Insight Brief

Our Perspectives on the US FDA Patient-Focused Drug Development (PFDD) Guidance 1 and 2

Generating robust data to understand patients' experiences with disease and its treatment

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Executive Summary

FDA is currently developing a series of four Patient-Focused Drug Development (PFDD) Guidance Documents for the healthcare industry. Guidance 1 and 2 are focused on ensuring that sponsors obtain robust, meaningful and interpretable patient input to understand their experience with their disease and its treatment to inform medical product development. Guidance 3 and 4 will thereafter address the COA selection and endpoint measurement. This document presents analyses of PFDD Guidance 1 and 2.

Generating information on what is important to patients for regulatory review is not a new practice. The FDA PRO Guidance (2009) outlined the importance of generating input from patients and caregivers on how disease affects their daily lives, what they find most troublesome, and the challenges, problems, and burdens of the treatments for the disease, to inform an outcome strategy intended for label claims. Sponsors commonly engage in qualitative concept elicitation research to this aim, generating conceptual disease models as a basis from which to inform endpoint development.

The PFDD guidance documents offer an opportunity to broaden the scope (beyond endpoint development), broaden research methods (beyond qualitative work), and offer guidance for how to do this in a scientifically rigorous way by selecting the right patients from whom to collect information and choosing the right method for answering clear questions.

Together the 3 guidances (PRO Guidance, PFDD-1 and PFDD-2) can provide all the information a sponsor needs to generate robust data to understand experience with disease and its treatment to inform development of endpoint measures for regulatory consideration.

BACKGROUND

Patient-Focused Drug Development (PFDD) is defined by FDA as a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation.

A key PFDD effort to develop a series of 4 methodological guidance documents was initiated in December 2016 with the signing of the 21st Century Cures Act into law.

This act mandated that FDA issue draft and final versions of one or more guidance documents over a period of 5 years regarding the collection of patient experience data and the use of such data and related information in drug development (Title III Section 3002). The Act included strict timeliness where a plan was due within 180 days of the signing of the act and at least one guidance final within 18 months. FDA responded by outlining the PFDD Guidance Series and planned timelines as summarized in Table 1.

Table 1: Summary of PFDD Guidance Timelines

GUIDANCE TITLE	PUBLIC WORKSHOP DATE	DRAFT DATES	FINAL DATES
PFDD-1: Collecting Comprehensive and Representative Input	12/18/17	6/13/18	June 2020
PFDD-2: Methods to Identify What is Important to Patients	10/15/18	10/1/19	Q1 2021
PFDD-3: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments	10/16/18	Q2 2020	Q4 2021
PFDD-4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision-making	12/6/19	Q2 2020	Q4 2021

Patient-Focused Drug Development (PFDD) is defined by FDA as a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation.

