



# National Health Council

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**Marc Boutin, JD**

Chief Executive Officer  
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December 14, 2018

The Honorable Scott Gottlieb, MD  
Commissioner, Food and Drug Administration  
Dockets Management Staff (HFA-305)  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

RE: Patient-Focused Drug Development Guidance: Methods To Identify What Is Important to Patients and Select, Develop, or Modify Fit-for-Purpose Clinical Outcome Assessments; Public Workshop; Request for Comments; Docket No. FDA-2018-N-2455

Dear Commissioner Gottlieb,

The National Health Council (NHC) is pleased to provide comments on the Food and Drug Administration's (FDA) discussion documents related to Guidance 2: "Methods to Identify What is Important to Patients" and Guidance 3: "Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments." The NHC appreciates the work and thought that the FDA is putting into the development of these draft guidance documents.

Founded in 1920, the National Health Council (NHC) is the only organization that brings together all segments of the health community to provide a united voice for the more than 160 million people with chronic diseases and disabilities and their family caregivers. Made up of more than 125 diverse national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient advocacy organizations, which control its governance and policy-making process. Other members include professional and membership associations; nonprofit organizations with an interest in health; and representatives from the pharmaceutical, generic drug, health insurance, device, and biotechnology industries.

## Overarching Comments

The National Health Council (NHC) provides the following overarching comments on the guidance discussion documents below.

### *Consideration of patients as partners*

The NHC believes that patient-focused drug development (PFDD) happens at two levels: (1) Patients engaged as partners informing the drug-development process, and (2) Patients participating as study subjects, such as those that provide data on the patient experience and in clinical trials that have been designed in a more patient-centered way. In general, the referenced discussion documents focus heavily on the latter and not enough on the former. We believe the focus should be both. For example, in addition to describing methods, such as reactive surveys, interviews, and focus groups, we recommend the guidance documents provide direction for how patients and patient organizations can contribute to the drug-development process, and survey and field guide development. This would help better capture the spirit and breadth of

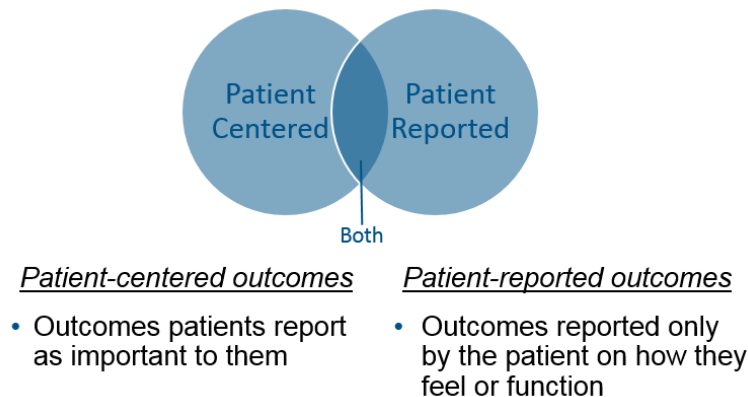
patient centricity in drug development where patients are involved as co-developers as well as being a source of patient-centered data.

*Patient centered versus patient reported*

FDA should reiterate and clarify that not all patient-reported outcomes (PROs) are patient centered and not all patient-centered outcomes are reported by patients, as confusion appears to be highly prevalent among many stakeholders. For an outcome measure to be patient centered, it must capture a concept(s) that patients identify as being highly important to them – these measures can be PROs, another type of Clinical Outcome Assessment (COA), or even a clinical measure. For example, during the 2014 Hemophilia A, Hemophilia B, von Willebrand Disease and Other Heritable Bleeding Disorders PFDD meeting, patients described joint pain as one of the most significant symptoms associated with their disease. This would be both a patient-centered and a patient-reported outcome. However, patients also described the importance of joint, soft tissue, muscle, and brain bleeding – these would be patient-centered outcomes, but none of these would be PROs.<sup>1</sup>

Understanding this distinction is important to help stakeholders differentiate among PROs developed without patient input and those developed with patient input and partnership. Currently, there are properly developed PRO tools available that are both patient reported and centered, but there are also those that are not patient centered. Continued confusion in the field will hinder evolution to patient-informed COAs. While it is inefficient to develop new measures when existing measures can be adopted or adapted, perpetuating continued use of non-patient-centered COA measures without needed adaptation runs counter to PFDD. FDA can support efficiency in this regard through dissemination of examples of good patient-centered and patient-reported measurement used in registrations by including information on how FDA views the level of patient-centricity in measure development. This could include qualitative research done with patients to determine if an existing measure is patient centered (e.g., how to demonstrate that the measure contains concepts important to patients).

