Assessment of the Use of Patient Experience Data in Regulatory Decision-Making

Final Report

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Table of Contents

Tables

Figures

Executive Summary

Patient-Focused Drug Development (PFDD) is "a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation."[1] Under the 21st Century Cures Act of 2016 (Cures Act) and the FDA Reauthorization Act of 2017 (FDARA), the Food and Drug Administration (FDA) has been expanding its work to support PFDD. Among other efforts, the Agency has issued (and is preparing more) guidance for industry and other stakeholders.[2] As directed by section 3001 of the Cures Act, FDA shall make public a brief statement regarding the patient experience data and related information reviewed and submitted as part of approved drug and biologic marketing applications; to comply with this requirement, FDA has included a Patient Experience Data Table as part of publicly available review documents.

As required by the Cures Act, in 2021, 2026, and 2031, FDA will conduct assessments of its use of patient experience data in regulatory decision-making, in particular with respect to the review of patient experience data and information on PFDD tools as part of applications approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)). FDA contracted with Eastern Research Group, Inc. (ERG) to conduct this first assessment and produce this initial report.

To perform the assessment, ERG examined FDA review documents and product labeling for approved applications in a three-year cohort to determine what patient experience data applicants submitted and where and how FDA used the data. ERG also conducted focus group interviews with FDA staff, applicants, and other stakeholders (patients, caregivers, clinicians, advocacy/research organizations) to obtain opinions about the collection and use of patient experience data. A summary of these data appears in Results.

Answers to Assessment Questions

ERG synthesized data collection results from the focus groups to answer the following assessment questions.

How does FDA use patient experience data in regulatory decision-making? In deciding whether to approve a drug or biologic, FDA reviewers shared that they view their primary mandate as weighing the product's risks and benefits based on sound science. For patient experience data, this usually takes the form of Patient-Reported Outcomes (PROs) or other types of Clinical Outcome Assessments (COAs). While PROs or COAs are used in clinical trials as the primary or co-primary endpoint for many symptomatic conditions, PROs or other COAs are often used as secondary or exploratory endpoints. Patient experience data tend to play a central role in FDA decisions when PROs or other COAs are used as primary endpoints. Patient experience data generally provide supporting information in situations where the condition is not well characterized, as with some rare diseases.

[1] *https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development*
[2] *https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical*

The variability in FDA's use of patient experience data likely reflects (1) the wide range of diseases it regulates, and (2) the state of the science and evolution of PFDD. For example, FDA reviews medical products for symptomatic disorders where COAs are the primary endpoint in clinical investigations. FDA also regulates medical products for conditions where patient experience data can provide contextual or supporting information (e.g., tolerability, patient priorities or concerns) but are unlikely to provide primary evidence of efficacy, such as clinical investigations where primary endpoints are laboratory values. Many interviewees observed that industry and FDA are in the middle of a learning curve – where many COAs have been established, and at the same time the science has not yet caught up with the need and desire for more and better integration of patient input in product development and review.

How do FDA staff, applicants, and other stakeholders describe FDA's use of patient experience data in regulatory decision-making? In interviews, most FDA reviewers described their use of patient experience data in reviews and decision-making as science-based and evolving. Some stated that they use qualitative patient experience data as background and context for the review. Many stated that they look forward to being able to work with more patient experience data as more fit-for-purpose tools are developed.

In interviews, applicants and other stakeholders (patients, caregivers, clinicians, representatives of advocacy/research organizations) stated that they do not know how FDA uses patient experience data in regulatory decision-making. They stated that they would like to understand how FDA uses patient experience data – both at the broad conceptual level and for specific drugs and biologics. Despite a lack of knowledge about how FDA uses patient experience data, most applicants and other stakeholders recognize that FDA is making efforts and commended the Agency for being on a positive trajectory in this regard.

What good practices and opportunities for improvement exist for use of patient experience data in regulatory decision-making? In interviews, FDA staff, applicants, and other stakeholders identified several good practices: early and frequent communication (between applicants and FDA, and between applicants and patients), applicant development of a solid data analysis plan, applicant use of patient experience data to help design clinical trials, FDA use of patient experience data to help frame the review, FDA consultation with internal COA experts, and FDA and applicant sharing of patient experience data with the patient community.

Those interviewed also offered suggestions for improvement: organize all-stakeholder meetings to share perspectives and identify collaborative ways to advance the practice of PFDD; develop a catalog of PFDD tools, endpoints, and outcome measures with practical information on appropriate use; broaden consideration of patient experience data in application reviews; and establish expectations for representation of the full diversity of the patient population in PFDD.

Findings and Recommendations

1) FDA's commitment to advancing PFDD, including use of patient experience data in regulatory decision-making, is evident to most internal and external stakeholders.

Recommendation: No action needed.

2) When FDA uses patient experience data in regulatory decision-making, it usually takes the form of considering PROs and other COAs for primary endpoints in the risk-benefit analysis for a marketing application. FDA staff also use other patient experience data as background and context for the review.

Recommendation: No action needed.

3) Whether and how FDA uses patient experience data in application approval decisions varies widely.

In part, this is because (1) applications vary in the need for clinical and patient experience data, (2) applicants vary in whether and how they develop and use patient experience data, (3) the availability of fit-for-purpose PFDD tools varies by therapeutic context, and (4) the quality, completeness, and relevance of submitted patient experience data vary. In addition, FDA staff openness to use of patient experience data varies across (and sometimes within) CDER and CBER review divisions.

Recommendation for Applicants: When pursuing a drug/biologic development program, consult FDA guidance, other PFDD resources, and FDA staff early and often to discuss the potential value of patient experience data, types of data to develop, fit-for-purpose tools to use, approaches to collecting complete data, and a data analysis plan.

Recommendations for FDA: Continue or expand collaborative programs to foster development of PFDD tools and COAs. Internally and externally, provide models of applicant development and presentation of patient experience data in marketing applications and FDA use of these data in various therapeutic contexts. Within and across review divisions, encourage sharing of additional examples of use of patient experience data in regulatory decision-making.

4) Applicants, patients, caregivers, and other stakeholders cannot easily determine how FDA uses patient experience data in regulatory decision-making.

Recommendations for FDA: In the Patient Experience Data Table, add a column for "Use in Review" with a straightforward list of options (e.g., Background/Context, Risk-Benefit Analysis, Factor in Decision, and Not Used). In the Patient Experience Data Table, add a column for Not Used: Reason with a straightforward list of options (e.g., Tool not Fit-For-Purpose, Data Incomplete, and Data not for Primary or Key Endpoint). As noted in #3, provide models of applicant development and presentation of patient experience data in marketing applications and FDA use of these data in various therapeutic contexts.

5) Applicants and other stakeholders see a need for greater clarity and specificity in FDA expectations for patient experience data.

Recommendations for FDA: Continue to develop and update PFDD guidance (as planned). Consider expanding FDA's compendium of COAs to delineate not-yet-accepted as well as accepted patient experience PFDD tools and COAs, with information about when they are or are not acceptable and why. Ask FDA reviewers to include the topic of patient experience data in meetings with sponsors/applicants (to be proactive in discussing applicant plans and provide advice throughout drug/biologic development).

6) FDA included a Patient Experience Data Table in 82% of NME NDA and BLA reviews in the assessment cohort. While FDA includes the table in most reviews of applications with clinical data, it does not do so every time. This finding might reflect that the assessment cohort spans multiple years starting from the implementation date of the Cures Act,[3] that the Patient Experience Data table was phased in, and that the content of the table has evolved over time.

Recommendation for FDA: Continue to remind FDA reviewers to include a Patient Experience Data Table in review documents, including those for applications containing no clinical or patient experience data.

7) Many applicants stated that they cannot always get a meeting with FDA reviewers early and often (in a timely manner) to discuss patient experience data during drug/biologic development.