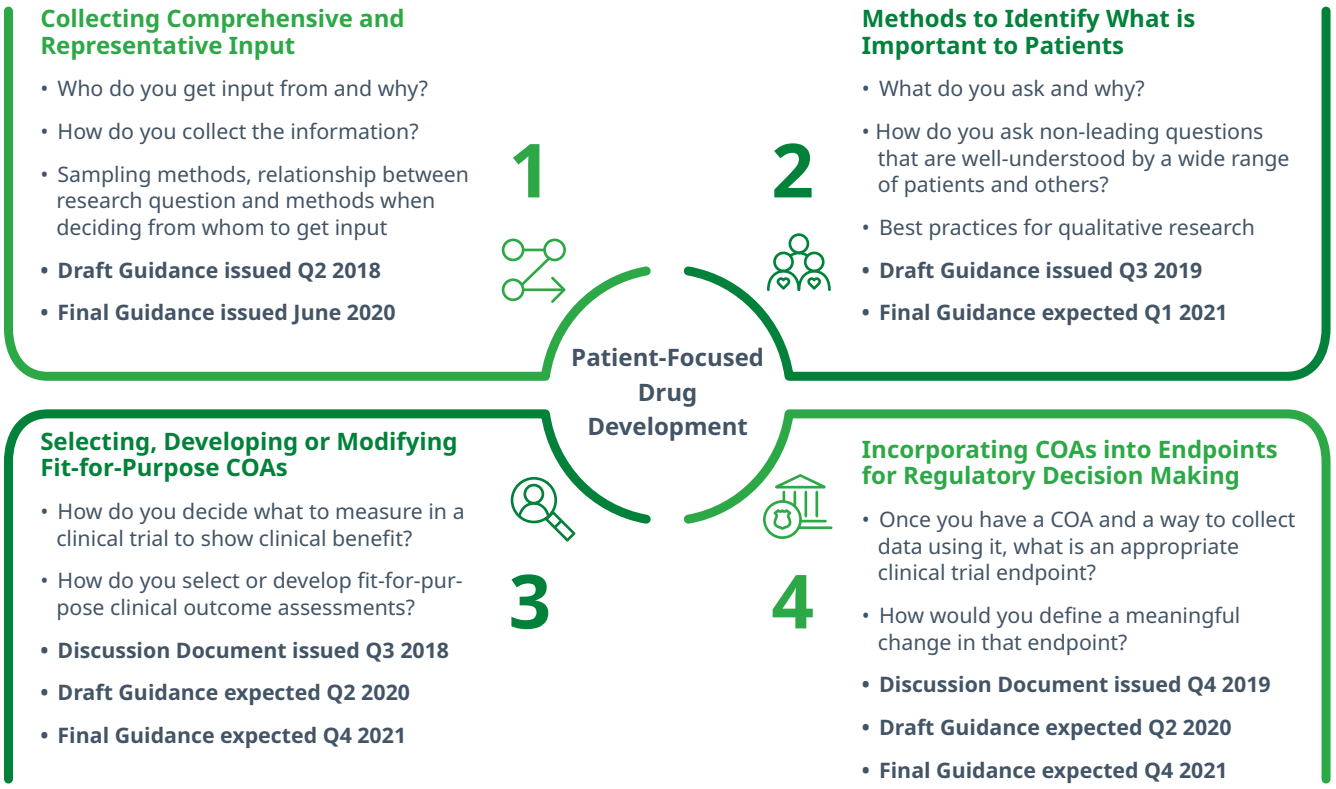
PFDD GUIDANCE SERIES OVERVIEW

The PFDD guidance series is meant to address in a stepwise manner how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision-making.

Figure 1 below briefly summarizes each guidance with the question it seeks to answer and how each question is addressed along with timelines for publishing the draft and final versions. Draft guidance for PFDD-1 was released in June 2018 and finalized in June 2020. Draft guidance for PFDD-2 was released in October 2019 and draft guidance for PFDD-3 and 4 is expected imminently. The timelines for finalization of PFDD-2 have been impacted by the COVID pandemic and updated timelines are not currently available.

While the focus of this document is on the recently developed PFDD Guidance Series, it's important to note that these guidance documents do not supersede the 2009 PRO Guidance (Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims). The PRO guidance is foundational and focused specifically on the use of PRO instruments to support labeling claims. This is clearly still very relevant for the industry, however, the PFDD series has a broader scope of not just the strict standards for claims but a shift to patient experience data that comes from many sources and has applications in drug development in addition to claims specifically for the regulatory purpose of benefit-risk assessments.

Figure 1: PFDD Guidance Series Overview



PFDD Guidance 1 – Collecting Comprehensive and Representative Input

OVERVIEW AND SUMMARY OF NEW INFORMATION

The first guidance document in the series starts from a logical starting place when considering integration of the patient voice. PFDD-1 presents best practices for collecting patient experience information. The objective is to answer the questions: *Whom do you get input from, and why?* and *How do you collect the information?* The guidance answers these questions with a presentation of sampling methods and methods for operationalizing and standardizing the collection, analysis and dissemination of patient experience data. Importantly, PFDD-1 also includes a glossary of terms used in all 4 documents.

Figure 2 is an overview with FDA's recommendation for stakeholders on how to study patient experience and each step is described in detail in the body of the guidance.

Key topics from the general steps outlined in Figure 2 below where FDA has provided new directions for industry are summarized in Table 2.

Figure 2: General Steps for Conducting Studies About Patient Experience

1 >	2 >	3 >	4 >	5 >	6 >	7 >	8
Define the research objective(s) and questions	Determine the target patient population from whom to collect information	Determine the study design and research setting, including instruments	Determine which analyses are required to achieve the research objectives	Construct the study sample	Collect the data and perform data management tasks	Analyze and interpret the data	Report study results