Fig. 1: Patient Centered Vs. Patient Reported



*Utility of patient experience data is not limited to COAs*

The NHC supports the FDA’s goal of developing guidance that provides structure for incorporating patient perspectives as a standard practice. The introduction section in both discussion documents states that the guidances will address how sponsors can “collect and submit patient-experience data and other relevant information from patients and caregivers for medical product development and regulatory decision making.” However, the content of the discussion documents primarily focuses on using the data collected as described in Guidance 2 for the development of COAs. Acknowledging that the statutory mandate requires FDA to develop the COA development guidance (Guidance 3) and implementation guidance

<sup>1</sup> Food and Drug Administration. The Voice of the Patient: Hemophilia A, Hemophilia B, von Willebrand Disease and Other Heritable Bleeding Disorders.  
<https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM513311.pdf>

(Guidance 4), the Agency should clarify other means by which patient-experience data can be used throughout the product lifecycle – including for FDA decision-making. Examples of how patient input is impactful as part of the review process, beyond COA data driving label claims, is needed to help create consistency across FDA review divisions and ensure parity in the use of such data. For example, patient perspectives can guide interpretation of benefits and risks. If there is an opportunity to describe these additional applications within the scope of forthcoming guidances, stakeholders would greatly benefit from that information. FDA could also consider developing a separate guidance that addresses these other uses of patient-informed data. Additionally, insights as to how patient experience data will be used in regulatory decision-making by FDA are important and should be described.

*Patient engagement is an evolving field, and flexibility is needed as methods and data sources evolve and advance*

As this evolving and emerging science advances forward – it would be helpful for the Agency to provide stakeholders with ample patient-engagement and patient-experience data examples. These could be hypothetical or real world and should span the PFDD continuum – from pre-competitive stages, throughout clinical-development plan implementation, regulatory review, and post-marketing activities. Examples should be methodologically sound, but not overly rigid, and describe a variety of methods and data sources. Examples of what would constitute acceptable representativeness also would be useful. Specifics to help readers understand why included examples, whether hypothetical or not, are deemed appropriate would be insightful.

Finally, while perhaps beyond the scope of Guidances 2 and 3, there appears to be confusion among stakeholders related to the distinction between the different types of patient preference studies. It would be helpful for the Agency to clearly articulate differences between these methodologies and study objectives for each, especially when it comes to studying preferences related to the disease outcome versus preferences related to treatment. Clarity regarding the Center for Drug Evaluation and Research's and the Center for Biologics Evaluation and Research's approach to preference data would be welcome.

### **Responses to Specific FDA Questions**

Below, we offer answers to the FDA's specific questions. Please note that we do not supply answers to every question.

#### **i. PFDD Guidance 2: Methods to Identify What is Important to Patients**

- 1. Identify best practices (qualitative and quantitative methods) for eliciting information about what aspects of symptoms, impacts of disease, and other issues important to patients that are representative of the target population of patients and caregivers. What level of detail of the methodology do you think is appropriate for this guidance?*

The NHC believes that it is too early to identify “best practices” and recognizes they may evolve over time. Opportunities for flexibility should be identified and encouraged, and practices should be assessed over time. Patients and their family caregivers need to have a more prominent role as co-developers to ensure that questions being asked during concept elicitation yield responsive, representative information.

It would be useful to understand whether FDA-sponsored or externally-led PFDD meetings are considered a good practice by the FDA for eliciting information about aspects of symptoms, impacts of disease, and other issues important to patients that are representative of the target population of patients and caregivers. Insights into whether/how data from a Voice-of-the-Patient report could supplement or be supplemented by other elicitation methods would be welcome.

