

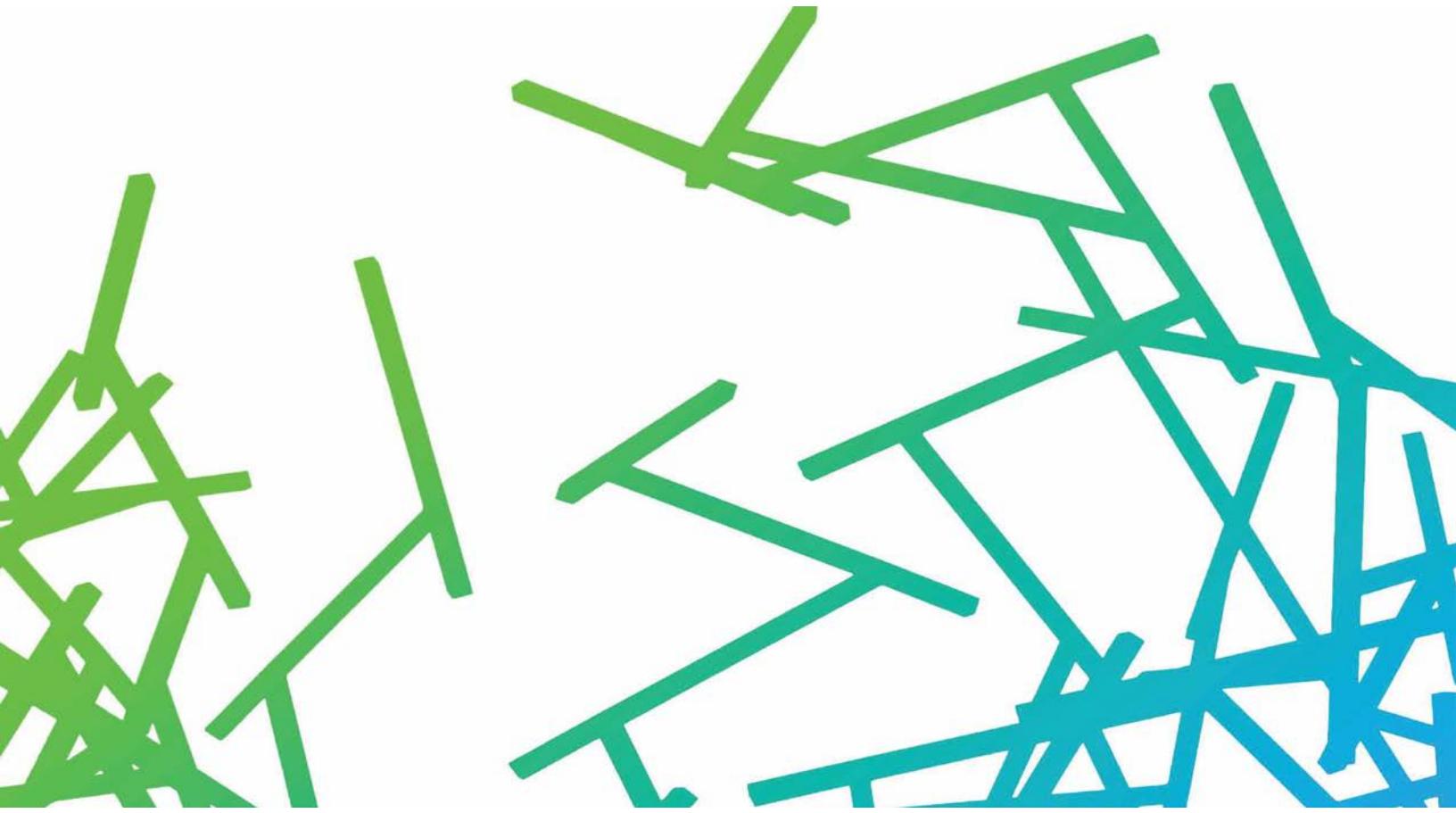
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# Integrating the Patient into the Drug Development Process: Developing FDA Guidance

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December 9, 2015  
Meeting Summary

*Released May 4, 2016*



## EXECUTIVE SUMMARY

Many stakeholders in the health care community have expressed a need for the U.S. Food and Drug Administration (FDA or the Agency) to provide guidance to encourage product sponsors (e.g., biopharmaceutical companies) to engage patients throughout the drug research and development lifecycle, illustrate how this can be achieved, and ensure the information collected is useful to the regulatory review process. Patients, researchers, and product sponsors alike welcome formal guidance from the FDA on how patients can be appropriately and meaningfully engaged.

To move this effort forward, the National Health Council (NHC) and Genetic Alliance (GA) convened a December 9, 2015, meeting with 36 multi-stakeholder participants. The objective of the meeting was to inform the scope and contents of a proposed FDA guidance document intended to guide industry, patient organizations, and other stakeholders in collecting input and information from patients to help inform drug research, development, regulatory review, and post-marketing activities, spanning the entire product lifecycle. The full-day meeting was held in Washington, DC, during which attendees participated in both large group discussions, as well as smaller breakout groups to delve deeper into specific topics and issues.