Recommendation for FDA: Conduct an assessment to better understand the extent that this has been the experience of applicants. If the experience is common or recurrent, conduct a root cause analysis to identify obstacles to scheduling meetings and allocating meeting time to discuss patient experience data early and often.

8) In collecting and reviewing patient experience data, some applicants and FDA staff focus on endpoints that are easily measured or of primary interest to clinicians. Patients would like greater attention to psychosocial, quality of life, and measures of ability to function.

Recommendation for FDA: See recommendations for 3 and 5.

9) In collecting patient experience data before and during clinical trials, engaging a representative and diverse patient population generates a greater understanding of patient concerns and enhances the utility and acceptability of patient experience data.

Recommendations for Applicants and Other Stakeholders: Refer to *FDA's PFDD Guidance 1*. Consult with a variety of patient organizations to help find diverse perspectives.

Recommendation for FDA: Continue to encourage and provide resources that support the collection of patient experience data in a manner that ensures its representativeness across the full diversity of the patient population.

[3] The assessment cohort encompasses three years of data, from Cures Act implementation in June 2017 to June 2020. Of FDA reviews of NME NDAs and BLAs in the cohort, 82% of those in the first year contain the Patient Experience Data Table, 77% of those in the second year contain the table, and 87% of those in the third contain the table. A few reviews contain a brief statement that no patient experience data were submitted instead of a table.

1. Introduction

This section presents background information as context for this assessment of the Food and Drug Administration's (FDA's) use of patient experience data in regulatory decision-making.

Note: Some terms in this report might not be familiar to all readers. To learn more about these terms, please visit the *BEST Glossary*, a product of an FDA-National Institutes of Health (NIH) Biomarker Working Group.

1.1 Regulatory Context

In 2012, the FDA Safety and Innovation Act (FDASIA) formally established a Patient-Focused Drug Development (PFDD) initiative to incorporate patient voice in drug and biologic development. FDA defines PFDD as "a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation."[4] The 21st Century Cures Act of 2016 (Cures Act) and the FDA Reauthorization Act of 2017 (FDARA) build on FDA's efforts under FDASIA, creating new directives and new opportunities for FDA to advance the science and efficiency of medical innovation, including in the area of PFDD.

Public Statement About Use of Patient Experience Data. Section 3001 of the Cures Act requires FDA to make public a brief statement on whether and how the Agency used any patient experience data and related information submitted by the applicant in reviewing a drug or biologic marketing application. The Federal Food, Drug, and Cosmetic (FD&C) Act, as amended by the Cures Act and FDARA, defines patient experience data as:

> "data that (1) are collected by any persons (including patients, family members, and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and (2) are intended to provide information about patients' experiences with a disease or condition, including (A) the impact (including physical and psychosocial impacts) of such disease or condition, or a related therapy or clinical investigation, on patients' lives; and (B) patient preferences with respect to treatment of such disease or condition."

This definition encompasses a wide range of types of patient experience data. Types of patient experience data and uses in regulatory decision-making are described in FDA's guidance on developing and submitting proposed draft guidance relating to patient experience data.[5]

For drug and biologic marketing applications received after June 12, 2017, FDA has been fulfilling the requirement to make public a statement about its use of patient experience data by including a Patient Experience Data Table in review documents for approved applications. FDA publishes these review documents at:

[4] *https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development*
[5] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/developing-and-submitting-proposed-draft-guidance-relating-patient-experience-data*

- *Drugs@FDA* for applications approved by FDA's Center for Drug Evaluation and Research (CDER).
- *Biological Approvals by Year* for applications approved by FDA's Center for Biologics Evaluation and Research (CBER).

The Patient Experience Data Table (Figure 1-1) provides a mechanism for reviewers to summarize the types of patient experience data that the applicant submitted as part of their application, whether they discussed the data in their review of the application, and whether they considered patient experience data from other sources.

Figure 1-1. Example of Patient Experience Data Table included in review documents for approved NDAs, BLAs, and supplemental applications

Patient Experience Data Relevant to this Application (check all that apply)

☐	**The patient experience data that were submitted as part of the application include:**			Section of review where discussed, if applicable
	☐	Clinical outcome assessment (COA) data, such as		
		☐	Patient reported outcome (PRO)	
		☐	Observer reported outcome (ObsRO)	
		☐	Clinician reported outcome (ClinRO)	
		☐	Performance outcome (PerfO)	
	☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)		
	☐	Patient-focused drug development or other stakeholder meeting summary reports		
	☐	Observational survey studies designed to capture patient experience data		
	☐	Natural history studies		
	☐	Patient preference studies (e.g., submitted studies or scientific publications)		
	☐	Other: (Please specify):		
☐	**Patient experience data that were not submitted in the application, but were considered in this review:**			
	☐	Input informed from participation in meetings with patient stakeholders		
	☐	Patient-focused drug development or other stakeholder meeting summary reports		
	☐	Observational survey studies designed to capture patient experience data		
	☐	Other: (Please specify):		
	Patient experience data was not submitted as part of this application.			

FDA Patient-Focused Initiatives. Section 3002 of the Cures Act requires FDA to issue new guidance regarding methods and approaches for capturing and measuring patients' experiences and perspectives. FDA held public workshops for each of the guidance documents to gather input from the community of patients, patient advocates, academic researchers, expert practitioners, drug developers, and other stakeholders. Information on these guidances can be found on FDA's PFDD guidance web page.[6] In addition to guidance, FDA also implements a variety of other Patient-Focused projects. [7]

Assessment of FDA Use of Patient Experience Data. Section 3004 of the Cures Act directs FDA to issue reports by June 2021, 2026, and 2031 assessing the use of patient experience data in regulatory decision-making, especially focusing on the review of patient experience data and information on PFDD tools as part of applications approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)).

1.2 This Assessment

FDA enlisted Eastern Research Group, Inc. (ERG) to conduct the first assessment of the Agency's use of patient experience data in regulatory decision-making and prepare a report for publication on FDA's website by June 2021.

ERG used a systematic process to identify, collect, and analyze comprehensive data for this assessment. This process involved developing assessment questions, determining the types of data needed to answer the questions, identifying data sources, designing data collection protocols and instruments, collecting and analyzing data, synthesizing results to answer the assessment questions, and distilling results into a cohesive set of findings and recommendations.

[6] *https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical*

[7] *https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development*

2. Results

To assess FDA's use of patient experience data in regulatory decision-making, ERG performed two types of data collections:

- **Examined FDA review documents and product labeling** for approved applications in a 3-year cohort to determine what patient experience data applicants submitted and where and how FDA used the data. The cohort included all 1,169 New Drug Applications (NDAs), Biologics License Applications (BLAs), and efficacy supplements that FDA received between June 12, 2017 and June 12, 2020 and approved by February 5, 2021 (Table 2-1). This approval cut-off date was chosen to allow time to collect data and complete the assessment. FDA publishes review documents and labeling for approved products at *Drugs@FDA* and *Biological Approvals by Year*.
- **Conducted focus group interviews with FDA staff, applicants, and other stakeholders** (patients, caregivers, clinicians, advocacy/research organizations) to obtain opinions about the collection and use of patient experience data. ERG interviewed 195 people in 62 groups.

The remainder of this section presents the results of these data collections.

Table 2-1. Distribution of application traits of NDAs, BLAs, and efficacy supplements* (n=1,169)

Trait	Categories	Distribution in Submissions
Application Type	NDAs	32%
	New Molecular Entity (NME) NDAs	*11%*
	Non-NME NDAs	21%
	BLAs	7%
	NME BLAs	*4%*
	Non-NME BLAs	*3%*
	Efficacy supplements	61%
	NDA efficacy supplements	*38%*
	BLA efficacy supplements	*23%*
Review Center	CDER	93%
	CBER	7%

*NDAs, BLAs, and efficacy supplements received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

2.1 Document Reviews

Mentions of Patient Experience Data in FDA Review Documents

For this assessment, ERG examined all NDAs, BLAs, and efficacy supplements in a three-year cohort. However, different types of applications vary in their need for clinical data. For example, applications for a new combination, formulation, manufacturer, or dosing regimen are much less likely to contain clinical data than applications for a New Molecular Entity (NME) or for a new indication for an existing product. The same is true for patient experience data.