Table 2: New Directions from PFDD-1 on Conducting Patient Experience Studies

	STEP	DETAIL
1	**Research Objective / Questions**	While definition of research objectives is not new, development of research questions is emphasized as the starting place in all PFDD guidances. FDA specifically recommends consultation with previously conducted studies and SMEs to determine appropriate questions to inform methods and study materials.
2	**Patient Population from Whom to Collect Information**	FDA recommends patients directly report their experience unless they cannot be expected to reliably self-report. In addition, the definition of a reporter as the person who will be providing the patient experience information is included and FDA further recommends reporter criteria (such as level of cognitive development, function, or mental status and health state) be set prior to study initiation. Similarly, FDA recommends that subgroups be pre-specified and care taken with the number of subgroups being proposed for analysis.
3	**Study Design – Sampling Methods**	A detailed presentation of probability and non-probability sampling approaches, selection strategies, examples and potential limitations to determine how individuals are selected to participate in the study is provided understanding that the intention of the research and population vary greatly in patient experience studies.
3	**Study Design – Representativeness**	The following 2 tests are provided for sample representativeness • Statements about patient experience based from the sample of patients are generalizable to the target population • Patients in the study sample consists of individuals of various characteristics that to some degree approximate the heterogeneity of the characteristics of the target population
4	**Analysis Planning**	While not a new concept FDA is consistent in recommending reference to the defined research question and considering the analytical strategy as qualitative, quantitative or a mixed method prior to selecting the study sample
5	**Study Sample**	When probability sampling is not feasible or required FDA presents factors to consider to achieve "sufficient representation" of: socioeconomic and demographic background, cultural background and spoken language, literacy, clinical characteristics. A discussion of international sampling is omitted from the guidance. While not explicitly mentioned, FDA requires representation from the US population in almost all cases.
5	**Study Sample**	Sampling frame construction and an emphasis that attempts should be made to minimize undercoverage of the target patient population in patient experience studies
6	**Additional Considerations** *Missing Data*	FDA recommends establishment of plans delineating strategies to minimize missing data and where missingness cannot be avoided to collect and determine the reasons why. To help understand extent and impact of missing data FDA recommends: • Table summary of missing data with frequencies, percentages, stratification by subgroups and reasons • Summary of missingness stratified by assessment visits or time points for longitudinal data
6	**Data Collection / Management**	Information is provided on types of data and potential advantages and limitations for consideration when determining data collection methods of: Interviews, Focus groups, Facilitated discussions, Observational methods, Documents, Audiovisual materials, Social media and verified patient communities, and Digital health technologies.
7	**Analysis / Interpretation**	FDA acknowledges that the analysis approach is dependent on the type of data, study conducted and research question and objectives. Additional discussion on interpretation is deferred for later guidance in the series.

IQVIA PCE DISCUSSION

The PFDD-1 Guidance is a highly informative document that is indicative of the shift in emphasis from regulators being purely focused on claims to better understand and integrate the patient voice. It differs from the 2009 PRO Guidance in its broad scope and openness for industry to collect information from patients in a scientifically sound manner from multiple sources for multiple purposes. Rather than being an overly instructional guidance with strict criteria, PFDD-1 focuses on preparation, understanding the research question and considerations for industry when defining approaches for collecting patient experience information.

As the first final guidance to be issued following the 21st Century Cures Act, it is worth noting that this is the first formal integration of the following definition of patient experience data.

Patient experience data: Defined in Title III, section 3001 of the Cures Act, as amended by section 605 of the FDA Reauthorization Act of 2017, and includes data that are collected by any persons and are intended to provide information about patients' experiences with a disease or condition. Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to:

1. the symptoms of their condition and its natural history;
2. the impact of the conditions on their functioning and quality of life;
3. their experience with treatments;
4. input on which outcomes are important to them;
5. their preferences for outcomes and treatments; and
6. the relative importance of any issue as defined by patients.

Prior to this guidance, the patient voice was limited to PRO data collected in a clinical trial. This new definition is important because it again emphasizes that while PRO information is critical, additional valuable information can and should be collected and analyzed for patient-focused drug development. Further, FDA details that patient experience data will be used for the regulatory purposes of informing clinical trial design, trial endpoint selection, and regulatory reviews including benefit-risk assessment as well as potential labeling (or other communications). This key difference is highlighted in Table 3 with other topics from the IQVIA PCE review of PFDD-1 along with our perspective on the opportunities and challenges for the biopharmaceutical industry when considering best practices for integration of the patient voice in drug development as described in PFDD-1.

This new definition of patient experience data is important because it again emphasizes that while PRO information is critical, additional valuable information can and should be collected and analyzed for patient-focused drug development.