This paper summarizes key themes and priorities arising from the stakeholder discussions. Key findings on where FDA guidance is needed, in order of priority, include:

1. Gaining alignment and clarity on key terminology
2. Demonstrating that the FDA encourages the collection and use of patient-provided<sup>1</sup> information in drug development
3. Providing clarity for stakeholders on the characteristics of appropriate and inappropriate patient interactions for collecting patient-provided information, with examples provided in the guidance
4. Providing clarity on acceptable methods and presentation of data and analyses for FDA review of patient-provided information
5. Emphasizing that the context in which a particular interaction with a patient occurs (e.g., stage of drug development, goals of the interaction) is key to assessing the appropriateness of the interaction and, as a result, context must be considered when determining methods and approaches to interacting with patients
6. Promoting transparency and communication across all aspects of patient-focused drug development to increase information-sharing and collaboration among patients, stakeholders, and the FDA, including how the FDA interacts and shares collected data with patients and other stakeholders
7. Enhancing clarity in the FDA's approach to evaluating and using patient-provided information in regulatory decision-making and product labeling, with examples of how the data can be used

These findings will be used to inform the development of draft FDA guidance language that will be submitted to the Agency for its consideration. It was suggested by the group that these key themes likely capture more content than what could be included in one guidance document and that multiple draft guidance documents might be appropriate. An outline for an initial draft guidance document, capturing the first three key themes, is attached as Appendix A. An outline of additional topics that stakeholders identified as important, but were not prioritized for the initial guidance document, is attached as Appendix B and should be considered for future draft FDA guidance documents.

## BACKGROUND

The health care community is increasingly recognizing that patient community<sup>2</sup> input during medical product research, development, regulatory approval, and post-marketing activities, spanning the entire product lifecycle, is critical to aligning approved treatments with patient needs to help them achieve their health goals. More than ever, stakeholders are seeking to engage patients before products enter the market to ensure therapies are developed with patient needs and priorities as the focal point.

The U.S. Food and Drug Administration (FDA or the Agency) has played a key role in expanding patient engagement in the pre-approval stages and throughout the product lifecycle. Over the past decade, the FDA has launched a number of initiatives aimed at soliciting patient input to inform medical product reviews. For example, provisions under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) led the Center for Drug Evaluation and Research (CDER) to create its Patient-Focused Drug Development (PFDD) Program.<sup>3</sup> CDER also includes patient representatives alongside technical experts on its advisory committees.<sup>4</sup> These efforts have ushered in a new wave of activities focused on helping FDA product reviewers understand more fully and consider more broadly patient needs in harmony with clinical, safety, and societal factors when making product approval decisions.<sup>5</sup>

Despite these advances, many stakeholders either do not know how or hesitate to fully incorporate patient engagement into their processes and integrate the patient perspective into their decision-making. To better understand the barriers hindering progress on this issue, the National Health Council (NHC) and Genetic Alliance (GA) co-hosted a meeting in March 2015 that brought together a multi-stakeholder group, including the FDA, to identify the barriers.

Participants of the March 2015 meeting identified the lack of guidance from the FDA on patient engagement efforts, in particular how regulations governing pre-approval promotion apply to pre-approval patient engagement to collect patient-provided information, as a fundamental barrier to patient involvement in research and development. Participants indicated that the risk, perceived or real, of violating these regulations may discourage product sponsors from proactively and meaningfully engaging patients in innovative ways and to the fullest extent possible. They agreed that clarity from the FDA could alleviate uncertainty and unpredictability, facilitate meaningful patient engagement, allow sponsors to more accurately estimate the return on investing in patient engagement, and reduce skepticism regarding patient engagement benefits. In addition, stakeholders also welcome FDA guidance regarding how the Agency will evaluate and use submitted patient-provided information.

To build on this momentum, the NHC and GA are spearheading an effort to leverage the collective experience and expertise of the patient and stakeholder communities to draft a proposed guidance document for the FDA's consideration. To inform the scope and content of the proposed FDA guidance, a working meeting was convened focusing on vetting and developing content areas to be included. This summary captures the key themes from this meeting, which was held in December 2015.

## INTRODUCTION

On December 9, 2015, the NHC and GA held a multi-stakeholder, invitational working meeting as an initial step in the process of drafting a proposed FDA guidance on patient engagement in drug<sup>6</sup> research and development. The aim of the meeting was to develop consensus on, describe, and prioritize the content that stakeholders recommend be included in the guidance document(s). The full-day meeting brought together 36 participants, representing multiple stakeholder groups, including patients, product sponsors, payers, and research organizations. See Appendix C for the full list of participants.