In examining FDA review documents for the applications in the assessment cohort, ERG observed that many do not mention patient experience data. This is because:

- Many applications do not need clinical or patient experience data.
- Of submissions with clinical data, some do not contain patient experience data.
- Of submissions with patient experience data, some of the data are provided for background or context rather than risk-benefit analyses and approval decisions.

In general, NME NDAs and BLAs are expected to contain clinical data due to the depth of evidence required to support efficacy and safety in the patient population. Similarly, these applications are among the most likely to include patient experience data. Although ERG collected data for all applications in the cohort, in this report we present data for NME NDAs and BLAs as a proxy for applications where patient experience data are most relevant.

Of NME NDAs and BLAs in the assessment cohort, 68% of FDA reviews mention patient experience data (Table 2-2). Eighty two percent of these reviews include a Patient Experience Data Table: 82% of NME NDAs and BLAs in the first year in the cohort, 77% of those in the second year of the cohort, and 87% of those in the third year of the cohort. ERG also examined applications with special features, such as priority review and orphan product designation. The results were similar to those for all NMEs NDAs and BLAs.

Table 2-2. Results of metrics for mentions of patient experience data in FDA reviews*

Metric		FDA Reviews of Approved NME NDAs and BLAs (n=176)		
		All (n=176)	Priority Review (n=112)	Orphan (n=87)
Percent of approved applications where review documents mention patient experience data		68%	70%	66%
	Percent of approved applications where review documents mention patient experience data from **the application****	66%	66%	62%
	Percent of approved applications where review documents mention patient experience data from **other sources****	7%	9%	11%

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**Percentages sum to more than 68% (all NME NDAs/BLAs), 70% (Priority Reviews) or 66% (Orphan designation) because some review documents mention patient experience data from both the application and other sources.

Results by Type of Patient Experience Data. The results above show overall values for patient experience data submitted by applicants and data from other sources. Many different types of patient experience data exist, however. Here ERG describes the types of patient experience data that FDA mentions in reviews of NME NDAs and BLAs: mainly Patient-Reported Outcomes (PROs) or other types of Clinical Outcome Assessments (COAs) (Table 2-3).

PROs and other COAs are the types of patient experience data most likely to serve as endpoints in clinical trials (and are therefore mostly likely to be considered in risk-benefit analyses and approval decisions) while other types of patient experience data are more often used to understand patient priorities and preferences, the disease or condition, or burden on patients (and are therefore mostly likely to be used for background and context). To generate PRO and COA data, applicants typically use surveys, questionnaires, diaries, rating scales, and similar fit-for-purpose instruments.

Of patient experience data from sources other than the application, FDA reviewers most often cite information from PFDD meetings[8] (4%) and natural history studies (3%). FDA reviewers occasionally cite data from human factors studies and patient listening sessions[9] as well.

Table 2-3. Types of patient experience data mentioned in FDA reviews

Metric	FDA Reviews that Contain PED for Approved NME NDAs and BLAs (n=120)
Of FDA reviews that mention patient experience data, percent that mention data from **applicants**	97%
• PRO	84%
• ClinRO	33%
• PerfO	9%
• ObsRO	7%
• Patient preference study	3%
Of FDA reviews that mention patient experience data, percent that mention data from **other sources**	11%
• PFDD meetings	4%
• Natural history study	3%

PED = Patient Experience Data. PRO = Patient-Reported Outcome. ClinRO = Clinician-Reported Outcome. PerfO = Performance Outcome. ObsRO = Observer-Reported Outcome.

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**Percentages sum to more than 100% because some review documents mention patient experience data from both the application and other sources.

[8] https://www.fda.gov/industry/prescription-drug-user-fee-amendments/fda-led-patient-focused-drug-development-pfdd-public-meetings

[9] https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-listening-sessions

Location of Patient Experience Data in FDA Review Documents. FDA's review documents are divided into sections that discuss different types of data and reviews (e.g., clinical, nonclinical). For the applications in the assessment cohort, mentions of patient experience data most often appear in the Clinical/Statistical sections of review documents. For NME NDAs and BLAs, this value is 90%.

As noted in Section 1, as of June 2017 FDA is required to publish a brief statement about patient experience data or related information that was part of a drug or biologic application. The Patient Experience Data Table serves this purpose. Of NME NDA/BLA reviews that mention patient experience data, 88% contain a Patient Experience Data Table.

Presentation of Patient Experience Data in FDA Review Documents. In its reviews, FDA may use patient experience and other data in a variety of ways. ERG describes these ways as follows:

- **Summary of Data** – FDA presents or describes patient experience data without further interpretation or analysis.
- **Interpretation of Data** – FDA provides comments or conclusions about the relevance of the patient experience data to the review.
- **Analysis of Data** – FDA provides its own analysis of patient experience data in a different way than originally presented by the applicant.
- **Factor in Decision** – FDA explicitly cites patient experience data in the Benefit-Risk Framework or in other discussions of factors contributing to a regulatory recommendation or decision.

Metrics related to the use and presentation of patient experience data are shown in Table 2-4. Patient experience data are often presented multiple ways within FDA review documents, with the vast majority (97%) of reviews providing at least a summary of the data reviewed, and a significant proportion (49%) of reviews presenting further interpretation.

Table 2-4. Presentation of patient experience data in FDA reviews*

Metrics	FDA Reviews that Contain PED for Approved NME NDAs and BLAs (n=120)
Percent of applications where review documents present patient experience data in the form of: **Summary of Data**	98%
Percent of applications where review documents present patient experience data in the form of **Interpretation of Data**	48%
Percent of applications where review documents present patient experience data in the form of: **Factor in Decision**	16%
Percent of applications where review documents present patient experience data in the form of: **Analysis of Data**	15%

PED = Patient Experience Data.

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**The percentages shown in this table represent the number of applications with patient experience data in the format noted divided by the total number of applications with patient experience data. Percentages sum to more than 100% because patient experience data are sometimes presented in multiple ways.

Mentions of Patient Experience Data in Approved Product Labeling

Approved product labeling contains information supported by data from the marketing application; this can include patient experience data. ERG found that 30% of approved product labeling for NME NDAs and BLAs in the assessment cohort mention patient experience data (Table 2-5).

In general, approved labeling for NME NDAs and BLAs with priority review (53%) is more likely to mention patient experience data than labeling for NME NDAs and BLAs as a whole (30%). Product labeling that mentions patient experience data most often belongs to one of three therapeutic areas: congenital, familial and genetic disorders, nervous system disorders, or skin and subcutaneous tissue disorders. Data for these and other therapeutic areas appear in Appendix B. Additional Results.

Of NME NDAs and BLAs with approved labeling that mentions patient experience data, nearly all mentions COAs (92%), with the majority of those being PROs (67%). The remainder of the COAs are Clinician-Reported Outcomes (25%), Observer-Reported Outcomes (3%), and Performance Outcomes (3%). The remaining 8% mention natural history studies (6%), observational survey studies (1%), and qualitative studies (1%).

Table 2-5. Results of metrics for patient experience data in approved product labeling*

Metric	Product Labeling for Approved NME NDAs and BLAs with FDA Reviews that mention Patient Experience Data (n=36)
Percent of approved product labeling that mentions patient experience data	30%
Special Feature	
Percent of approved product labeling with patient experience data for applications with special feature: **Priority Review****	53%
Percent of approved product labeling with patient experience data for applications with special feature: **None****	44%
Percent of approved product labeling with patient experience data for applications with special feature: **Orphan****	39%
Therapeutic Area	
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Congenital, familial and genetic disorders****	17%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Nervous system disorders****	14%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Skin and subcutaneous tissue disorders****	14%

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**The percentages shown in this table represent the number of approved product labeling with patient experience data with the therapeutic area noted divided by the total number approved applications where FDA reviews mention patient experience data.