Table 3: PFDD-1 Opportunities and Challenges

TOPIC	OPPORTUNITY	CHALLENGE
Patient experience data definition and integration	The emphasis on patient experience represents an opportunity to develop products that truly make a difference in patient's lives	Traditional drug development where studies are designed without the patient voice may need revision and/ or concurrent work to support that the patient experience is informing development / appropriately integrated into the outcomes
Use of patient experience data for regulatory purposes	The expansion of FDA's interest in the patient voice provides the opportunity for sponsors to practically expand the utility of patient experience data beyond claims to better demonstrate product meaningfulness and inform benefit-risk decisions with data from well-defined research. This may strengthen applications for approval decisions, provide stronger information for medical product communications and potentially improve trial designs for studies that are easier to recruit and/or have increased retention rates	Sponsors that approach drug development using traditional methods without incorporation of patients may be unprepared for the changing regulatory environment and expectations for patient-centered research. Additional expertise and time in development may be required for these programs
Planning and Preparation – Research Question The breadth of the types of studies and data addressed by this document requires that sponsor's understand specifically their research objectives and questions	The information presented provides the ability to thoughtfully design studies where patient experience is well understood and likelihood of regulatory acceptance of the data is high	Time to prepare is often limited and research objectives may change. Few organizations have integrated teams focusing on all aspects of "patient experience" as outlined in the definition
Planning and Preparation – Patient Population Incorporation of reporter and subgroup criteria	Better defined criteria of the reporters and subgroups upfront that define cognitive function and health state provides interpretable and representative data	Time to prepare and is often limited
Sample definition	FDA has provided recommendations, selection criteria, examples and information to ensure the sample is appropriate for a given scenario	Patient experience studies can be challenging to recruit and variability from the ideal sample needs consideration
Data sources – social media and DHTs	FDA's openness to new sources of data allows companies to stay current and integrate technology into patient experience research	Novel data collection methods introduce risk that sponsors may not be interested in adding (or have expertise to add) to the drug development program. Evidentiary standards (such as verified patient communities) for using these methods to collect well-defined, reliable and valid data are still being developed

SUMMARY OF CHANGES BETWEEN THE DRAFT AND FINAL PFDD-1

IQVIA PCE offers the following summary of the changes between the draft and final versions with PCE interpretations (in green) for consideration where appropriate:

- Matured introduction with emphasis on the expansive definition of patient experience
- Addition of "How would you define a meaningful change in that endpoint?" to the prior question of "How do you incorporate a given COA tool or set of measures into a defined clinical study endpoint?" to the description of PFDD-4
  Indicative of more emphasis on definition of clinically meaningful change in the upcoming PFDD-4 draft guidance
- Refinement of patient experience data description language to:
  "Patient experience data include the experiences, perspectives, needs, and priorities of patients related to:
  - » The signs and symptoms patients experience and how these signs and symptoms affect their day-to-day functioning and quality of life
  - » The course of their disease over time, including the effect the disease has on patients' day-to-day function and quality of life over time, and the changes that patients experience in their symptoms over time
  - » Patients' experience with the treatments for their disease: the symptoms and burdens related to treatment
  - » Patients' views on potential disease or treatment outcomes and how they weigh the importance of different possible outcomes
  - » How patients view the impact of the disease, treatment, and outcomes, and their view of potential tradeoffs between disease outcomes and treatment benefits and risks"

  This revision provides more patient-centric language such as replacing "natural history" with "course of disease over time" and reflects feedback received from patients
- Removal of reference to patient partners and the journey being enriched or informed by their input
  This change and others throughout the document reflects a dissuasion to allow others to speak on behalf of patients. Expert consultation is de-emphasized and was removed in the 'defining the research objectives and questions' section
- "Data Characteristics" removed from Methodological Distinctions for Collecting Patient Experience Data table (Table 1)
  Minor change as this method is a bit obscure
- Addition of "feasibility of leveraging existing literature and data" to list of factors that are important to consider when selecting a research approach
  This is a hopeful sign that FDA is more open to integration of published information
- Additional information in the 'Determining who will be providing patient experience data' section as follows:
  - » Restatement of the reference to include input from patient partners with a focus on appropriateness of methods before determining self-report data would be unreliable

  - » Addition of the qualification of 'valuable but distinct' information may still be obtained from caregivers, patient advocates, clinicians, and others
  - » Removal of age as factor to consider when deciding whether and how self-report may be included
  - » To what extent can patients reliably and validly self-report is added to reporter criteria

  Inclusion of data from anyone other than the patient is dissuaded and considerations for researchers to design appropriate methods for challenging patient populations are offered as preferable to incorporating clinicians, caregivers or patient advocates

- Subgroups are removed as a separate topic but remain integrated in discussion of considerations of sample size with a footnote definition
- Undercoverage sampling frame figure is removed and reference to example patient registries at the NIH website is added
- Missing data section updated with FDA recommendations to provide tabular summaries of missing data

  Addition of practical directions indicate FDA interest in preventing and understanding missingness – integration of SISAQOL findings
- Removal of all detail on qualitative, quantitative and mixed-methods research

  FDA provided updated section on analysis being driven by the research question and setting and reference to upcoming guidance. Information may have been seen as redundant with PFDD-2
- Changes to Operationalizing and Standardizing Data Collection and Management section
  - » Addition of Focus Groups, Facilitated discussions and social media to collecting data
  - » Replacement of "Questionnaires" with "Survey Instruments" and updated information

  Helpful clarification to define survey instruments and to provide reference to PFDD-3 for a discussion of COAs
- Examples of AV materials provided with addition of standardization requirements