The meeting consisted of large group discussions to establish consensus on the general areas that should be covered in the guidance, as well as smaller breakout group sessions allowing stakeholders to deliberate and prioritize key issues within those general areas. Informed by learnings from the March 2015 meeting, this meeting focused on key areas of patient and stakeholder interest, including what constitutes appropriate patient-sponsor interactions, methods, and best practices for collecting and submitting patient-provided information, and how the FDA will evaluate and use patient-provided information submitted by sponsors. Participants were also able to suggest additional key areas for discussion.

Throughout the day, several key themes emerged as high-priority areas for an initial FDA guidance. **Clarity is needed on: (1) definitions for terms; (2) FDA support for patient engagement; (3) methods for patient interactions; (4) methods of data capture, analysis, and presentation; (5) transparency from the FDA to sponsors and other stakeholders and between patients, sponsors, FDA, and other stakeholders; and (6) the importance of context.** In addition to determining what specific topics should be covered in the guidance, themes involving the approach and tone of the guidance were also raised throughout the conversations.

The purpose of this summary is to capture the key themes to inform the development of proposed draft guidance language. While most of the discussions focused specifically on the development and approval of drugs and biologics, the learnings and recommendations may also apply to devices, as well as patient engagement occurring in the post-marketing setting. A working draft outline for the initial FDA guidance document is attached as Appendix A. While discussion was robust during the full-day meeting, this summary is not meant to be an all-inclusive transcript.

Further, the group recognized that the amount of content discussed was likely too extensive for one draft guidance document and that several documents may be required. Thus, the content as prioritized and identified as potential priority areas for a second or subsequent FDA guidance document is captured in Appendix B.

## KEY THEMES TO INFORM GUIDANCE DEVELOPMENT

### Clear Definitions for Terms

Participants called for a common lexicon to facilitate understanding and standardization of conversations on topics related to patient engagement in drug development. Recognizing that current terminology is highly fragmented and that the same term can be used differently among stakeholders or differently around the world, participants expressed how important it is for any guidance to precisely define terms so that stakeholders understand and use a common, standardized language.

Some of the terms that stakeholders noted as needing clear definitions include:

- patient
- patient engagement
- patient-provided or patient-generated information
- patient data
- patient preference
- stated preference
- patient value
- patient centered
- patient reported
- patient-reported outcome
- patient impact
- patient-informed drug development
- patient-generated data
- patient generated

While necessary as a baseline or foundation, definitions will not dictate product sponsor or FDA commitments or actions regarding patient engagement in drug development. While this list is not exhaustive, it represents some of the key terms participants believe should be defined in the guidance. (See Appendix A for other terms included in the draft guidance outline.) As one example, many participants stated that the term “patient” should include family caregivers, patient advocates, and family members, as well as individuals diagnosed with a particular condition. In addition, many participants also reiterated the need to clearly define “patient-provided information,” which refers to the views, experiences, preferences, needs, priorities, opinions, and other perspectives of patients, caregivers, family members, and other members of the patient’s support community, as well as patient advocates. A specific definition helps prevent an unduly broad understanding of “patient-provided information” that might otherwise include anything from genetic information to pathology results.

Some participants suggested defining types of research, including “clinical research,” “commercial,” “human subjects research,” and “natural history” to provide clarity as to what specific issues the guidance aims to address. The guidance should also include definitions of different types of patient engagement interactions. The group suggested that existing FDA guidance or other FDA documents be used as the foundation for this work.

## FDA Support for Patient Engagement

Participants highlighted a need for the FDA to use the guidance document to publicly express its support for meaningful patient engagement across the product lifecycle, not a requirement for product approval. Participants also discussed how the guidance should include a clear commitment from the FDA to support opportunities for stakeholders to engage with and receive guidance from the Agency on patient engagement. The guidance should also state that the FDA expects meaningful patient engagement to be the norm, along with early and frequent communication with the FDA to discuss patient engagement plans.

## Clarity on Patient Interactions

In addition, participants identified the need for clarity on the FDA's view of pre-approval sponsor-patient interactions, which are fundamental to supporting patient-focused drug development. Stakeholders are eager for guidance from the FDA to help determine how to appropriately and meaningfully engage patients and collect the most relevant information and input. Guidance from the FDA could alleviate sponsor fears or perceptions that they are violating pre-approval promotion regulations; these perceived risks may be a barrier to meaningful patient engagement. While some product sponsors are innovating on this front, others weigh the risk as too high and forgo patient interactions for this reason. Guidance should identify characteristics of patient interactions the FDA considers in assessing promotional activities. Participants were clear that they did not want the guidance to prescribe what sponsors (or other stakeholders) *had to* or *should do* (and therefore stifle innovation in this space), but rather focus on defining boundaries or "guardrails" to guide sponsors.

