadmap and Rubric

*To guide decision-making on representativeness for each patient-engagement activity, establish the following, prior to initiation of engagement and with patient input:*

	Guiding Questions to Consider	Good Process	Poor Process
<b>1. Define – Clearly define the objective(s) for each engagement effort.</b>			
	<ul style="list-style-type: none"> <li>What is the objective(s) of the engagement activity?</li> <li>What information or learning is desired from the activity?</li> <li>Have patients been involved in crafting the objective?</li> </ul>	<ul style="list-style-type: none"> <li>Objective for engagement is clearly articulated with patient input and guidance.</li> <li>The process to define engagement objective is documented and transparent.</li> </ul>	<ul style="list-style-type: none"> <li>Objective for engagement is unclear or not articulated at all.</li> <li>Processes to define the objective are not documented or transparent.</li> <li>Effort appears to be a “fishing expedition” to gather data to support an activity that has already transpired.</li> </ul>
<b>2. Understand – Understand as much as possible about the full population and subpopulations and challenges to reaching them.</b>			
	<ul style="list-style-type: none"> <li>What is known about the full patient population of interest?</li> <li>What sources of information about this population are available?</li> <li>Are the sources outdated or inaccurate?</li> <li>Have discussions occurred with patient(s)/patient group to best understand the</li> </ul>	<ul style="list-style-type: none"> <li>All publicly available sources of information about the population are identified through literature review, opinions from specialists, and patient input.</li> <li>Patients are engaged in helping describe the full patient population, subgroups, and anticipated challenges and burdens.</li> <li>Issues with feasibility or</li> </ul>	<ul style="list-style-type: none"> <li>There is a poor understanding of the full and target populations.</li> <li>Sources of information on the full population were not tapped or were ignored.</li> <li>Patients were not consulted when trying to understand the full and target populations</li> <li>Feasibility for reaching the target population was not considered.</li> <li>Challenges were poorly understood and not considered.</li> </ul>

	<p>full population?</p> <ul style="list-style-type: none"> <li>• Is the target patient population for the engagement activity the full population or a subpopulation?</li> <li>• What is the degree of heterogeneity in the full or subpopulation?</li> <li>• Have you considered viewpoints from a diverse number of patient groups or patients? How will you balance perspectives?</li> <li>• Is the target population easily identifiable?</li> <li>• Are there any anticipated challenges to reaching the target population?</li> </ul>	<p>lack of resources to get to the target are considered.</p> <ul style="list-style-type: none"> <li>• The process to define the target population is documented and transparent.</li> </ul>	
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<p><b>3. Specify – Develop a description of the minimum target(s) for representativeness for the engagement activity.</b></p>			
	<ul style="list-style-type: none"> <li>• Has patient input been incorporated to define the minimum representativeness target(s)?</li> <li>• What is the minimum target(s) of patient representativeness for this interaction?</li> <li>• What are the target patient characteristics sought?</li> <li>• What are the target patient numbers sought?</li> <li>• Are the patients desired for</li> </ul>	<ul style="list-style-type: none"> <li>• Clearly defined minimum target(s) for patient representativeness are established including the specific patient characteristics sought.</li> <li>• Patients are ready to engage.</li> </ul>	<ul style="list-style-type: none"> <li>• No targets were established in terms of patient characteristics or numbers.</li> <li>• Targets were established but the rationale for them is unclear.</li> <li>• Processes are unclear.</li> </ul>

	the engagement ready to contribute in a meaningful way?		
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<b>4. Plan – Develop a plan to achieve the minimum target(s) defined.</b>			
	<ul style="list-style-type: none"> <li>• Have patients contributed to defining plans to achieve and assess patient representativeness target(s)?</li> <li>• Do the engagement plans articulate the patient responsibilities?</li> <li>• Are there power imbalances inherent in the plans? Are there ways to mitigate these?</li> <li>• What burdens to patient exist with this target? Are there plans to minimize burdens?</li> <li>• Are your plans defensible?</li> </ul>	<ul style="list-style-type: none"> <li>• The plan for achieving representativeness includes appropriate and feasible efforts not just those that are convenient.</li> <li>• Patient responsibilities are clearly articulated.</li> <li>• The plans and processes are transparently documented with rationale.</li> </ul>	<ul style="list-style-type: none"> <li>• There is no plan to meet representativeness targets.</li> <li>• Plans are poorly described or not feasible.</li> <li>• No rationale for plans are described.</li> </ul>