  This addition is helpful to ensure better quality data
- Social media – replacement of "Designed online communities" with "Verified patient communities" and removal of "Spontaneous online communities" (Table 3)

  Reflection of the emphasis on verified communities provided in PFDD-2. This may be interpreted as FDA's interest in the reliability of social media data for drug development
- Removal of discussion of Digital Health Technology (retained as a data collection method)

  The rationale for this change is unclear at this time
- Addition of Data Analysis

  Flexible, brief description in lieu of prior extensive detail as discussed above
- Removal of Appendix 3 – considerations for data management

  Potentially redundant with other clinical data management guidance documents

PFDD Guidance 2 – Methods to Identify What is Important to Patients

OVERVIEW AND SUMMARY OF NEW INFORMATION

The second guidance in the series builds on the first where now that the methods to identify whom to get information from and how to collect that information are understood, how then do we determine what is most important to those patients. This guidance seeks to answer the questions of: *What do you ask, and why?* and *How do you ask non-leading questions that are well-understood by a wide range of patients and others?* The guidance answers these questions with methods to identify what matters most to patients regarding burden of disease and burden of treatment to guide medical product development. The guidance does not address methods for collecting and analyzing COA data or PPI data, rather these are methods to gain information that may inform the selection or development of COAs and the generation and use of PPI. Importantly, PFDD-2 also includes appendices that are highly practical for conducting patient experience research such as study materials, and information on screening and exit interview studies.

FDA again emphasizes the definition of research questions and patient population by first conducting background research with expert input in order to have a baseline characterization of the disease and available treatments. PFDD-2 then moves to a thorough discussion on qualitative, quantitative and mixed-methods research methods and then addresses specific populations and considerations for social media. While the 2009 PRO guidance describes the requirement of patient input to demonstrate content validity of a PRO intended to support label claims and mentions data from interviews and focus groups for this purpose, the information on available methods and how to best determine what is important to patients was limited. Therefore, much of the draft PFDD-2 guidance includes new directions for industry and is summarized in Table 4 on page 14. The final PFDD-2 guidance is anticipated to be issued in 2021.

PFDD Guidance 2 uses methods to identify what matters most to patients regarding burden of disease and burden of treatment to guide medical product development.