Participants agreed that the best way to frame this section of the guidance is to start with the assumption that patient interactions are appropriate and extend to a discussion of characteristics of appropriate interactions. Participants suggested the guidance document not define (or list examples of) "good" and "bad" interactions, but take a more nuanced approach to describing what may be considered "appropriate" interactions by focusing on characteristics of interactions. Participants recognized that assessing these characteristics will be context dependent. Some participants suggested that looking at other, existing standards might provide valuable insights (e.g., standards for talking to doctors, for conducting clinical trials). Others recommended that the guidance interpret and reference existing law, address common misperceptions, and include examples.

Examples of the characteristics discussed include, but were not limited to, the following (See draft guidance outline, Appendix A.):

- Source(s) of information
- Type of product information shared with patients
- Types of questions (e.g., disease state vs. product-specific; open-ended vs. closed; real data or hypothetical data)
- Context of questions and intent of the questioner
- Transparency of intended use of information gathered and if/how the information will be shared
- Role of sponsor staff involved (i.e., marketing, scientific)
- Expectation of patient exclusivity (i.e., patient may not engage with other sponsors)

Some participants talked about using a framework that illustrates characteristics that may be perceived as gauging the intent of the engagement, where variation in the characteristic could fall on a continuum

between “high” and “low” risk of being perceived as promotional intent. However, participants recognized that there is nuance to designating a rating scheme, as it depends on the specific context.

## Clarity on Methods of Data Capture, Analysis and Presentation

Participants agreed that stakeholders need better resources, tools, and guidance to enhance and optimize patient engagement efforts. This encompasses all aspects of patient engagement from determining the best ways for product sponsors to integrate the patient perspective into its processes to identifying what methods should be used to collect a specific type of patient-provided information and designing studies. Several participants highlighted stakeholder uncertainty regarding how the FDA would like to see sponsors engaging with patients, as well as patients’ expectations. **For example, many in the health care community have voiced a desire for patients to be meaningfully integrated in the drug development process. However, what that ultimately looks like in practice (i.e., how to meet both patient and FDA expectations) has not been clearly defined.** Participants also pointed out that understanding among stakeholders of available patient engagement methods and how to use them varies widely. These are just a few of the gaps cited as potential areas to be addressed in FDA guidance.

Participants emphasized the importance of capturing the patient story and understanding the patient’s lived experience, as they view these to be the most valuable aspects of patient-provided information. However, they also recognize the challenges associated with capturing qualitative information. To ensure that processes for collecting patient-provided information optimizes both patients’ experience of the interaction and stakeholders’ ability to gather the information they need, participants recommend that the guidance focus on describing how stakeholders can partner with patients to enhance the engagement process and collaborate on the study design, with sufficient examples.

With regard to collecting patient-provided information, participants recognized that an area of research on the science of patient input is emerging and encouraged stakeholders to leverage existing knowledge and to learn from experts in the field. **However, participants noted gaps in understanding regarding what methods can be used, should be used, and when.** In addition, they explained that studies conducted to obtain patient-provided information should meet a high quality standard. Namely, the studies should be reproducible, representative, and the methods used to collect the information should be rigorous and methodologically sound. As such, participants welcome guidance from the FDA that describes how studies should meet that threshold; sets appropriate expectations for how patients should be engaged; outlines the need for mixed-method approaches; and considers patient-centered communication and documentation (i.e., messaging that takes into account health literacy and health numeracy considerations). **In addition, the guidance should outline methods without prescribing that any specific method must be used at any point in drug development.** Many participants also supported the idea of a toolkit comprising validated and reliable data collection instruments. However, some noted that an initial guidance should place emphasis on communicating the expectation that instruments are used properly and effectively, rather than elaborating on the contents of a potential toolkit.

Several participants highlighted the importance of training and effectively implementing the methods. Many considered training for those who would be designing patient engagement plans and collecting patient-provided information to be critical to advancing patient engagement. Participants raised the idea that FDA guidance could include recommendations for product sponsors on training and capacity building.

While methods for patient engagement was a key discussion point and a high-priority topic for inclusion in an FDA guidance, some suggested that addressing this in the first guidance document might be premature given that clarity on the FDA's use of patient-provided information in regulatory decision-making and the type of information that the FDA will consider may impact what an FDA guidance on methods should include. Instead, they suggested that an initial proposed guidance might first address the FDA's expectations for the contents of a patient-provided information package submission (i.e., what is submitted to the Agency). Some suggested the inclusion of a template guiding stakeholders on how to organize and present the information would be helpful. Participants agree that early communication with the FDA regarding study designs, patient engagement plans, and patient-provided information submission packages is key to determining what to collect and how to collect it.