Regarding the question on the level of detail, the Patient-Centered Outcomes Research Institute (PCORI) encountered the challenge of determining the level of detail to include when developing their PCORI Engagement Rubric. To avoid being overly prescriptive and encourage methodological innovation, they developed broadly applicable Principles and Key Considerations<sup>2</sup>. Similarly, the Medical Device Innovation Consortium (MDIC) developed “A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology” that FDA could consider developing or adapting a similar method.<sup>3</sup>

2. *What sample size will elicit sufficient information about the patient experience to assure representativeness but is feasible?*

Sample size and representativeness depend on the research question at hand and disease prevalence. Researchers should first identify what kind of representativeness is needed based on the objective of the research. Sample size and sampling technique are dependent on the desired representativeness based on the question and objective. If these are not clearly articulated, representativeness cannot be determined.

A decision framework should be used to ensure representativeness in patient-centered research. The NHC Patient Representativeness Roadmap and Rubric is an example of one such approach. It is intended to guide decision-making on representativeness for a given patient-engagement activity.<sup>4</sup> The steps in that framework include: defining the objective of engagement, understanding the full population and subpopulations, specifying minimum targets for representativeness, planning to achieve minimum targets, evaluating progress against goals, and documenting the process. We suggest the FDA consider this kind of framework.

Importantly, pre-specifying a desired sample size for every engagement encounter may not be appropriate and can be a barrier to engagement, especially rare-disease patient engagement or engagement for a research question that is limited to narrowly defined subpopulations. Certain methodologies are appropriate with very small sample sizes where power calculations are inappropriate. For example, the purpose of ethnographic research is to “provide rich, holistic insights into people’s views and actions, as well as the nature (that is, sights, sounds) of the location they inhabit, through the collection of detailed observations and interviews.”<sup>5</sup>

Malterud and colleagues<sup>6</sup> developed a useful guiding framework for considering the role of sample size in qualitative research. Their framework suggests that the importance of sample size is influenced by:

- (a) Aim of the study;
  - E.g., Among patients with foot ulcers: understanding ease of changing bandages would require fewer participants than to understand patient experiences with the health care system more broadly
- (b) Sample specificity;
  - E.g., Smaller samples may be sufficient when engaging homogenous samples (ex. sample of foot ulcer patients from a specific location with similar characteristics) whereas larger samples may be needed for highly heterogeneous samples (ex. nationally representative sample of foot ulcer patients)

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<sup>2</sup> Patient-Centered Outcomes Research Institute. Engagement Rubric [updated June 2016] Patient-Centered Outcomes Research Institute. Feb 4 2014. <http://www.pcori.org/sites/default/files/Engagement-Rubric.pdf>.

<sup>3</sup> Medical Device Innovation Consortium. A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology. [http://mdic.org/wp-content/uploads/2015/05/MDIC\\_PCBR\\_Framework\\_Web1.pdf](http://mdic.org/wp-content/uploads/2015/05/MDIC_PCBR_Framework_Web1.pdf)

<sup>4</sup> National Health Council. Tackling Representativeness: A Roadmap and Rubric.

<https://www.nationalhealthcouncil.org/sites/default/files/Representativeness%20in%20Patient%20Engagement.pdf>

<sup>5</sup> Reeves Scott, Kuper Ayelet, Hodges Brian David. Qualitative research methodologies: ethnography BMJ 2008; 337 :a1020

- (c) Use of established theory (e.g., reliance on existing theoretical framework may require fewer participants; absence of a theoretical foundation may require more participants);
- (d) Analysis strategy (e.g., exploratory analyses may require more participants than in-depth analyses of narratives from a smaller selection of patients).<sup>6</sup>

The author's also describe the quality of the dialogue; however, this aspect is not as relevant to inform regulatory decision-making. When possible or appropriate, FDA should provide examples related to this topic.

- 3. *What other data (e.g., data from social networks, accelerometry, room surveillance) can be used to elicit or derive information about the patient experience in a feasible manner?*

These data are all potentially appropriate – their appropriateness depends on the aim of the study. For example, using digital sources to collect information about a patients' activity within the scope of a clinical trial will have different ethical and regulatory considerations than when using these sources to make diagnostic or treatment recommendations. Intended use will contribute to the decision regarding whether they are fit for purpose.

- 4. *Use of social media is recognized as a potential data collection method to elicit information regarding patient experience.*
  - a. *Will information collected from social media sources meet the goals of Guidance 2 (e.g., collecting representative information on important symptoms, burdens, and related issues)? If yes, how do we determine the adequacy of data from social media sources?*

Information collected from social media can be very useful. For example, it may offer opportunities to engage individuals with disabilities or individuals who struggle with face-to-face communication.<sup>7</sup> However, its usefulness is context-specific and as with other data sources is dependent on study objective, data quality, representativeness, known biases, etc. It may be appropriate to supplement other sources with social media and vice-versa.