2.2 Interviews

This section highlights key themes and feedback from focus group interviews with FDA staff, applicants, and other stakeholders. For this assessment, ERG interviewed:

- 26 groups of FDA staff: a total of 91 FDA staff members across a broad array of CDER and CBER offices, divisions, and roles.
- 11 biopharmaceutical companies: a total of 29 people representing various roles in their companies. ERG selected applicants who represent a variety of company sizes, levels of experience submitting applications to FDA, regulatory outcomes for applications, and therapeutic areas.
- 25 groups of other stakeholders (patients and caregivers, clinicians, and research, education, support, and advocacy organizations): a total of 75 people representing a wide range of therapeutic areas. In addition, ERG selected stakeholders who represent a wide range of demographics and circumstances: by race/ethnicity, age, dis/abilities, sexual orientation, gender identity, socioeconomic status, geographic region, population density, and other identifying traits. Most of these individuals have experience partnering with FDA and/or industry for medical product development. For example, many had participated or were participating in FDA and other PFDD meetings, Advisory Committee meetings, listening sessions, focus groups, and clinical trials.

Table 2-6 presents a summary of interview comments that ERG received during these interviews.

Table 2-6. Interview comments from FDA staff, applicants, and other stakeholders (patients, caregivers, clinicians, advocacy/research organizations), by topic

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
Collection of Patient Experience Data		
• FDA reviewers rely mainly on data collected by applicants. • FDA reviewers sometimes seek patient experience data from PFDD meetings and Voice of the Patient reports, patient workshops and symposiums, patient testimony at Advisory Committee meetings, patient listening sessions, patient advocacy group meetings, clinical practice, and the medical device reporting system. • These sources provide valuable therapeutic context for what patients find meaningful in treating their condition, which provides a frame of reference for application reviews. • A few interviewees noted that a limitation of these sources is that they give voice to a relatively small percentage of patients who might not be representative of the larger patient population. • Patient experience data in the form of adverse events reported to FDA inform the Agency's surveillance efforts. **Good practice for FDA:** • Use patient experience data from a variety of sources as a frame of reference for evaluating the clinical meaningfulness of endpoints and other data submitted in applications to support drug/indication approval. **Good practice for applicants:** • Ensure that patient experience data collection is convenient and not too burdensome for patients. **Challenges for applicants:** • Fit-for-purpose instruments are not yet available for all endpoints and other measures of interest. • Instruments that are fit-for-purpose for some indications cannot always be used for other indications. • Some study designs do not adequately consider patients' circumstances that might constrain their ability to complete questionnaires and other clinical trial activities.	• The amount and types of patient experience data that applicants collect vary with several factors, including company culture, disease area of focus, and company size. Types of patient experience data collected can include: ○ None. ○ A limited number of PROs known to be accepted and valued by FDA. ○ Data to help determine how to design clinical trials in ways that minimize the burden to patients. ○ Data to help select clinically meaningful endpoints and other measures. ○ A robust array of patient experience data from the pre-competitive period through post-marketing. ○ Patient experience data to support the needs of other stakeholders, especially payers. • Perceived FDA expectations influence the amount and types of patient experience data that applicants collect. Ultimately, applicants need to invest time and resources in areas that will advance product development and contribute to positive regulatory outcomes. **Challenges for applicants:** • Difficult to justify patient experience data internally without knowing whether or how FDA will use it. • Inconsistent openness to patient experience data across FDA review divisions, which sends mixed signals to applicants about the value of the data. • Lack of fit-for-purpose tools and instruments to collect patient experience data. • The time and expense involved in establishing these tools and instruments.	• Patient experience data should be collected and used to understand: ○ How to make it as easy as possible for patients to participate in clinical trials (to maximize diverse participation and data completeness). ○ Context, priorities, benefit-risk tradeoffs, practical and logistical issues, psychosocial issues, and other factors that shape patient perspectives. ○ Natural history of condition, burden and impacts of condition, burden and impacts of treatment, expectations for benefits, tolerance for risks and uncertainties, and unmet medical needs. ○ PROs and other COAs that help establish product safety and efficacy. **Challenges for all** • Variability in applicants' commitment to inclusion of patient voice throughout product development. • Insufficient guidance, expectations, or mandates from FDA to collect and present patient experience data in a robust manner (though this is evolving). • Gaps in the science and development of fit-for-purpose tools and instruments. • The time and expense involved in establishing these tools and instruments. • Insufficient diversity in PFDD, resulting in gaps in knowledge about concerns of people of varying demographics and circumstances. • Insufficient attention to psychosocial, mental health, activities of daily living, and other measures of ability to function, quality of life, and similar concerns that are important to patients and caregivers. • Disproportionate attention on endpoints that are easily measured or primarily of interest to clinicians.

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
Patient Experience Data Submitted in Applications		
• Applications vary widely in the amount and types of patient experience data included. To some extent, this varies by indication; for example, conditions with mild symptoms or mainly laboratory findings are less often associated with patient experience data than conditions that are chronic or otherwise burdensome to patients and caregivers. • The types of patient experience data most often found in applications are PROs and other COAs from surveys, questionnaires, diaries, rating scales, or other instruments. • The quality and completeness of the data are variable. In fields with well-established endpoints and fit-for-purpose tools, the quality and completeness of data are high – comparable to any other type of clinical trial data. However, PROs and other COAs are sometimes compromised by missing data. • With diseases that are less well-characterized, with less well-defined endpoints, patient experience data are sometimes less complete and lower quality. **Good practices for applicants:** • Begin discussing patient experience data with FDA early and often in order to facilitate optimum clinical trial design and selection of endpoints (and appropriate data collection methods) that are most clinically meaningful. • Develop a scientifically sound analysis plan that addresses methodological, quality, and completeness issues.	• PROs and other COAs are the primary types of patient experience data submitted in NDAs, BLAs, and efficacy supplements. • Some applicants also submit other types of patient experience data to (1) provide background or context for their applications or (2) justify their selection of endpoints, measures, and data collection tools. • Some applicants refrain from submitting more types of patient experience data until they receive more information from FDA about whether reviewers will accept the data, value the data, and use the data in risk-benefit assessments or regulatory decision-making. **Good practices for applicants:** • Engage and maintain contact with patient communities throughout the product development lifecycle to collect high-quality patient experience data and to foster transparency and confidence. • Meet with FDA reviewers and COA experts as early as possible to discuss patient experience data. • Refer to FDA guidance, which clearly defines types of patient experience data and methods for collecting patient experience data. • Other good resources include patient organizations and registries, and PFDD and other similar meetings. **Challenges for applicants:** • Meeting and discussing patient experience data with reviewers and FDA COA experts early and often is sometimes limited by FDA availability. • FDA acceptance and use of patient experience data appear to be inconsistent across (and sometimes within) review divisions, leading to a lack of predictability in FDA expectations. • Evidentiary standards for use of patient experience data are unclear. This is true for background or contextual	**Good practices for applicants:** • In applications, use patient experience data to justify selection of endpoints and other measures to FDA reviewers. • Submit a broad range of patient experience data: for background/context, to establish clinical meaningfulness of endpoints and other measures, and to demonstrate outcomes that matter to patients as well as clinicians.