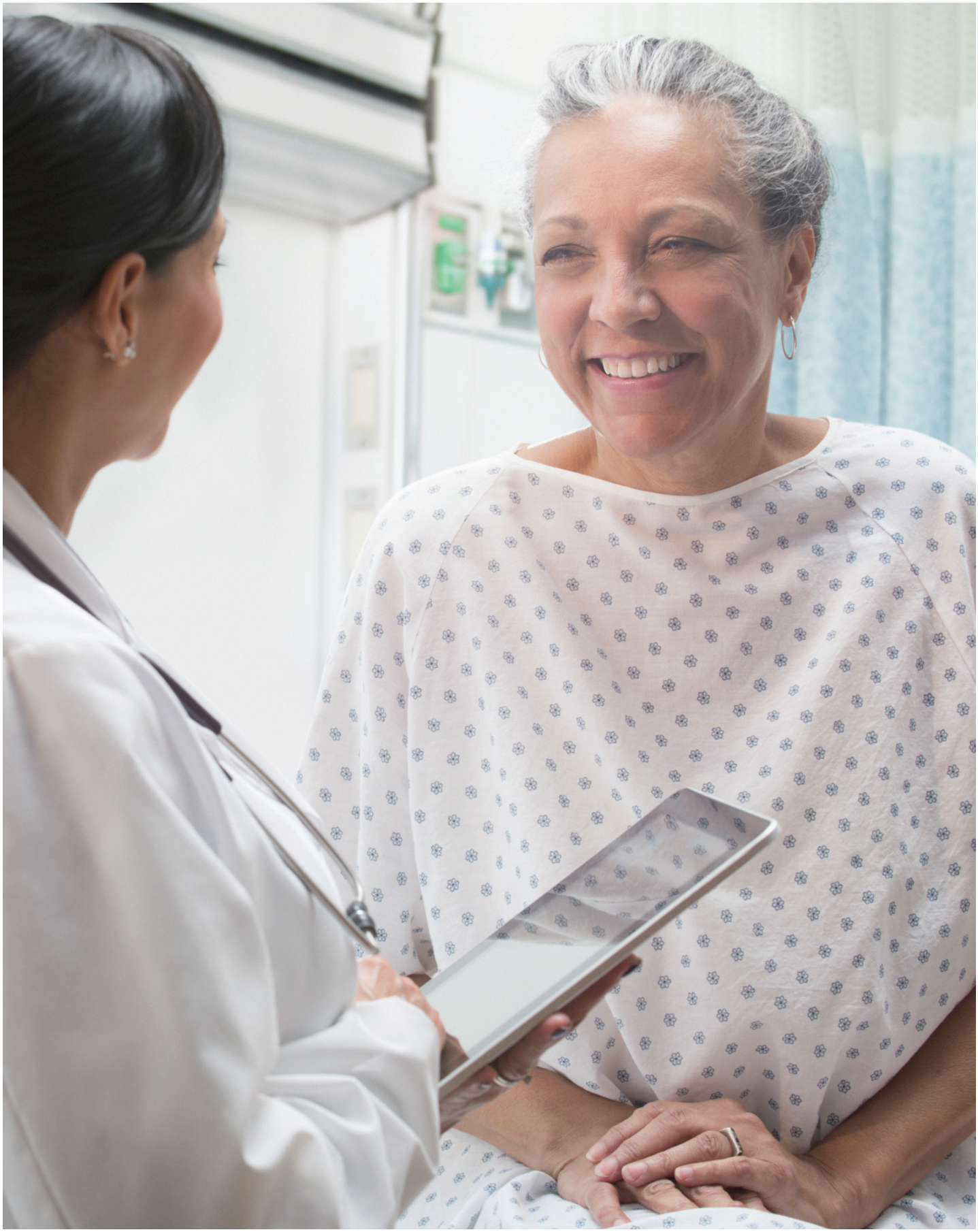


Table 4: New Directions from PFDD-2 on Identifying What is Important to Patients

TOPIC	DETAIL
Qualitative Research Methods	The following qualitative research methods are described by FDA with complete descriptions of the Agency perspective on potential strengths and limitations: one-on-one interviews, focus groups, Delphi methods, observational methods, and facilitated discussions at patient meetings and survey instruments with open-ended questions
Qualitative Research Methods One-on-one Interviews	As a common qualitative research method, FDA provides additional guidance on one-on-one interviews and recommend that sponsors determine the interview type method of administration of semi-structured, structured or unstructured interviews and then consider the following: • Number of interviews to conduct • Design interview questions and guide • Pilot test interview guide • Select/train interviewers • Recruitment strategy
Qualitative Research Methods One-on-one Interviews	The guidance again emphasizes that the interview plan should be tailored to the target population, study characteristics and design. FDA does not provide a preference in interview type but rather includes reference to a "growing body of literature" that suggest no differences in the accuracy of the data collected between modes
Qualitative Research Methods Focus Groups	FDA also provides further guidance on the other most common qualitative research method of focus groups where a moderator leads a discussion with a group of 5-10 participants. A presentation of the strengths and weaknesses of in-person focus groups and telephone or online focus groups is presented along with considerations for: • Number of focus groups to conduct • Sample size for each focus group
Qualitative Research Methods	FDA describes spontaneous responses as ideal but when prompting is required recommends specific approaches for collecting unbiased patient input of: • Use of a semi-structured interview guide • Not suggesting an answer • Not assuming to know what the participant is thinking or feeling • Not asking questions that cast judgment or imply that you prefer one response versus another Examples of problematic probing questions that are leading or cast judgment are also provided.
Qualitative Research Methods	FDA has provided specific considerations for the content of the following qualitative study materials: • Study protocol • Interview/discussion guide • Training material • Glossary • Coding dictionary • Data analysis plan
Analysis of Qualitative Data	Detail and examples for the qualitative analysis steps outlined in PFDD-1 including modes for displaying qualitative data and an example concept saturation table
Quantitative Research Methods	FDA guidance on survey instruments (not COAs for study endpoints) is focused on 1. Mode of administration (self or interviewer-administered) 2. Design and testing of instructions, questions and response options

TOPIC	DETAIL
Quantitative Research Methods	Considerations for development of survey instructions and questions are described such as: • Well-aligned with the research objective • Specific to concept of interest • Formatted simply • Assessed for potential social desirability bias Question formats to be avoided are provided such as: • Incomplete questions • Double-barreled or multi-barreled questions • Leading questions FDA includes examples for illustration
Quantitative Research Methods	Strengths, potential limitations and examples of closed-ended and open-ended survey questions are provided
Quantitative Research Methods	FDA also provides guidance with considerations and examples for design of the following response option types: • Checklist • Dichotomous • Rankings • Rating scales • Visual analog scale
Mixed Methods	FDA recommends that the goals and objectives of a mixed methods approach and how the results of both qualitative and quantitative research components are intended to be used together is well understood. The guidance provides questions and potential reasons for using a mixed method approach (such as supplementing or clarifying results from another method or expanding scope of the research question)
Mixed Methods	Examples of approaches are provided for: • Mixed-method study based on qualitatively driven concurrent design • Mixed-method study based on quantitatively driven sequential design • Mixed-method study with equal status sequential design
Specific Populations	Detailed considerations for populations that include children, cognitively impaired, rare diseases and patients from different cultures
Social Media	Careful selection of the source of the social media with the research question in mind is recommended. FDA prefers data from communities where personal information is provided to allow verification of personal characteristics
Social Media	Data analysis should address potential limitations (lacking mechanisms to verify patient characteristics) and how they can affect data integrity and interpretation.
Screening and Exit Interview Studies	Implementation of screening/exit interviews in clinical trials is discussed as helpful for understanding specific topics and strengths and weaknesses are described. Importantly, FDA recommends the interviews are done before or after patients complete the main portion of the trial to avoid potential to compromise trial integrity