<b>5. Evaluate – Develop an evaluation plan to assess progress on achieving target(s) or if they need to be adjusted based on new information.</b>			
	<ul style="list-style-type: none"> <li>• Has a reasonable effort been made to achieve patient representativeness?</li> <li>• Have patient representativeness target(s) been reached (or as close as possible)?</li> <li>• How will target(s) be refined throughout the engagement effort?</li> <li>• At what points in the</li> </ul>	<ul style="list-style-type: none"> <li>• Every reasonable effort is made to achieve patient representativeness targets in the plan.</li> <li>• A plan is created to assess patient representativeness throughout the engagement.</li> <li>• As part of the assessment, plans to meet the target(s) are refined throughout the engagement effort.</li> </ul>	<ul style="list-style-type: none"> <li>• No assessment plan exists, no evaluation is conducted.</li> <li>• Targets are not met but it unclear why.</li> <li>• Challenges were encountered, but limitations and learnings are not documented or shared.</li> </ul>

	<p>engagement efforts is patient representativeness assessed? Is that often enough?</p> <ul style="list-style-type: none"> <li>• Are engagement plans flexible enough to incorporate new information throughout the project?</li> <li>• What is the rationale for what actions were or were not taken to ensure representativeness?</li> <li>• What insights are documented on barriers encountered?</li> </ul>	<ul style="list-style-type: none"> <li>• Issues and challenges are addressed as best possible and not avoided.</li> <li>• When target patient representativeness could not be achieved, there is clear documentation of limitations, challenges, and barriers.</li> <li>• All work is transparently documented to share learnings.</li> </ul>	
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<b>6. Document – Record how patient representativeness was defined, targeted, achieved, and assessed.</b>			
	<ul style="list-style-type: none"> <li>• Does complete documentation exist on the process and rationale for why decisions were made?</li> <li>• Have the plans considered limitations, missing data, challenges, and barriers, innovative techniques, and explained them in the documentation?</li> </ul>	<ul style="list-style-type: none"> <li>• All processes and decisions (including rationale) to create plans, revise plans are transparently documented.</li> <li>• Limitations, missing data, challenges, and barriers are documented and explained.</li> <li>• The documentation uses clear and easily understandable language.</li> <li>• Key learnings and best practices are being shared publically.</li> </ul>	<ul style="list-style-type: none"> <li>• Documentation does not exist or is incomplete, unclear, and/or not transparent.</li> <li>• Learnings are not shared.</li> </ul>

## Appendix B. Case Examples

The Patient Representativeness Roadmap and Rubric is intended to guide decision-making on representativeness for a given patient engagement activity. The Roadmap and Rubric consist of six guiding principles with examples of what “good” and “poor” processes look like.

The six key principles are:

1. *Define* – Clearly define the objective(s) for each engagement effort.
2. *Understand* – Understand as much as possible about the full population and subpopulations and challenges to reaching them.
3. *Specify* – Develop a description of the minimum target(s) for representativeness for the engagement activity.
4. *Plan* – Develop a plan to achieve the minimum target(s) defined.
5. *Evaluate* – Develop an evaluation plan to assess progress on achieving target(s) or if they need to be adjusted based on new information.
6. *Document* – Record how patient representativeness was defined, targeted, achieved, and assessed.

The following four case examples are organized to demonstrate alignment with each of the six key principles of the Roadmap and Rubric.