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
	patient experience data, for patient experience data used to justify selection of endpoints, and for patient experience data used for secondary and exploratory endpoints. • Evidentiary standards for including patient experience data in labeling are unclear.	
Use of Patient Experience Data in FDA Reviews		
• PROs and other COAs are the main types of patient experience data used for clinical trial endpoints. PROs and other COAs of sufficient quality and completeness are treated the same as other data; they are not explicitly called out as patient experience data in risk-benefit analyses and decisions. • Other types of patient experience data sometimes provide a frame or context for reviews – for example, to demonstrate that the endpoints or outcomes used are clinically meaningful or important to patients. • Data for primary or co-primary endpoints are integral to risk-benefit analysis and approvability decisions. Data for secondary endpoints may be less applicable or rigorous, and might be considered based on the acceptability of the tools used. • Exploratory endpoints and qualitative or subjective patient experience data collected in non-standardized ways might not provide support for the risk-benefit analysis; these are supplementary or descriptive data that provide context rather than a basis for decision-making. • In rare diseases, a broader range of patient experience data is important in contextualizing the impact of the disease on patients in terms of characterizing a disease, symptomology and natural history, burden on patients, unmet needs, clinically meaningful endpoints, and therapeutic priorities. These elements are essential to designing clinical trials with small populations and conducting risk-benefit analyses of the data.	• A close reading of review documents shows that FDA uses patient experience data (mainly PROs and other COAs) in at least some application reviews and regulatory decision-making. • How FDA uses patient experience data in reviews and decision-making is generally unknown. • FDA appears to focus on objective data and endpoints. • Seeing mentions of PROs or other COAs in review documents suggests that FDA appears to be increasing its use of these data. • Patient experience data do not often appear in labeling, except in some instances where specific PROs or other COAs contributed to product approval.	• How FDA uses patient experience data in reviews and decision-making is generally unknown. • FDA review documents are too lengthy, technical, and regulator-oriented to be useful to most people who are not physicians or scientists. • FDA review documents do not explain the role of patient experience data in regulatory decision-making. • Product labeling rarely includes information about patient experience data. • Based on experience participating in PFDD meetings, listening sessions, and Advisory Committee meetings, FDA's commitment to the use of patient experience data appears to be expanding – and this is to be commended.

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
• Some FDA reviewers frequently work with patient experience data, while others rarely do. To some extent, this varies by therapeutic area or indication (as noted above). **Challenges for FDA (from a few FDA staff):** • Determining whether ratings used in scales are clinically meaningful to patients. • Determining whether PROs have bias that might skew results. • Determining whether patient testimonials at Advisory Committee meetings represent the experience of opinion leaders or a majority of the patient population. • Deciding where to include patient experience data in reviews when data are not efficacy/safety assessments. • Addressing use of patient experience data to justify unsubstantiated claims of superiority (to a competitor product) in labeling and promotional materials.		
Patient Experience Data in FDA Review Documents and Approved Product Labeling		

• FDA uses the Patient Experience Data Table to identify the locations of patient experience data in the review without describing the role that the data played in the review.
• FDA cites patient experience data in Benefit-Risk Frameworks when the data are central to the risk-benefit analysis.
• When PROs or other COAs are used to justify claims, they may be included in labeling. Most labeling does not reference framing or contextual patient experience data because they cannot be used to justify claims.
Good practice for FDA:
• Work with COA experts within FDA as needed because they are valuable resources in evaluating patient experience data.
	• PROs or other COAs appear in labeling when they contribute to product approvability.
	• Other types of patient experience data do not generally appear in labeling.
	Suggestions to FDA (from a few applicants):
	• In labeling, include more information about patient experiences with treatment so clinicians can offer advice to patients on what to expect and how to manage any side effects.
	• Provide patient experience data in Plain English in a separate (new) section of the label or in a patient information sheet. Dissenting view: Doing so might have the unintended consequence of people perceiving these data to be less important than other types of data.
		Suggestions to FDA:
		• In review documents, explicitly identify patient experience data as such and explicitly describe how reviewers weighed these data in the risk-benefit analysis and decision-making.
		• In the label or a separate patient information sheet:
		  ○ Explicitly identify the contributions of patient experience data to the information presented.
		  ○ Provide Plain English information about patient experience data of interest to clinicians and patients; if possible, structure this in a consistent format that is digestible and facilitates comparison of similar information across labeling/information sheets.

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
Suggestions to Advance Development of or Communication About Patient Experience Data		

• Continue the many PFDD initiatives the Agency has already begun.	• A roadmap articulating what patient experience data FDA considers useful or valuable under what circumstances.
	• Expanded FDA guidance on development of new fit-for-purpose COAs and other patient experience data – by therapeutic area or indication, where appropriate.
	• Collaborative initiatives (encompassing all stakeholders) to develop new fit-for-purpose COAs and other patient experience data.
	• A public inventory of tools that FDA considers acceptable or unacceptable, under what circumstances (e.g., in what indications and populations), and why.
	• A dedicated meeting pathway for discussing patient experience data with FDA.
		• Improve communication on how FDA uses data collected via PFDD meetings and other forums.
		• Improve communication on how FDA uses data in specific application reviews.
		• Disseminate information about FDA's use of patient experience data to stakeholders by:
		  ○ Emails, newsletters, social media, and other methods of communication.
		  ○ Further developing and leveraging partnerships with patient advocacy organizations to disseminate the information through their networks.
		• Organize more public meetings in which FDA, industry, clinicians, patient advocacy and research organizations, and patients and caregivers can share ideas and constraints – to enhance understanding across stakeholders and innovate development of paths forward that are both feasible and meaningful.
		• Further develop collaborations between these parties to identify, design, and develop new patient experience data tools and metrics – to speed development of better tools while avoiding burdensome costs for any single party.
		• Develop and maintain a catalog of accepted (and not-yet-accepted) patient experience data-based endpoints, outcome measures, and data collection tools – flagged by indications or other considerations where appropriate – as a reference for the Agency, industry, and other stakeholders. This could be an expansion of FDA's compendium of COAs.[10]
		• Broaden consideration of patient experience data in application reviews: context-setting use of these data, and consideration of endpoints and measures that are not yet fully or widely accepted in order to (1) contribute to a body of knowledge and evidence that could bolster or

[10] *https://www.fda.gov/drugs/development-resources/clinical-outcome-assessment-compendium*

FDA Staff Comments	Applicant Comments	Other Stakeholder Comments
		refine their use in the future, (2) share information that is useful for clinicians and patients, even if it cannot be used for decision-making, and (3) gain a fuller picture of patient experience with the disease or therapy. • Establish expectations for representation by all demographics and circumstances that are important in the patient population. This might include race/ethnicity and culture, gender, age, dis/abilities, gender identity, sexual orientation, language, socioeconomic status, proximity to research sites, access to transportation, access to technology, etc. This will enhance patient voice and clinical trial design in ways that are practical and meaningful for patients. Note: *FDA published the final Patient-Focused Drug Development Guidance 1[11] in June 2020, which provides guidance on collecting comprehensive and representative input from patients. This guidance addresses some but not all types of patient demographics and circumstances proposed by stakeholders.*

[11] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input*

3. Assessment Questions and Answers

This section provides answers to the assessment questions based on analysis and synthesis of the results presented in Section 2 of this report.

3.1 How does FDA use patient experience data in regulatory decision-making?

In interviews, FDA staff defined regulatory decision-making mainly in terms of reviewing marketing applications and deciding whether to approve the new drugs/biologics (or the new indications or other new claims for previously approved drugs/biologics). To answer this question, therefore, ERG focuses primarily on FDA's use of patient experience data in reviewing NDAs, BLAs, and efficacy supplements.

According to staff interviewed for this assessment, in deciding whether to approve a drug or biologic FDA's primary mandate is to weigh the product's risks and benefits based on sound science. Therefore, staff mainly consider safety and efficacy data from well-designed studies. For patient experience data, this usually takes the form of PROs and other COAs. While PROs or COAs are used in clinical trials as the primary or co-primary endpoint for many symptomatic conditions, PROs or other COAs are often used as secondary or exploratory endpoints. Patient experience data tend to play a central role in FDA decisions when PROs or other COAs are used as primary endpoints. Patient experience data provide supporting information in situations where the condition is not well characterized, as with some rare diseases.