## **Greater Clarity & Transparency throughout the Drug Development and Approval Process**

Some of the key discussion points from participants focused on important cross-cutting themes. Among those repeatedly raised were: (1) enhancing clarity of the FDA's expectations and how the Agency will evaluate, use, and communicate patient-provided information in regulatory decision-making and product labeling; and (2) the importance of promoting transparency, communication, and information-sharing between patients, stakeholders, and the FDA. This was raised with regard to the FDA's evaluation and use of patient-provided information, sponsor-patient interactions, and information sharing. While stakeholders' concerns in these areas are important for the FDA to eventually address in detail, participants emphasized that acknowledging the broader themes of promoting transparency by all regarding patient engagement and enhancing clarity should be messaged in an initial FDA guidance.

**Meeting participants described their frustration at the lack of clarity and structure from the FDA on how it will evaluate and factor patient-provided information into its regulatory decision-making.** Clarity from the FDA on these matters will assist sponsors in their collection of patient-provided information and also enable sponsors to report back to patients regarding how their engagement impacts a product's development process. While participants agreed there is a need for FDA to clarify how it will evaluate patient-provided information, participants suggested the FDA also provide clarity on what a patient-provided information package submitted to the Agency should include to meet the FDA's evidentiary and methodological standards. Some participants noted that, given the early stages of evolution regarding patient-provided information, guidance should identify guardrails and expectations that leave room for innovation as opposed to prescribed methods.

**Attendees also expressed that sponsors (including third parties working on behalf of sponsors), patient organizations, and other stakeholders collecting patient-provided information have an obligation to be transparent about the terms or conditions of each interaction.** For example, product sponsors should be transparent about financial relationships with patients and patient groups. Participants also emphasized the need for sponsors to share important information with patients, and suggested including in FDA guidance relevant examples of the types of disclosures sponsors might use. Examples include the relationships of the party collecting patient-provided information with product sponsors, how information provided would be used or shared, and the funding source supporting the study. These disclosures should be communicated clearly and in a manner that is sensitive to the health literacy and numeracy needs of the patients. A concern that arose was whether disclosure of certain information, such as funding source, should be mandatory. Participants recognized that different disclosures may necessitate differing disclosure timing. For example, some things should be disclosed prior to patient interaction (e.g., terms of the interaction), some after the interaction (e.g., study results), and some may simply be available on request.

**Finally, participants emphasized that guidance should stress the importance of being transparent about the terms of patient-provided information ownership.** While opinions diverged regarding whether patient-provided information should be “owned” by any one company, participants agreed that sponsors have an obligation to both patients and the broader stakeholder community to communicate results of studies involving patients (e.g., peer-reviewed and scientific communications), including unfavorable results. The importance of publications in achieving this end was raised but the ability of a publication strategy to fully disseminate results was questioned given that some data may not be publishable for a variety of reasons, so this is not something that could be mandated.

## **Context Matters**

Participants voiced the need for any guidance from the FDA to be flexible enough to account for the wide range of possible interactions between product sponsors and patients. In particular, participants stressed that the context and circumstances in which a sponsor interacts with a patient will ultimately inform what actions or decisions stakeholders should take. Participants reasoned that the tools, methods, and approaches stakeholders find useful will vary depending on the context of the engagement. Therefore, FDA guidance should avoid rigid or prescriptive recommendations that may lead to greater uncertainty and/or stifle innovation. Rather, guidance should serve to help frame stakeholders’ thinking on how to plan and approach patient interactions.

**Context<sup>7</sup> is key to informing the selection of methods and best practices for collecting patient-provided information.** Meeting participants voiced that any FDA guidance on methods for engaging patients should address factors that help stakeholders determine which methods to use. Another area where context is critical is in characterizing appropriate product sponsor-patient interactions. Similar to the myriad factors that are considered to determine what methods to use in a particular situation, determining whether a patient interaction will violate regulations or policies governing an interaction can also be very complex. Given that certain product sponsor-patient interactions may be appropriate in one context but not in another, guidance on this topic should be mindful of the context in which the interaction takes place.

For example, sponsors must carefully consider who from within their companies engages and interacts with patients. Participants noted that the presence of marketing staff (i.e., a staff member from the marketing department or with a marketing title) could predispose FDA to the perception the interactions is promotional in nature. However, they also pointed out that there are contexts in which a marketing staff member could provide valuable, non-promotional expertise to patient interactions as well as broader engagement efforts. Certainly, if a marketing staff member is providing patients with information about a current product that is about to launch or about a potential expanded indication for an existing product, this would give the Agency cause to scrutinize the interaction. However, if a marketing staff member has expertise in survey methods or has extensive experience in facilitating focus groups, leveraging the individual’s skills could greatly enhance the patient interactions. The sponsor should demonstrate and document the research-based intent for collecting patient-provided information. This is one of many examples that illustrates how context matters in ultimately determining whether sponsor-patient interaction are in compliance with regulatory policies around promotion.

**While ensuring appropriate recognition of context may seem obvious, as the FDA makes decisions on a case-by-case basis, the issue raised fundamental questions on how the FDA can best account for these nuances in a guidance document.** To that end, participants suggested that any FDA guidance discussing appropriateness of patient interactions or decisions involving the collection, use, or communication of

patient-provided information should highlight the multitude of factors that contextualize those interactions and decisions.