An important advantage of collecting information through social media sources is that more data can be collected less expensively. Without flexibility, many of the useful aspects of social media cannot be realized as the field is evolving. We encourage flexibility and evaluation. Because it is an emerging field, there will be a period of trial and error. During this period, FDA should facilitate dissemination of new learnings, both positive and negative to encourage good practices. As available, guidance would be useful from FDA regarding acceptability of the data and evidentiary standards required based on a study's objective.

- b. *Is there a need for patient verification if social media is the data collection method to elicit information about the patient experience?*

The need for patient verification depends on the objective, data, and data source. It may also differ depending on characteristics of the disease. For example, is it a chronic versus acute condition? Prevalent? Frequently misdiagnosed? Is the disease easily recognizable by the patient (e.g. menstrual cramps versus heart failure)? In addition to patient verification, the use of data from social media sources may raise questions regarding consent and privacy (i.e., how do we ensure that patient social media data is being used with appropriate consent and confidentiality?).

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<sup>6</sup> Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. *Qual Health Res.* 2015 Nov 27. pii: 1049732315617444.

<sup>7</sup> Hemsley B, Murray J. Distance and proximity: research on social media connections in the field of communication disability. *Disabil Rehabil.* 2015;37(17):1509-10. doi: 10.3109/09638288.2015.1057031.

Again, FDA should allow for experimentation and flexibility, and disseminate examples of good practices as they emerge.

5. *Important considerations are needed for special populations, such as pediatrics, the cognitively impaired, and rare diseases. What other special populations (beyond pediatric, cognitively impaired, and rare diseases) should be identified for this FDA Guidance? Are there any other factors to consider when eliciting information from special populations?*

“Special populations” can be context-specific and mutable. For example, patients with low health literacy may be considered a “special population.” Additionally, sensory (vision, hearing, tactile) limitations may impact ability to respond to PRO measures and may require accommodations.

Matza and colleagues described good practices related to pediatric PRO research, including strategies for concept elicitation and cognitive interviews with children.<sup>8</sup> Similarly, Benjamin and colleagues published good practices related to use of PROs and ObsROs in rare disease clinical trials.<sup>9</sup> In many cases, Institutional Review Boards have already developed general human subjects’ protections specific to many special populations. FDA guidance about special populations should be consistent with these requirements.

6. *The level of rigor needed for generating patient experience data can vary across studies and will depend on the intended use. However, there are certain elements common to all studies such as a protocol, structured data collection, and analysis. How much detail about each aspect would be useful in guidance? On a website? Elsewhere?*

As stated, the level of rigor needed varies depending on the objective of the study. Importantly, many of the proposed patient engagement methods already have dedicated methods textbooks and resources published toward that end. While it is important for FDA to provide direction on the types of elements industry should consider and the relevant fields of expertise from which they should obtain guidance and resources, the guidance itself does not need to be overly detailed. There are already existing resources (e.g., Registries for Evaluating Patient Outcomes)<sup>10</sup>. This approach will also allow researchers to adopt emerging methods and data sources. Clearly outlining opportunities for stakeholders to discuss specifics with FDA staff ensures that stakeholders have the opportunity to seek additional insights as needed. This also helps the FDA demonstrate flexibility and encourage methodological innovation.

De-identified or hypothetical examples and FAQs published on a website or in an appendix would be helpful for stakeholders to understand why FDA accepted (or did not accept) a proposed study design, methodological approach, or data source.

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<sup>8</sup> Matza LS, Patrick D, Riley AW et al. Pediatric patient-reported outcome instruments for research to support medical product labeling: Report of the ISPOR PRO good research practices for the assessment of children and adolescents task force. *Value Health* 2013;16:461-79.

<sup>9</sup> Benjamin K, Vernon MK, Patrick DL et al. Patient Reported Outcome and Observer Reported Outcome Assessment in Rare Disease Clinical Trials - Emerging Good Practices: An ISPOR COA Emerging Good Practices Report. *Value Health* 2017; (7):838-855.