IQVIA PCE DISCUSSION

The PFDD-2 Guidance again continues the theme of presenting methodologies instead of directives to incorporate the patient voice for a broad spectrum of purposes in drug development. This guidance provides a thorough presentation of summarized information, considerations, and examples to guide the decision-making of researchers that are looking to develop products that are informed by issues that are important to patients.

A clear take-away from PFDD-2 is that FDA is interested in prompting researchers to employ thoughtful methodologies that are supported by a proactive rationale. Good research practices of defining the objective, patient population and employing background research are emphasized as standard practice, but the specific method (e.g., interviews, focus groups, surveys, social media) to then determine what is important to patients should be informed by that foundation and each method has varied strengths and limitations. Once the method is selected, the implementation should then incorporate standards to optimize the quality of data. FDA provides specific directions on asking appropriate questions and identification of the strengths and weaknesses of interpretability due to potential data collection limitations. Table 5 on page 17 discusses these expectations along with other topics from the IQVIA PCE review of PFDD-2 including our perspective on the opportunities and challenges for the biopharmaceutical industry when considering methods for determining what is important to patients.

Conclusion

Guidances 1 & 2 fit together to outline the FDA expectations for sponsors generating a patient insight strategy. They provide clear guidance to ensure that sponsors use appropriate methodologies to obtain robust, meaningful, generalizable and interpretable patient input to understand their experience with their disease and its treatment to inform medical product development.

PFDD-1 and 2 can be used alongside the PRO Guidance to generate effective, patient-centered strategies to yield robust data to understand experience with disease and its treatment to inform development of endpoint measures for regulatory consideration. Table 6 on page 18 outlines some key questions sponsors may have in generating data to understand experience with disease and its treatment to inform development of endpoint measures, and provides reference to the FDA guidance document which should be consulted to provide direction.

Guidance 3 & 4, when available, will focus on measuring what is most important to patients in a reliable and interpretable manner using fit for purpose COAs in well-controlled clinical trials, and on structuring associated endpoints to inform regulatory decision-making.

Table 5: PFDD-2 Opportunities and Challenges

TOPIC	OPPORTUNITY	CHALLENGE
Determination of appropriate methodology (qualitative, quantitative or mixed-method) to determine what is important to patients	Researchers have flexibility to determine a patient-centric methodology that is appropriate for the specific research they are conducting which may yield better quality information leading to improved product development decision-making	This decision needs to be based on the research objective and made thoughtfully. Time, resource constraints as well as information silos may represent a challenge in supporting the methodology with an appropriate rationale
Selection of a qualitative method to determine what is important to patients	The qualitative method is not pre-specified and the array of options and detailed considerations provide ability to design creative studies that maximize the possibility of gaining meaningful data	In the event that a qualitative method is used with a weak rationale (such as 'we always do it this way') the incorporation of the conclusions may be poor or not supported
Direction on asking non-leading questions that are well-understood by a wide range of patients	FDA's recommendations are clear and present an opportunity to optimize data quality and reduce confusion when interpreting patient experience data	Investment in training interviewers and careful review and planning is required
Design of survey instruments as a quantitative method for determining what is important to patients	The recommendations from FDA provide opportunity to incorporate survey instrument information in determining meaningful concepts	Off the shelf surveys may need revision to ensure they comply with the guidance
Incorporation of a mixed-method approach to determining what is important to patients	Incorporation of different methods presents an opportunity to investigate unclear or "gray area" concepts using multiple techniques	The need for a mixed method approach may not be evident at the beginning of the research project and implementing it needs clear communication in order to not be seen as post-hoc or cherry picking
Incorporation of information from social media sources to determine what is important to patients	The openness of FDA to consider information from social media is important as a wealth of patient data exists on these platforms that may be useful to better understand what is meaningful to patients	Acceptability of data collected from social media where patient characteristics cannot be confirmed is unclear
Incorporation of Screening/Exit Interview or Survey Studies	Gain valuable patient feedback on experience with the product, trial and/or COA that can inform development	Cost and burden on site staff and patients in addition to the clinical protocol requirements

A clear take-away from PFDD-2 is that FDA is interested in prompting researchers to employ thoughtful methodologies that are supported by a proactive rationale.