These factors include but are not limited to (See Appendix A):

- Goals, intent, or reason for the interaction
- Setting in which the interaction is taking place
- Stage in the development lifecycle of the product for which the interaction is taking place
- Entities involved in the engagement
- Type(s) of information needed
- Compensation arrangement(s) between entities

Participants cautioned that any guidance provided by the FDA should not be overly specific, so as to inadvertently cause stakeholders to feel more restricted. However, participants did agree that any initial guidance should at a minimum acknowledge the need to consider context where appropriate and, to the extent possible, account for variability. Furthermore, context should continue to be a key theme and be integrated into future guidance documents discussing patient interactions.

## ADDITIONAL TAKEAWAYS FOR FUTURE CONSIDERATION

Participants identified many issues for consideration that were important but of lower urgency to the group. As mentioned above, these will be considered for a second or subsequent guidance document(s). Examples of topics included:

- Specific information on considerations and factors regarding the FDA's evaluation and use of patient-provided information in drug labeling
- Protection of patient interests by promoting full disclosure from sponsors
- Protection of personally identifiable patient health information (i.e., protected health information)

Some important questions raised during the meeting arguably fall outside the scope of an FDA guidance, such as how stakeholders other than FDA will or should use patient-provided information, where to store patient-provided information, how to create a data repository that could be used to capture and share sponsor-submitted information, and how to train all stakeholders so that they acquire the skills necessary to implement meaningful patient engagement. In addition, participants stated it was important to think through how patient-provided information will be used in care delivery. Participants expressed hope in finding other forums to discuss and address these important areas that affect the success of patient-centered health care as a whole.

## **CONCLUSION**

At the December 9 2015, meeting, participants explored a vast range of ideas and offered suggestions and considerations for a proposed FDA guidance. Those ideas were organized around key themes discussed in this summary.

Specifically, participants expressed that the initial FDA guidance should focus on clarifying and defining key terms, reinforcing and enhancing the FDA's support of patient engagement in drug development, affirming the FDA's commitment to incorporating patient perspectives into the Agency's decision-making processes, and helping stakeholders understand the characteristics of patient interactions that might be perceived as promotional. Further, participants would like the proposed guidance to address methods and acknowledge cross-cutting issues of transparency and proper context.

The outputs and learnings from this meeting will serve as the basis of a proposed draft FDA guidance document. Once thoroughly vetted, NHC and GA will submit the draft guidance document to the FDA for its review and consideration. The goal is for the FDA to adopt ideas, sections, or even the entire document. Longer term, NHC and GA will decide on actions for subsequent FDA guidance documents based on the additional topics not addressed in the initial guidance.

## **APPENDIX A**

### **Outline for Draft Guidance Language**

#### I. Introduction

- a. Promotes patient input early in drug research and development and across the product lifecycle to help streamline development, shorten timelines, enhance decision-making, and more closely align products with patient needs and desires – resulting in better patient outcomes
  - i. References experiences with regulator support for patient involvement in non-US countries, notably Europe (i.e., Patient Focused Medicines Development)
- b. Sets the tone that the FDA supports patient engagement throughout the drug-development lifecycle and utilizes input derived from patient experiences and perspectives when evaluating drugs.

#### II. Overview and Scope

- a. Describes the purpose and scope of the guidance document
- b. Introduces why patient engagement is important to patients, other stakeholders, and regulatory review
- c. Emphasizes that the submission of patient-provided information is strictly voluntary, but if submitted, will be utilized
- d. Highlights the FDA's support for sponsor-patient interaction throughout the entire product lifecycle continuum and encourages sponsors to meaningfully engage patients

#### III. Define Terms Used in this Guidance

- a. Identifies a number of commonly-used terms that may have slightly varying definitions depending on how they've been used and by whom they've been used, and defines the terms for the purposes of this guidance
  - i. Sponsor (sponsor of marketing application)
  - ii. Patient (broader than just an individual with a condition, includes the entire patient community: caregivers, family members or guardians, and other members of the patient's support community, as well as patient advocates and patient advocacy groups)
  - iii. Meaningful patient engagement
  - iv. Patient centered
  - v. Patient engagement
  - vi. Patient-identified information
  - vii. Patient interaction
  - viii. Patient-provided or generated information
  - ix. Patient preference
  - x. Patient-prioritized outcome
  - xi. Patient reported
  - xii. Patient-reported outcome (PRO)
  - xiii. Patient-focused drug development
  - xiv. Patient-directed drug development

- xv. Patient value
- xvi. Patient input
- xvii. Patient communication
- xviii. Risk aversion
- xix. Risk tolerance
- xx. Types of research
  - 1. Clinical research
  - 2. Market research
  - 3. Human subjects research
  - 4. Natural history of disease
  - 5. Burden of disease
  - 6. Assessment of current therapies
- xi. Types of patient engagement interactions
  - 1. Patient as research subject, stakeholder, advisor, consultant, partner, etc.