<sup>10</sup> Gliklich R, Dreyer N, Leavy M, eds. *Registries for Evaluating Patient Outcomes: A User’s Guide*. Third edition. Two volumes. (Prepared by the Outcome DEcIDE Center [Outcome Sciences, Inc., a Quintiles company] under Contract No. 290 2005 00351 TO7.) AHRQ Publication No. 13(14)-EHC111. Rockville, MD: Agency for Healthcare Research and Quality. April 2014. <http://www.effectivehealthcare.ahrq.gov/registries-guide-3.cfm>.

7. *What document structure and content would be most useful for this guidance?*

This guidance document would benefit from questions and answers with applicable examples. Previous FDA guidance documents have successfully provided information about FDA's thinking on a topic using this format.

8. *Many potential research methods are available and not all could be included in the discussion document. Is it clear the Agency is open to discussion of the methods described and other methods, both within medical product programs and in the pre-competitive space?*

Direct and clear articulation that FDA is aware that the field of patient engagement is evolving and that flexibility is needed during this evolution, would be helpful. Additionally, outlining mechanisms for these discussions would be helpful to ensure that this point is clearly conveyed and well understood.

9. *What are the most important timepoints when FDA input could be maximally helpful?*

Patient engagement throughout the development process (beyond patient-engagement study participation) is integral. This should start as early in the process as possible and is the newest and most evolving aspect of PFDD. FDA must be prepared to provide input on this aspect of patient engagement early and throughout development.

We also anticipate that FDA's input will be helpful during the design of a patient-experience study. However, it is important that opportunities exist throughout the drug development continuum, including during the pre-competitive phase and within the scope of specific clinical development plans, etc.

FDA should clearly articulate when, how, and who can request FDA input. The feedback should be timely, specific, and actionable. In addition to industry-requested meetings, we recommend that opportunities for patient organization-requested meetings also be clearly described. The Agency can outline its expectations for when a sponsor should approach the Agency and in what ways the Agency can help at each time point.

We expect that the level of FDA involvement required will be significant now and in the near future. However, it is likely that the level of involvement needed will decrease in the future as good practices evolve, and stakeholders will be able to utilize them with a lesser degree of direction needed from the FDA.

## **II. PFDD Guidance 3: Select, Develop, or Modify Fit-for-Purpose Clinical Outcome Assessments**

While not covered in any of the questions in the document, it is important that FDA clearly states that the suitability of measures is not limited to the psychometric properties of an instrument. The overall patient centrality of clinical development plan and trial design are also critical for PFDD. Additional considerations (beyond psychometric properties) include trial design, frequency that PRO data is requested from patients, frequency of administration, etc.

1. *Does the Roadmap Diagram (Figure 3) in the Guidance 3 discussion document capture the appropriate elements to strategize for the selection and/or development of a COA for use in clinical trials? If not, what are other factors that should be considered and where should they be positioned in the diagram?*

Currently it appears that lettered items A-D listed in Column One of the Roadmap convey a particular order that should be followed to gather information to understand a disease or condition. We recommend that FDA revise this formatting to more clearly depict that this process is much more iterative in nature. For example, patient/caregiver perspectives, which are currently listed in Box D, are important for understanding, from the patient perspective, the natural history of the disease or condition, currently listed

in Box A. This could be achieved through development of a Column One-specific wheel-and-spoke-type diagram. Corresponding text can make it clear that data gathering is unlikely to be as linear as this column in the Roadmap might seem to imply.

It also should be noted that “patient/caregiver *perspectives*” refers to a specific patient-provided data type, whereas “natural history of the disease or condition,” “patient subpopulations,” and “health care environment” refer to broader kinds of information. We suggest that reference to patient/caregiver-provided information be made more prominent and it be made clearer that it refers to patient/caregiver experiences, perspectives, and preferences and other information. These contribute to understanding the patient journey, which should inform COA measure development and operationalization.

Additionally, examples of appropriate methods for engaging patients to identify their perspectives and experiences related to natural history of disease, subpopulations, and the health care environment would be useful. The NHC’s Patient Perspectives on Disease Impact and Treatment Options: A Stratification Tool and corresponding Implementation Manual provide suggestions on gathering, translating, and sharing this information.<sup>11,12</sup>

2. *Does the decision tree diagram (Figure 6) in the Guidance 3 discussion document capture the process to select, develop, or modify a COA sufficiently? If not, what are other factors that should be considered in this process and where should they be positioned in the diagram? Should this diagram replace the “Wheel and Spokes” diagram in the current PRO Guidance (Figure 3 in FDA PRO Guidance)?*

We believe that it could be made clearer in the first step that the concept of interest should be a product of following Step 1 (Column One of the Roadmap). As a result, the concept of interest is one that has demonstrated importance to patients. It should also be made clearer that the specification of the context of use should be one that has been informed by patient input (Column One flowing into Column Two).