Table 6: Common questions in generating data to understand experience with disease and treatment

QUESTION	HIGH LEVEL ANSWER	FDA GUIDANCE DOCUMENT FOR MORE INFORMATION
Why is patient experience data needed in drug development?	FDA values the use of patient input to help foster the development and availability of safe and effective medical products. The collection of patient input helps FDA gain a better understanding of the patient experience and expected clinical benefit Patients are experts in their own experience of their disease or condition and the ultimate consumers of medical products. The collection of patient experience data is important because it provides an opportunity to inform medical product development and enhance regulatory decision making to better address patients' needs	PFDD-1
How can I use patient experience data to support drug development?	Patient experience data is used to help inform clinical trial design, trial endpoint selection, and regulatory reviews including benefit-risk assessments as well as potential labeling (or other communications) Engaging patients actively in the development process can potentially improve rates of trial enrollment and retention and increase applicability to patients Patient experience data can be used to help identify unmet medical needs and important clinical outcomes to be studied, as well as inform the design of future clinical trials. Further, patient experience data can help inform COA development and selection, as well as analyses and communication of benefit-risk	PFDD-1
Who should I collect patient experience data from?	Without adequate documentation of patient input, a PRO instrument's content validity is likely to be questioned	PRO Guidance (2009)
	For the collection of patient experience data, FDA recommends direct reports from patients, unless they are unable to reliably report on the concept of interest (e.g., young children, individuals with cognitive problems)	PFDD-2
How do I collect patient experience data?	Patient experience data can be collected in a variety of research contexts, including (but not limited to): clinical trials, observational studies, advisory boards, public meetings, and other novel settings (e.g., online patient communities) The level of rigor needed for patient experience data generation can vary across studies and will depend on the intended use When studying patient experience, it is important to obtain patient experience data that are not only relevant, objective, and accurate, but also representative of the target population. PFDD-1 provides information on how to improve quality of research	PFDD-1
	PRO content validity is supported by evidence from qualitative studies	PRO Guidance (2009)
	Qualitative research methods (e.g., through interviews or focus groups), quantitative research methods (e.g., through survey instruments), or mixed-methods research (e.g., through open-ended and fixed-response items in a survey instrument) can be used to identify what is important to patients. These methods can be used either independently or complementarily When selecting an appropriate research method, FDA recommends carefully considering the research objectives PFDD-2 provides information on these methods and can be used as a basis from which to select the most appropriate method of collecting patient experience data	PFDD-2
Why is patient experience data needed to inform endpoint development?	FDA require evidence that any outcome measure comprehensively measures the concept of interest including evidence that the items and domains of an instrument are appropriate and comprehensive relative to its intended measurement concept, population, and use. This is called content validity. Testing other measurement properties will not replace or rectify problems with content validity.	PRO Guidance (2009)
How and when should I share patient experience data with FDA?	FDA encourages stakeholders considering collecting and submitting patient experience data to FDA to have early interactions with FDA during the design phase of such studies and obtain feedback from the relevant FDA review division	PFDD-1
	FDA encourages stakeholders to have early interactions with FDA and obtain feedback from the relevant FDA review division when considering collection of patient experience data related to the burden of disease and burden of treatment	PFDD-2

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As senior principal and head of Scientific and Analytic Research for the Patient Centered Sciences team at IQVIA, Matt provides scientific oversight and support to PCE consulting projects, and other PCE services that require scientific participation, with a focus on patient insight generation and COA.

Matt has extensive experience in COA development, implementation, analysis and interpretation.

He has worked across academic, consulting, clinical and industry settings and is an active leader in the COA science industry. Matt joined IQVIA in 2019.

Matt has a BS in Psychology, and an MS in Health Psychology. He is a Chartered Practitioner Health Psychologist and a Chartered Scientist. Matt has been awarded Fellowships by the Royal Society of Medicine and the Royal Society of Public Health and an Associate Fellowship by the British Psychological Society.

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As an associate principal and senior regulatory advisor for the Patient Centered Sciences team at IQVIA, Joy provides leadership in integration of the patient voice into effective data-driven regulatory strategies.

Joy has a broad industry background as a regulatory and quality professional. She has held leadership positions in multiple drug development programs with a consistent focus on the patient in all aspects, including heading up regulatory programs with patient experience data as a primary measure of effectiveness, establishment of quality systems in drug product manufacturing and oversight of clinical compliance for late-stage trials. Joy joined IQVIA in 2019.

Joy has a BS in General Biology from the University of California at San Diego.

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