The variability in FDA's use of patient experience data likely reflects (1) the wide range of diseases it regulates, and (2) the state of the science and evolution of PFDD. For example, FDA reviews medical products for symptomatic disorders where COAs might be the primary endpoint. It also regulates medical products for conditions where patient experience data can provide contextual or supporting information (e.g., tolerability, patient priorities or concerns) but are unlikely to provide primary evidence of efficacy, such as certain conditions where primary endpoints are laboratory values. Many interviewees observed that industry and FDA are in the middle of a learning curve – where many COAs have been established, and at the same time the science has not yet caught up with the need and desire for more and better integration of patient input in product development and review. Many FDA staff expressed interest in using more patient experience data as the field evolves.

FDA staff, applicants, and other stakeholders stated their belief that some of this variability stems from the extent to which:

- The application includes clinical data.
- The application includes patient experience data.
- The patient experience data are scientifically sound – that is, PROs or other COAs from fit-for-purpose tools and of sufficient completeness and quality for analysis.
- The patient experience data are relevant to FDA's risk-benefit analysis for the application.

In turn, these factors stem from the extent to which:

- Patient experience data are central to understanding safety and efficacy for the product's indication. For example, patient experience data sometimes play a minor role in asymptomatic conditions where the main endpoints are laboratory results and acute conditions with mild symptoms. At the other extreme are chronic conditions that are life-threatening, that severely impact the patient's ability to function, or that involve major psychosocial concerns.
- Fit-for-purpose tools exist for collecting the types of patient experience data that are clinically meaningful and relevant to the product's indications. Many interviewees stated that they would like to provide or review more or different types of patient experience data – that better reflect patients' concerns and priorities – but fit-for-purpose tools do not exist. Design and development of new tools are time-consuming and expensive, so some applicants are unable to develop them in a timely fashion or at all.
- Applicants believe that FDA will accept and consider the types of patient experience data that they are able to collect. Many interviewees stated that FDA focuses primarily on scientifically sound data, by which they mean data that meet FDA methodological standards for completeness and quality.
- The applicant chooses to collect patient experience data and include them in the application. Interviewees stated that the culture of a company and the value it places on including the voice of the patient in medical product development vary – and this variability is independent of the therapeutic area, company size, or level of experience the company has in product development.

Some FDA staff noted that they use other (non-COA) patient experience data from applicants – as well as data from other sources, such as PFDD meetings, other workshops, focus groups, listening sessions, and literature searches – as context to help frame their review. The information helps them understand patient concerns and priorities, which provides valuable context for considering the relevance and clinical meaningfulness of the safety and efficacy data that they are reviewing. These staff stated that they begin talking with applicants about the need for patient experience data – and how they will be used in clinical trial design and implementation – early in the drug development process.

Outside of application reviews, some FDA staff described using patient experience data for other purposes, such as monitoring postmarket safety and revising product labeling.

3.2 How do FDA staff, applicants, and external stakeholders describe FDA's use of patient experience data in regulatory decision-making?

FDA Staff. In interviews, most FDA reviewers described their use of patient experience data in reviews and decision-making as science-based. They expressed the view that their central task is to perform a scientifically sound risk-benefit analysis as a basis for decision-making. Therefore, they stated that they mainly consider validated and widely accepted PROs (and other COAs) in their risk-benefit analyses and regulatory recommendations and decisions. Some reviewers also described their use of other types of patient experience data as providing context; they use patient experience data to assess the clinical meaningfulness of the endpoints in the clinical trials.

Many FDA interviewees also described the Agency's use of patient experience data as evolving. They stated that this is an evolving field, with FDA staff, applicants, patients, caregivers, and other stakeholders at varying points on the learning curve. Many FDA interviewees expressed an interest in receiving, reviewing, and using more patient experience data (as long as the patient experience data are scientifically sound). Some interviewees, particularly those who review products that rely on laboratory findings, expressed the belief that patient experience data will continue to play a minor role in their fields, even as the use of patient experience data grows in other therapeutic areas or review domains.

Applicants and Other Stakeholders. These interviewees noted that they do not know how FDA uses patient experience data in regulatory decision-making. These groups vary in the extent to which they read FDA reviews of marketing applications for new drugs and biologics. According to the people we interviewed, applicants read the reviews consistently; some advocacy/research organization staff and clinicians who partner with industry and FDA read the reviews; and most other advocacy/research organization staff, clinicians, and patients and caregivers do not read the reviews. Those who do read FDA's review documents rarely find information about how FDA uses patient experience data in its risk-benefit analyses and decisions. All interviewees stated that they would like to understand how FDA uses patient experience data in regulatory decision-making – both at the broad conceptual level and for specific drugs and biologics. In addition, many applicants stated that FDA staff openness to patient experience data appears to vary across (and sometimes within) CDER and CBER review divisions; this perception is based on their experience with FDA staff during meetings.

By contrast, all applicants and other stakeholders (except patients) read product labeling. During the review process, the applicant and FDA staff work to establish language for product labeling that can be justified based on data from the marketing application. Therefore, the two parties have an opportunity to include patient experience data in labeling to the extent that these data support the information in the labeling. In interviews, FDA staff, applicants, and other external stakeholders agreed that patient experience data rarely appear in product labeling. ERG examined the package inserts of approved applications in our assessment cohort. In contrast to the perceptions of internal and external stakeholders interviewed for this assessment, we found that 30% of approved NME NDAs and BLAs with patient experience data mentioned in review documents also contain references to patient experience data in their labeling – mainly PROs and other COAs. It is possible that interviewees underestimate the prevalence of patient experience data in labeling because they:

- Perceive patient experience data as not yet central to regulatory decision-making.
- Do not easily notice or recognize patient experience data in Section 14 of the package insert (where clinical trial data are discussed) because this section is dense and technical.

In interviews, applicants and other stakeholders also commented that they rarely hear from FDA about its consideration of patient experience data through other mechanisms – such as follow-up after PFDD or Advisory Committee meetings. In some cases, they are told that FDA will use the information, but afterward they generally do not hear whether or how it has been used. In some cases, patients and other stakeholders stated that they believe that FDA considered their input in Advisory Committee meetings because of the decisions that were made, but they were not told this explicitly.

Despite a lack of knowledge about how FDA uses patient experience data in regulatory decision-making, most applicants and other stakeholders recognize that FDA is making efforts in this regard. Indeed, many stated that FDA should be commended for its commitment to expanding use of patient experience data in drug development and regulatory decision-making. Even if much more work is needed, many interviewees believe that FDA is on a positive trajectory in this regard.

3.3 What good practices and opportunities for improvement exist for use of patient experience data in regulatory decision-making?

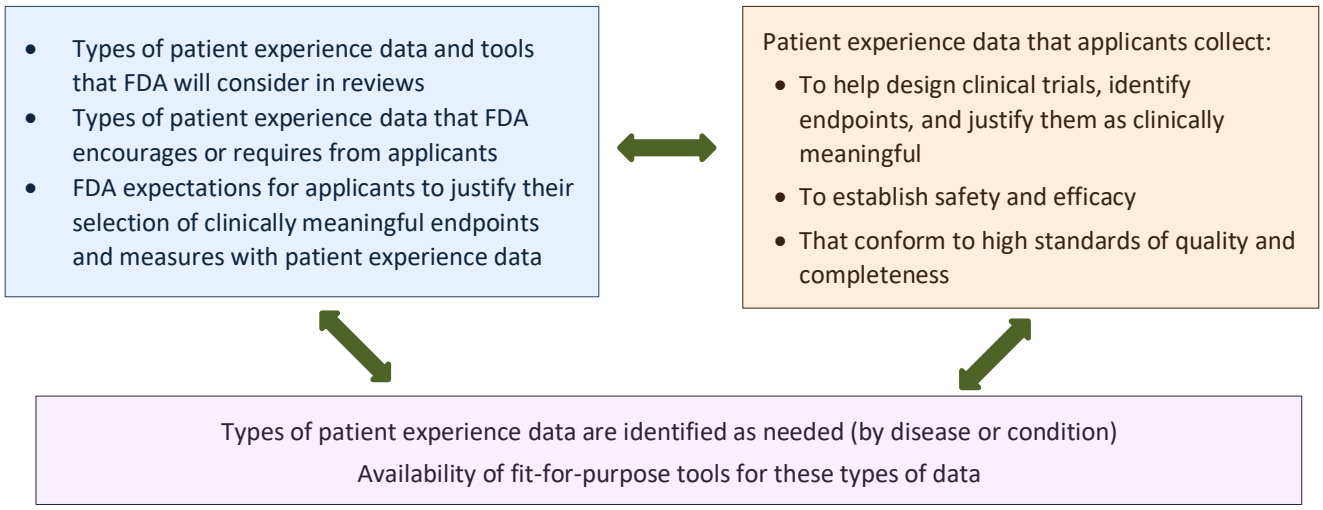
FDA staff and applicants interviewed for this assessment identified some good practices related to the use of patient experience data in regulatory decision-making. Those identified as being suitable for broader adoption appear in Table 3-1.