#### IV. Background

- a. What is patient-focused drug development (PFDD)?
  - i. Describes PFDD in a manner that is consistent with the FDA's previous use of the term and discusses the FDA's rationale for expanding programs and initiatives around PFDD
  - ii. Explains that patient engagement is broader than the FDA's PFDD Program
- b. What is "patient-provided information"?
  - i. Introduces the concept of "patient-provided information" and describes what it entails (e.g., encompasses the entirety of potential patient-provided information, anecdotes, preference information, etc. that can be collected from an interaction with a patient)
  - ii. Addresses that some existing terms may be defined differently by other organizations or in different contexts and explains why it is being referred to as such in this guidance
  - iii. References Section III, which will more comprehensively discuss and define each of the specific terms used
- c. Why include patient-provided information in regulatory decision-making?
  - i. Addresses why patient-provided information is important to the FDA
  - ii. Describes potential points in the review process where patient-provided information might be considered
  - iii. Acknowledges potential uses for patient-provided information in different regulatory analysis, review, and decision processes, such as benefit-risk assessments
- d. Who is involved in patient engagement?
  - i. Identifies the potential entities involved (e.g. patients, drug sponsors, third parties, etc.)
    - 1. References definitions established in Section III
  - ii. Describes what a patient interaction entails and emphasizes there are many different roles patients can assume in interactions (e.g., patient as research subject, stakeholder, advisor, etc.).
  - iii. Delineate between formal and informal interactions

- e. What are the methods used to collect patient-provided information?
    - i. Acknowledges there are many existing methods for collecting patient-provided information (but does not go into detail about each method)
    - ii. Gives examples of contexts in which patient-provided information can be collected (e.g. clinical research, commercial, human subjects research, natural history, etc.)
  - f. When and how might the FDA consider patient-provided information during the drug review process?
    - i. Acknowledges that patient-provided information can be considered at many points during the drug review process and describes at a high-level some ways in which patient-provided information can be used by the FDA (e.g., determining benefit-risk, informing drug labeling)

#### V. Factors to Consider Regarding Interactions with Patients

- a. Establishes that sponsor-patient interactions throughout all stages of discovery, research, development, and marketing review can be appropriate (i.e., will not violate pre-approval promotion restrictions, etc.)
  - b. Acknowledges that the appropriateness of an interaction is always determined on a case-by-case basis and that context for the interactions is important
  - c. Provides characteristics the FDA can consider regarding sponsor-patient interactions to assess whether the interactions have a promotional intent:

Factor	Potential Risk of Being Perceived as Engagement with Promotional Intent	
	(Lower)	(Higher)
<b>Sponsor Representation</b>		
What is the job function and/or title of the sponsor's representative(s)?	Patient liaison/medical/scientific	Commercial/marketing
How many sponsor representatives are involved in the interaction?	Low sponsor-representative to patient ratio	High sponsor-representative to patient ratio
How many sponsors support/are involved in the engagement?	Multiple sponsors	Single sponsor
<b>Subject Matter</b>		
What topic is discussed during the engagement?	Disease/condition/symptoms	Specific product
What materials are shared with patients?	Disease/condition/symptom content	Product/pre-product content

Factor	Potential Risk of Being Perceived as Engagement with Promotional Intent (Lower)  (Higher)	
<b>Timeframe</b>		
At what point in the product lifecycle is the interaction taking place?	Premarket/early development	Launch/post market
<b>Setting</b>		
What is the venue for engagement?	Academia/research/clinical environment	Launch event
<b>Purpose</b>		
What is the rationale for the interaction?	Collecting natural history, disease symptoms, quality of life	Discuss characteristic of a specific product
<b>Methods</b>		
What are the logistics for the engagement?	Structured <sup>8</sup>	Unstructured
Is there <i>a priori</i> planning for the engagement interaction?	<i>A priori</i> protocol	Unplanned, informal
How informed are patients about the goals and intent behind the interaction and research?	Complete transparency	Treated as completely proprietary
Exclusivity requested of patients?	No <sup>9</sup>	Yes <sup>10</sup>
Types of questions posed to patients?	Broad, open ended	Specific, narrow, closed ended, leading
In what direction is the flow of information?	Primarily patient to sponsor	Primarily sponsor to patient
Are patients being compensated for their time?	Appropriate compensation for the level of interaction	Disproportionate Compensation
Are financial arrangements with patients or any third party disclosed?	Full disclosure	Limited/no disclosure