Key Principles	Case Study #1	Case Study #2	Case Study #3	Case Study #4
<p><b>1. <u>Define</u> engagement activity objective:</b></p>	<ul style="list-style-type: none"> <li>• A biopharmaceutical company wants to engage patients in <b>interviews</b> to understand the impact of a rare disease on patients’ lives.</li> <li>• The company has little experience with the disease or therapeutic area.</li> <li>• This is early-stage engagement, pre-clinical work.</li> </ul>	<ul style="list-style-type: none"> <li>• A biopharmaceutical company wants to engage patients through <b>a survey</b> to understand the impact of different disease symptoms and treatment side effects as they relate to treatment decision making.</li> <li>• This engagement is intended to augment other data obtained through clinical trials and literature review.</li> </ul>	<ul style="list-style-type: none"> <li>• A biopharmaceutical company wants to engage patients through <b>a survey</b> to understand the emerging needs of both people living with a disease and their partners.</li> </ul>	<ul style="list-style-type: none"> <li>• A patient advocacy organization wants to engage its members by developing a <b>leadership council</b> to understand patient perspectives on a variety of issues related to the organization’s disease focus.</li> </ul>

<p><b>2. <u>Understand the full population:</u></b></p>	<ul style="list-style-type: none"> <li>• There are only case reports.</li> <li>• The population is estimated to be approximately 50,000 children in the US.</li> <li>• Two small patient advocacy groups exist. Interviews were conducted with the lead person from each.</li> <li>• One of the patient groups has a publicly accessible blog. Qualitative data was reviewed collaboratively with the patient group.</li> <li>• A clinical specialist was identified by both patient groups as the leading expert.</li> <li>• A local patient, a child, and his family were recruited to be advisors.</li> <li>• It is difficult to have a complete understanding of the full population due to the nature of this rare disease. However, symptoms change over time.</li> <li>• It was recommended the researchers consider population fatigue, impact of the disease on the family and siblings, and difficulty in getting an accurate</li> </ul>	<ul style="list-style-type: none"> <li>• The patient population has known cognitive impairments, which necessitate specific approaches to get meaningful feedback.</li> <li>• Advocacy organization reach is limited to high-functioning and highly motivated patients/ caregivers.</li> <li>• Thus, outreach is needed beyond those patients involved in advocacy organizations to get a full picture of the population.</li> </ul>	<ul style="list-style-type: none"> <li>• The demographic profile of patients has changed over time and by geography, making multinational representation important.</li> <li>• The disease also covers a wide age range.</li> <li>• The survey was developed in collaboration with an external, multinational Steering Committee of patients/ representatives.</li> <li>• A preliminary phase of qualitative research was carried out with 24 patients across four countries to help understand the key areas of focus.</li> <li>• It was decided to concentrate on adults, so the survey was designed for patients 18 years and older.</li> </ul>	<ul style="list-style-type: none"> <li>• The disease of interest has many different forms.</li> <li>• The organization had the goal of engaging people that encompassed the variety of diagnoses and experiences.</li> <li>• Candidates for the Council were “scored” based on criteria created to highlight the array of perspectives ranging from one disease form to another, and to capture greatest likelihood of success in promoting the goals of the council.</li> <li>• After this initial research, discussion and considerable thought the organization arrived at the specific criteria needed.</li> </ul>
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	<p>diagnosis due to lack of clinicians' familiarity with the disease.</p> <ul style="list-style-type: none"> <li>The number or percent of undiagnosed cases is difficult to determine; impacts on minority and under-served populations are not well understood.</li> </ul>			
<p><b>3. Specify target (based on information learned from #2):</b></p>	<ul style="list-style-type: none"> <li>Recruit 10 child/parent dyads for interviews, to get patient and parent perspectives.</li> <li>Be sure to include children with a range of ages from 2 to 12 years, to capture changes over time.</li> <li>Structure interviews to be by telephone (to capture geographic range) and for no more than one half-hour with the child due to fatigue from the illness. Parent interviews can be longer. Multiple interviews with the child, in half-hour, increments may be needed if acceptable to patients and families.</li> <li>Strive for racial and cultural diversity as much as possible in recruitment with the understanding this may be limited.</li> </ul>	<ul style="list-style-type: none"> <li>Recruit patients through a partnership with a community clinic group.</li> <li>The clinic group covers a large geographically and socially-economically diverse, real-world patient population.</li> <li>Strive for racial and cultural diversity as much as possible in recruitment with the understanding this may be limited at this point.</li> </ul>	<ul style="list-style-type: none"> <li>An in-depth quantitative survey was carried out in nine countries.</li> <li>Patient respondents were sought worldwide.</li> <li>A plan was created to gather diversity by geography, disease history, sexual orientation, gender, co-morbidities and age.</li> </ul>	<ul style="list-style-type: none"> <li>Twelve Council members were identified with a pre-specified range of diversity in perspectives (to encompass different forms of the disease), commitment to the disease community and the likelihood of a successful, robust role on the council.</li> </ul>