FDA staff, applicants, and other stakeholders interviewed for this assessment identified several suggestions for improving the use of patient experience data in regulatory decision-making. In so doing, many acknowledged that some suggestions might not be feasible in the short term and some might be outside FDA's purview. Some interviewees also commented on the interrelationships between the state of the science, FDA expectations, and industry behavior (Figure 3-1), all of which influence what patient experience data FDA can use in regulatory decision-making.

Table 3-1. Good practices for using patient experience data in regulatory decision-making, as identified by FDA staff, applicants, and other stakeholders (patients, caregivers, clinicians, advocacy/research organizations) interviewed for this assessment

FDA	• Talk with applicants early and often in drug development about good practices in collecting and using patient experience data • Emphasize to applicants the need for a solid analysis plan before gathering patient experience data • Use patient experience data from applicant, FDA meetings, and other sources to provide context, help frame the review, and identify or select relevant and important concepts of interest • Obtain internal COA expertise when needed
Applicants	• Establish a company-wide culture and expectation of patient inclusion in drug development • Talk with FDA early in drug development about good practices in collecting and using patient experience data • Include patients/caregivers in advisory boards to help identify meaningful endpoints and outcome measures, design clinical trials, and review and refine clinical trials in progress • Develop a solid analysis plan for patient experience data, with feedback from FDA
Other Stakeholders	• Collect patient experience data to determine how to make it as easy as possible for patients to participate in clinical trials (to enable generation of data that meets goals for completeness), and to identify what endpoints and other measures are meaningful to patients • Consult with patients throughout entire drug/biologic development lifecycle (to obtain insights that can improve methodologies at every stage of development) • Share results of patient experience data collections with study participants and patient advocacy groups (to maintain positive relationships and obtain additional, ongoing insights)

Figure 3-1. Interplay between factors that influence FDA use of patient experience data



Suggestions for improving use of patient experience data in regulatory decision-making encompass the full drug development process because of the interrelationships described in Figure 3-1. Suggestions offered by applicant and other stakeholder interviewees include:

- Organize meetings in which FDA, industry, clinicians, patient advocacy and research organizations, and patients and caregivers can share their perspectives, ideas, and challenges. This will foster greater understanding across groups as well as development of paths forward that are both feasible and meaningful to all parties.
- Help develop collaborations between these parties to identify, design, and develop new PDFDD tools and metrics. This will speed development of better tools while avoiding burdensome costs for any single party.
- Develop and maintain a catalog of accepted (and not-yet-accepted) PFDD tools, endpoints, and outcome measures – flagged by indications or other considerations where appropriate – as a reference for the Agency, industry, and other stakeholders.
- Broaden consideration of patient experience data in application reviews. This includes the context-setting use of these data described above. It also includes consideration of endpoints and measures that are not yet fully or widely accepted in order to (1) contribute to a body of knowledge and evidence that could bolster or refine their use in the future, (2) share information that is useful for clinicians and patients, even if it cannot be used for decision-making, and (3) gain a fuller picture of patient experience with the disease or therapy.
- Establish expectations for representation of the full diversity of the patient population – in order to better represent patient voice, design clinical trials in ways that are practical and meaningful for patients, and generate patient experience data that prescribers can consider in treating patients of varied identities and circumstances.

4. Findings and Recommendations

This section provides findings and recommendations regarding the use of patient experience data in regulatory decision-making.

1) FDA's commitment to advancing PFDD, including use of patient experience data in regulatory decision-making, is evident to most internal and external stakeholders.

Recommendation: No action needed.

2) When FDA uses patient experience data in regulatory decision-making, it usually takes the form of considering PROs and other COAs for primary endpoints in the risk-benefit analysis for a marketing application. FDA staff also use other patient experience data as background and context for the review.

Recommendation: No action needed.

3) Whether and how FDA uses patient experience data in application approval decisions varies widely.

In part, this is because (1) applications vary in the need for clinical and patient experience data, (2) applicants vary in whether and how they develop and use patient experience data, (3) the availability of fit-for-purpose PFDD tools varies by therapeutic context, and (4) the quality, completeness, and relevance of submitted patient experience data vary. In addition, FDA staff openness to use of patient experience data varies across (and sometimes within) CDER and CBER review divisions.

Recommendation for Applicants: When pursuing a drug/biologic development program, consult FDA guidance, other PFDD resources, and FDA staff early and often to discuss the potential value of patient experience data, types of data to develop, fit-for-purpose tools to use, approaches to collecting complete data, and a data analysis plan.

Recommendations for FDA: Continue or expand collaborative programs to foster development of PFDD tools and COAs. Internally and externally, provide models of applicant development and presentation of patient experience data in marketing applications and FDA use of these data in various therapeutic contexts. Within and across review divisions, encourage sharing of additional examples of use of patient experience data in regulatory decision-making.

4) Applicants, patients, caregivers, and other stakeholders cannot easily determine how FDA uses patient experience data in regulatory decision-making.

Recommendations for FDA: In the Patient Experience Data Table, add a column for "Use in Review" with a straightforward list of options (e.g., Background/Context, Risk-Benefit Analysis, Factor in Decision, and Not Used). In the Patient Experience Data Table, add a column for Not Used: Reason with a straightforward list of options (e.g., Tool not Fit-For-Purpose, Data Incomplete, and Data not for Primary or Key Endpoint). As noted in #3, provide models of applicant development and presentation of patient experience data in marketing applications and FDA use of these data in various therapeutic contexts..

5) Applicants and other stakeholders see a need for greater clarity and specificity in FDA expectations for patient experience data.

Recommendations for FDA: Continue to develop and update PFDD guidance (as planned). Consider expanding FDA's compendium of COAs to delineate not-yet-accepted as well as accepted patient experience PFDD tools and COAs, with information about when they are or are not acceptable and why. Ask FDA reviewers to include the topic of patient experience data in meetings with sponsors/applicants (to be proactive in discussing applicant plans and provide advice throughout drug/biologic development).

6) FDA included a Patient Experience Data Table in 82% of NME NDA and BLA reviews in the assessment cohort. While FDA includes the table in most reviews of applications with clinical data, it does not do so every time. This finding might reflect that the assessment cohort spans multiple years starting from the implementation date of the Cures Act,[12] that the Patient Experience Data table was phased in, and that the content of the table has evolved over time.

Recommendation for FDA: Continue to remind FDA reviewers to include a Patient Experience Data Table in review documents, including those for applications containing no clinical or patient experience data.

7) Many applicants stated that they cannot always get a meeting with FDA reviewers early and often (in a timely manner) to discuss patient experience data during drug/biologic development.