3. *Important considerations are needed for special populations, such as pediatric, the cognitively impaired, rare diseases, and patients from different language and cultural groups. Does the Guidance 3 discussion document capture all the relevant special populations? What other populations should be identified for this FDA Guidance? Are there any other factors to consider when selecting, developing, and implementing COAs for these populations?*
  - a. *What other factors need to be considered when determining a reasonable minimum age to self-report in a reliable and valid manner?*
  - b. *What other factors need to be considered when determining a reasonable minimum level of cognitive function to self-report?*
  - c. *How to address selection of COAs for people who move between a self-report status and inability to self-report?*
  - d. *What are other factors and/or approaches to consider when using COAs in multinational, multicultural, and/or multiregional studies?*
  - e. *Does the Guidance 3 discussion document appropriately present the important considerations for selection, development, and/or modification of COAs in rare diseases in sufficient detail and in a feasible manner? If not, what are other factors and/or approaches to consider?*

Patients and their families and caregivers should be involved in making these determinations and setting cut points (e.g., determining a reasonable minimum age to self-report in a reliable and valid manner).

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<sup>11</sup> National Health Council. Patient Perspectives on Disease Impact and Treatment Options: A Stratification Tool.

[http://www.nationalhealthcouncil.org/sites/default/files/NHCPatientInformationToolandinstructions\\_0.pdf](http://www.nationalhealthcouncil.org/sites/default/files/NHCPatientInformationToolandinstructions_0.pdf)

<sup>12</sup> National Health Council. Implementation Manual: How to Operationalize the National Health Council’s Patient Information Tool. <http://www.nationalhealthcouncil.org/sites/default/files/Patient-Information-Tool-Manual.pdf>



Matza and colleagues state that considerations for age cut-offs among children and adolescents include: level of independence required of child respondents and cognitive and developmental variability within populations.<sup>8</sup> Parents or family caregivers can provide unique insights into these patient characteristics.

4. *Does the Guidance 3 discussion document capture the most appropriate and feasible methods to determine within-patient meaningful score changes in COA instruments? Are there any other methods to consider?*

Determining what is meaningful should be informed by patient and caregiver input, including selection of a meaningful concept of interest to establishing meaningful change. For example, Morgan and colleagues examined how adolescents with juvenile idiopathic arthritis (JIA), parents, and clinicians defined minimally important differences (MID) on Patient Reported Outcomes Measurement Information System (PROMIS®) measures. The authors found that perspectives on MID, especially for mobility and pain interference, differed between stakeholder groups. Engaging patients and their family caregivers ensures that these differences are considered during validation. The corresponding paper describes their methodology.<sup>13</sup>

6. *FDA strives to maintain flexibility in our evaluation of evidence, taking into account feasibility and practicality. Does the discussion document appropriately describe how FDA will assess whether a COA is fit for purpose?*

To this end, FDA could help stakeholders by providing examples that indicate which types of evidence will be generally accepted for different regulatory objectives in the development and application of COAs.

9. *How do the good measurement principles presented in this discussion document apply to PerfOs and ClinROs, and what other evidence is needed?*

Good measurement principles apply to all COAs. However, the selection of concepts for COAs should be focused on outcomes that are meaningful and important to patients. Thus, selection of COA concepts that are not important to patients and that are not patient reported should be supported by clear justification for non-patient-centered selections regardless of COA type.

There is existing literature related to PerfOs and ClinROs (e.g., PerfO White Paper<sup>6</sup> and ISPOR Task Force ClinRO paper). FDA's reference of these documents would be useful, in particular as the focus of the discussion document is primarily on PROs. To ensure that the most patient-centered tools are incorporated into clinical development plans, it would be helpful if the Guidance was more inclusive of other types of COAs.

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<sup>13</sup> Morgan EM, Mara CA, Huang B, et al. Establishing clinical meaning and defining important differences for Patient-Reported Outcomes Measurement Information System (PROMIS®) measures in juvenile idiopathic arthritis using standard setting with patients, parents, and providers. *Qual Life Res.* 2016;26(3):565-586.