<p><b>4. <u>Plan for achieving targets:</u></b></p>	<ul style="list-style-type: none"> <li>• A partnership is formed with both patient groups and the leading clinical expert to recruit the patient/parent dyads from both the academic setting, and through both patient groups' websites.</li> <li>• A plan is put into place to capture target characteristics.</li> </ul>	<ul style="list-style-type: none"> <li>• The survey was kept purposely short, to be completed without the assistance of clinic staff.</li> <li>• All patients with the condition and their caregivers were asked to complete the survey with no exclusions.</li> <li>• The survey was co-developed with advocacy partners who helped "test" the instrument with patients to refine test questions, language, length and format. This confirmed that to reach the most diverse patient population the final survey needed to be simple, short and use parallel question formats to meet the cognitive needs of the patient population (e.g., a caregiver questionnaire also developed).</li> </ul>	<ul style="list-style-type: none"> <li>• Participants were recruited in multiple ways, including: working with the Steering Committee members (who supported recruitment via their own connections and networks), collaborating with charities, patient support organizations, non-governmental organizations, disease-related online communities, and promoting the research via social media.</li> </ul>	<ul style="list-style-type: none"> <li>• The twelve top-scoring candidates were placed in a matrix that noted how each person's qualities and characteristics matched up with the key domains.</li> <li>• The organization examined how well the domains were represented by the top-scoring candidates, and then iteratively added and removed candidates until we achieved the desired coverage across the pre-specified criteria was achieved.</li> </ul>
<p><b>5. <u>Evaluate progress:</u></b></p>	<ul style="list-style-type: none"> <li>• It is expected that recruitment will be completed in a one-month period. Interviews should be completed within two weeks of recruitment.</li> </ul>	<ul style="list-style-type: none"> <li>• Due to significant work at the outset to define the research goal, identify limitations of different research methods, and gather input from both patient organizations and individual patients no changes were required.</li> </ul>	<ul style="list-style-type: none"> <li>• When it was noted that the response rate was greater in some countries than others, efforts were made to increase outreach to the patient groups and online support groups in those countries.</li> </ul>	<ul style="list-style-type: none"> <li>• Duplicates (meaning two candidates with identical domain profiles) were re-evaluated for relative strengths and weaknesses. One of was tentatively removed and placed on the standby list.</li> </ul>



	<ul style="list-style-type: none"> <li>• Each week, recruitment and completion status were evaluated. Barriers and challenges encountered were minimal and documented.</li> <li>• No change to the plan was required.</li> </ul>			<ul style="list-style-type: none"> <li>• As gaps were filled, additional duplicates were created; and as duplicates were removed, new gaps opened. The exercise took many rounds before landing on the best slate possible per the criteria.</li> </ul>
<p><b>6. <u>Document</u> each step:</b></p>	<ul style="list-style-type: none"> <li>• All steps and decisions were documented with rationale for each decision.</li> </ul>	<ul style="list-style-type: none"> <li>• All steps and decisions were documented with rationale for each decision.</li> </ul>	<ul style="list-style-type: none"> <li>• All steps and decisions were documented in a report with rationale.</li> <li>• Survey results were posted.</li> <li>• The results have been presented at medical conferences. The data is available on a public website designed to be a quality of life resource for patients.</li> </ul>	<ul style="list-style-type: none"> <li>• All steps and decisions were documented throughout the process with rationale for each decision.</li> <li>• The criteria for selection were publicly announced prior to the call for nominations.</li> </ul>