Recommendation for FDA: Conduct an assessment to better understand the extent that this has been the experience of applicants. If the experience is common or recurrent, conduct a root cause analysis to identify obstacles to scheduling meetings and allocating meeting time to discuss patient experience data early and often.

8) In collecting and reviewing patient experience data, some applicants and FDA staff focus on endpoints that are easily measured or of primary interest to clinicians. Patients would like greater attention to psychosocial, quality of life, and measures of ability to function.

Recommendation for FDA: See recommendations for 3 and 5.

9) In collecting patient experience data before and during clinical trials, engaging a representative and diverse patient population generates a greater understanding of patient concerns and enhances the utility and acceptability of patient experience data.

Recommendations for Applicants and Other Stakeholders: Refer to *FDA's PFDD Guidance 1*. Consult with a variety of patient organizations to help find diverse perspectives.

Recommendation for FDA: Continue to encourage and provide resources that support the collection of patient experience data in a manner that ensures its representativeness across the full diversity of the patient population.

[12] The assessment cohort encompasses three years of data, from Cures Act implementation in June 2017 to June 2020. Of FDA reviews of NME NDAs and BLAs in the cohort, 82% of those in the first year contain the Patient Experience Data Table, 77% of those in the second year contain the table, and 87% of those in the third contain the table. A few reviews contain a brief statement that no patient experience data were submitted instead of a table.

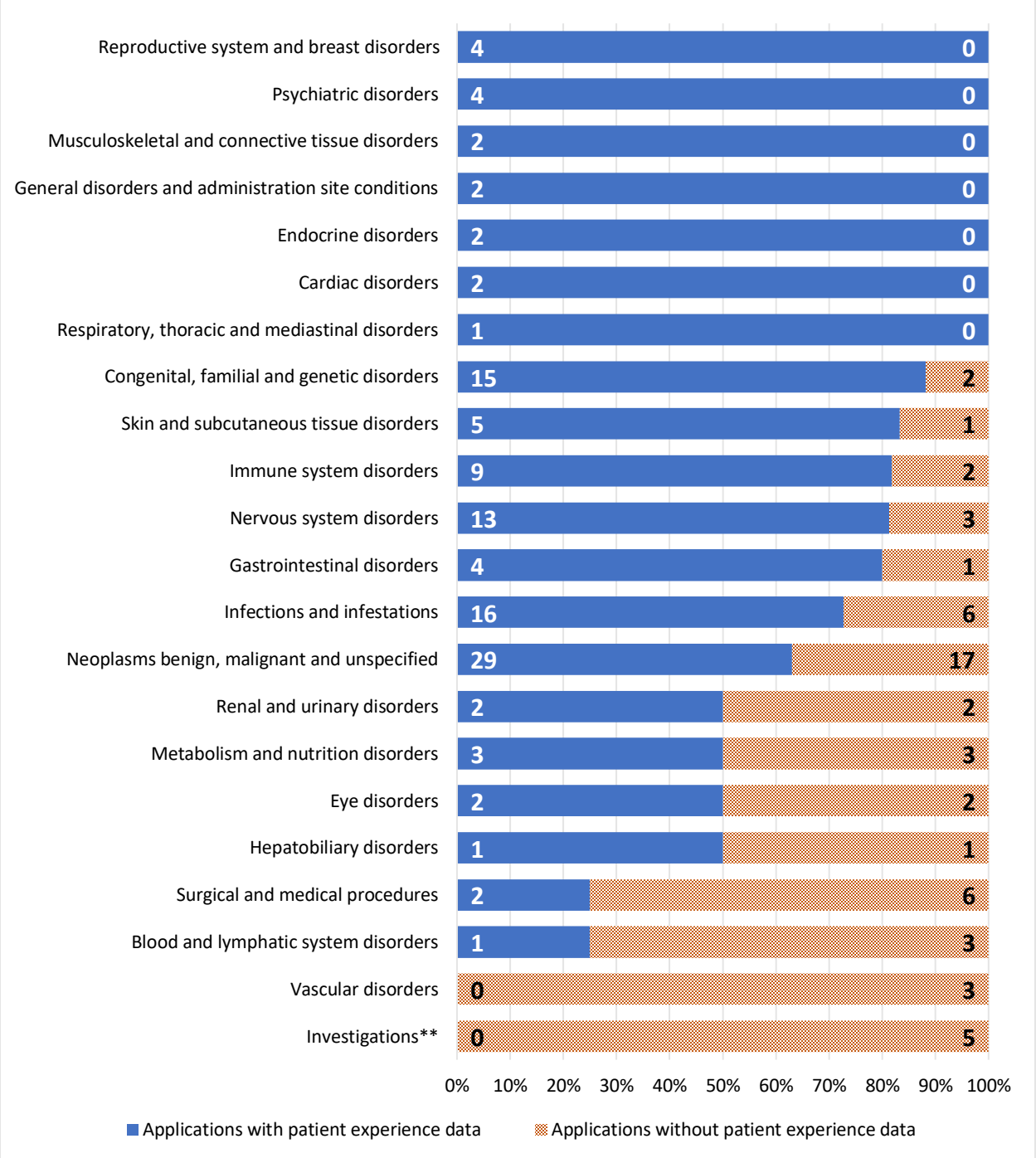
Appendix A. Acronyms and Abbreviations

Acronym / Abbreviation	Term
BLA	Biologics License Application
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
ClinRO	Clinician-Reported Outcome
COA	Clinical Outcome Assessment
DCOA	Division of Clinical Outcome Assessments
ERG	Eastern Research Group, Inc.
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act
FDASIA	FDA Safety and Innovation Act
FD&C Act	Federal Food, Drug, and Cosmetic Act
MedDRA	Medical Dictionary for Regulatory Activities
NDA	New Drug Application
NIH	National Institutes of Health
NME	New Molecular Entity
ObsRO	Observer-Reported Outcome
PED	Patient Experience Data
PerfO	Performance Outcome
PFDD	Patient-Focused Drug Development
PRO	Patient-Reported Outcome

Appendix B. Additional Results

Results by Therapeutic Areas of Applications. The therapeutic areas represented by approved NME NDAs and BLAs in the assessment cohort are shown in Figure B-1, with applications containing patient experience data highlighted. ERG identified therapeutic areas by using the primary Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class associated with the indication(s) proposed in each NDA or BLA. Applications in the "neoplasms benign, malignant and unspecified" therapeutic area were most numerous, comprising 26% of the total number of approved NME NDAs and BLAs. Among approved NME NDAs and BLAs, most of the therapeutic areas had a majority of applications with patient experience data.

Figure B-1. Proportions of approved NME NDAs and BLAs with and without patient experience data considered in FDA reviews, by therapeutic area* (n=176)



*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**Examples of "investigations" are positron emission tomogram, colonoscopy, myocardial scintigraphy/scan myocardial perfusion, and diagnostic procedure.

Mentions of Patient Experience Data in Approved Product Labeling. Metrics for mentions of patient experience data in approved product labeling for NME NDAs and BLAs by therapeutic area appear in Table B-1.

Table B-1. Results of metrics for patient experience data in approved product labeling*

Metric	Product Labeling for Approved NME NDAs and BLAs (n=36) with FDA Reviews that Reference Patient Experience Data
Percent of approved product labeling that mentions patient experience data	30%
Therapeutic Area	
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Congenital, familial and genetic disorders****	17%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Nervous system disorders****	14%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Skin and subcutaneous tissue disorders****	14%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Immune system disorders****	14%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Gastrointestinal disorders****	8%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **General disorders****	6%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Neoplasms benign, malignant and unspecified****	6%
Percent of approved product labeling with patient experience data for applications with therapeutic area: **Reproductive system and breast disorders****	6%

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**The percentages shown in this table represent the number of approved product labeling with patient experience data with the therapeutic area noted divided by the total number approved applications where FDA review reference patient experience data. Less than 3% of product labeling in other therapeutic areas contain references to patient experience data.