<b>Factor</b>	<b>Potential Risk of Being Perceived as Engagement with Promotional Intent</b>	
	(Lower)	(Higher)
<b>Data</b>		
What is the quality of the collected information?	High quality data (i.e., publishable in a peer-reviewed journal)	Low quality, unstructured notes
Will the information be distributed?	Disseminated, shared, open source	Proprietary
How will the information or results be distributed?	Dissemination plan for public communication <sup>11</sup>	Internal use only
Who will own the collected information?	Made publicly available	Company intellectual property

## VI. Other Considerations

- a. Submission of patient-provided information
  - i. Briefly provides instructions on ways to submit patient-provided information to the FDA (not exhaustive list – intent is to acknowledge there is pathway for this)
  - ii. Reiterate that drug sponsors' submission of patient-provided information is voluntary
- b. Communicating with the FDA
  - i. Acknowledges the FDA's willingness to work with sponsors to discuss patient engagement strategies or plans
    - 1. Relays the message of "Come talk to us"
    - 2. Outlines existing pathways for stakeholders to contact the FDA regarding patient engagement and study design
    - 3. Recommends sponsors talk to the Agency early about their patient engagement plans

## APPENDIX B

### Topics Under Consideration for Inclusion in Future FDA Guidance Documents

- Methods and best practice considerations for collecting patient-provided information
  - Describes methods that can be used to collect patient-provided information
    - Include both quantitative and qualitative
    - Ensure instruments are validated, reliable, valuable
  - Describes qualities of a methodologically rigorous study
    - Developing a protocol
    - Ensuring information is reproducible, representative, etc.
    - Ensuring methods used are planned and documented
  - Addresses methodological challenges (e.g., heterogeneity in subgroups)
  - Describes best practices for engaging with patients
    - Emphasize bidirectional engagement that is "meaningful"
    - Consider burden on patients
    - Provide patients with appropriate disclosures
    - Consider context when selecting methods (i.e., optimal along continuum)
    - "Set the floor" on each stage of design and development
    - Consider patient communication (i.e., health literacy, numeracy)
    - Indicate when certain discussions with patients can take place (e.g., end of Phase 2 meeting)
    - Consider when and for what direct patient input is expected (e.g., burden of disease, burden of treatment, relative risk tolerance, etc.)
- Contents of a patient-provided information package submission
  - Characterizes what should go into a complete patient-provided information package for submission to the FDA
- FDA's evaluation and use of patient-provided information
  - Describes how the FDA will accept patient-provided information (i.e., in what forms)
  - Describes how the FDA will evaluate submitted patient-provided information
  - Describes how the FDA can and might use submitted patient-provided information (i.e., regulatory decision-making, safety surveillance)
- Use cases, e.g.,
  - Patient-provided information in drug labeling
    - Describes ways patient-provided information can be incorporated into product labeling
    - Describes ways to incorporate patient-provided information into labeling
- Patient protection
  - Informed consent issues

## APPENDIX C

### Integrating the Patient Perspective into the Drug Development Process: Developing FDA Guidance December 9, 2015, Meeting Participants

#### *Stakeholder Participants*

##### **Mark Allegretta, PhD**

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#### **National Health Council and Genetic Alliance Participants**

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*For more information about the National Health Council/Genetic Alliance initiative on Integrating the Patient Perspective into the Drug Development Process: Developing FDA Guidance, contact Eleanor Perfetto at [eperfetto@nhcouncil.org](mailto:eperfetto@nhcouncil.org) or 202-973-0546.*

## COMMENTS AND REFERENCES

<sup>1</sup> “Patient-provided information” is any information coming directly from members of the patient community and includes, but is not limited to, views, experiences, preferences, needs, opinions, and priorities. It is an umbrella term used to include patient-generated information, patient-perspective information, and patient-driven information.

<sup>2</sup> We use the term “patient community” to include patients, caregivers, family members, and other members of the patient’s support community, as well as patient advocates and representatives of patient advocacy organizations.

<sup>3</sup> See FDA website, Patient-Focused Drug Development: Disease Area Meetings Planned for Fiscal Years 2013-2017, available at: <http://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm347317.htm> (accessed March 16, 2016)

<sup>4</sup> See FDA website, Learn About FDA Advisory Committees, <http://www.fda.gov/ForPatients/About/ucm413274.htm> (accessed March 16, 2016).

<sup>5</sup> PDUFA Reauthorizations Performance Goals and Procedures Fiscal Year 2013 Through 2017  
<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf> (accessed Jan. 21, 2016).

<sup>6</sup> The term “drug” is meant to encompass both drugs and biologics.

<sup>7</sup> The term “context” is used to refer to the circumstances surrounding a particular event or action, in this case, the patient interaction. See also: FDA’s definition of “Context of Use” in reference to clinical outcome assessments:  
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm370262.htm#COU>

<sup>8</sup> i.e., formal process, clear goals, and a protocol

<sup>9</sup> No restrictions are placed on patients

<sup>10</sup> Expectation of exclusivity to sponsor

<sup>11</sup> e.g., peer-reviewed journal