**III. Conclusion**

The NHC fully supports the FDA's PFDD initiative and the enhancement of patient engagement in medical product development. FDA's commitment to using patient experience data to inform decision-making is important and appreciated. We thank the Agency for the opportunity to comment and participate in the past workshops.

Please do not hesitate to contact Eric Gascho, our Vice President of Policy and Government Affairs, if you or your staff would like to discuss these issues in greater detail. He is reachable by phone at 202-973-0545 or via e-mail at [egascho@nhcouncil.org](mailto:egascho@nhcouncil.org).

Sincerely,

A handwritten signature in black ink, appearing to read "MBoutin", with a long horizontal stroke extending to the right.

Marc Boutin, JD  
Chief Executive Officer  
National Health Council

## Appendix A.

According to the RFI, CCOAES “would reflect measures, tools, and endpoints that assess a minimum list of impacts that matter most to patients and are likely to demonstrate change relating to disease burden, treatment burden, and, if applicable, physical function.” The Core Outcome Measures in Effectiveness Trials (COMET) initiative defines COS as “an agreed minimum set of outcomes or outcome measures... It is a recommendation of ‘what’ should be measured and reported in all trials in a specific area.” They define a Core Outcome Measurement Instrument Sets (COMISs) as “details on the instruments or tools to use to measure the outcomes in a COS.”<sup>14</sup> COMET’s definition that a COS may refer to outcomes or outcome measures results in ambiguity.

Our interpretation is that a COS is a broad range of possible outcomes identified through multi-stakeholder consensus building. Outcomes comprising a COS may include those that are patient-centered (i.e., identified and prioritized by patients) and not patient-centered (i.e., not prioritized by patients). A COS includes all types of outcomes including, COAs, biomarkers, survival outcomes, etc. A COMIS is an extension of a COS meaning it includes a broad range of measures associated with the COS. A COMIS includes patient-centered and non-patient-centered outcome measures (see Figure 1). A CCOASES is subset of a COMIS and includes only patient-centered outcome measures falling under the COA umbrella: patient-reported outcomes measures (PROMs), clinician-reported outcome measures (ClinRo), observer-reported outcome measures (ObsRO), and performance outcome measures.

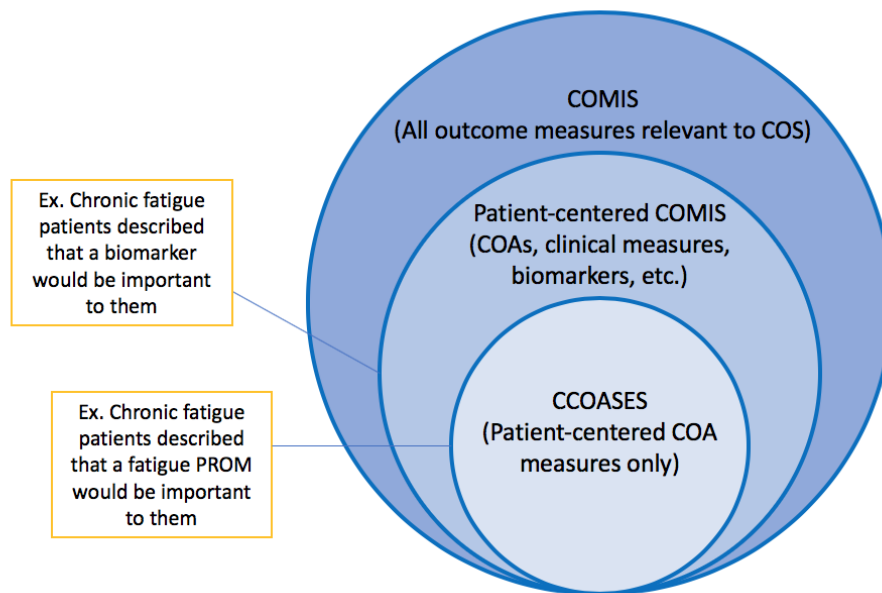


Figure 1. COS vernacular

<sup>14</sup> Core Outcome Measures in Effectiveness Trials. Core Outcome Set (COS) Glossary. <http://www.comet-initiative.org/glossary/cos/>