PCR143

Regulatory Recommendations for Patient Experience Data in North America, Europe, and Asia Pacific

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BACKGROUND

- Patient experience data (PED) offers insights into patients' experiences of a disease/condition and/or with a treatment/clinical investigation.
- There is currently no standard definition of PED, but the US Food and Drug Administration (FDA) advises that "PED can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to, e.g.:[1]
  - Symptoms of their condition and natural history
  - Impact of condition on functioning and quality of life (QoL)
  - Experiences with treatment
  - Patient preferences for outcomes and treatments"
- Other aspects of PED include patient satisfaction, treatment adherence, and perceptions of clinical trials, healthcare systems, and/or procedures.[2]
- PED in drug development can be generated using several methods, including:
  - Clinical outcome assessments (COAs), which assess how patients feel, function, or survive[2]
  - Preference studies
  - Qualitative research
  - Natural history examinations
- PED is increasingly being embraced by regulatory agencies to support their review and decision-making processes.
  - Each regulatory body independently decides whether to develop its own PED guidance.

OBJECTIVE

- To describe guidance relating to PED across regulatory agencies in North America, Europe, and Asia Pacific.
- Key questions of interest:
  1. Have identified regulatory agencies within scope issued:
     a) Standalone PED-related guidance documents?
     b) Other regulatory submission or clinical trial guidance documents including PED-related recommendations?
     c) Disease-specific guidance documents including PED-related recommendations (in specific therapy areas [TAs] of interest)?
  2. If yes, are the PED recommendations related to COA or other forms of PED (e.g., preference studies, qualitative research, natural history examinations)?
  3. If PED recommendations are related to COA, which types of COA evidence do regulatory agencies expect to see?

KEY RESULTS

- Overall, 39 guidance documents across regulatory agencies in North America, Europe, and Asia Pacific were identified and reviewed.
- No standalone PED-related guidance documents have been issued by the Canadian, UK, Australian, or Japanese regulatory agencies.
  - However, most of these agencies are working on PED-related initiatives or have published disease-specific guidance documents that mention COAs as key endpoints, although they lack detailed COA-related recommendations.

CONCLUSIONS

- Through PED, the patient voice is increasingly being recognized as an important factor contributing to regulatory decisions on the market authorization of new drugs.
- The FDA is leading the way in advancing PED measurement standards and expectations.
  - Europe and China are mostly aligned with the FDA's approach.
  - PED is of interest to other regulatory authorities that have not yet published specific PED-related guidance.
- Regulatory agencies considering PED-related initiatives in the context of international clinical trials should think about aligning their approach with other stakeholders in the drug development process.
  - Harmonization will advance standards, enable consistent decisions regarding drug approval, simplify the process of drug development, and thus facilitate patients' access to beneficial drugs.

Methods – Scope of interest

Table 1. Countries and respective regulatory agencies within scope

Country/continent	Regulatory agency
Canada	Health Canada (HC)
United States	Food and Drug Administration (FDA)
Europe	European Medicines Agency (EMA)
United Kingdom	Medicines and Healthcare products Regulatory Agency (MHRA)
Australia	Therapeutic Goods Administration (TGA)
China	National Medical Products Administration Center for Drug Evaluation (NMPA-CDE)
Japan	Pharmaceuticals and Medical Devices Agency (PMDA)

- Regulatory agency websites were systematically searched to identify published standalone guidance documents on how PED should be included in regulatory submissions.
  - The search was conducted in 2021; however, the new guidance issued by NMPA-CDE in 2022 was included as well
- If no standalone PED-related guidance was identified, general guidance on regulatory submissions and/or clinical trial development was searched for PED-related information.
- Terms for both searches included COA, PED, patient perspective, patient centric, patient preference, patient-reported outcome (PRO), patient engagement, and patient-centered endpoint.
  - Search terms were translated into local language when English version of guidance document was not available.
- The search was repeated to identify guidance on the generation and use of PED in specific TAs of interest.

Table 2: Therapy areas of interest

Therapy area
Alzheimer's Disease
Atopic Dermatitis (AD)
Diabetes
Oncology
Systemic Lupus Erythematosus (SLE)
Ulcerative Colitis (UC)

Methods – Continued

- All guidance documents were reviewed to obtain information related to:
  - Types of COA evidence required or expected by regulatory agencies, e.g.:
    - Expectations regarding concepts of interest and instruments
    - Requirements for COA validation, analysis, and interpretation
    - Requirements for study design elements (including missing data)
    - Considerations for endpoint definitions
  - The value of other types of PED beyond COA.

Results: Regulatory guidance documents

	FDA (United States)	HC (Canada)	EMA (Europe)	MHRA (UK)	TGA (Australia)	NMPA-CDE (China)	PMDA (Japan)
Standalone PED-related guidance document(s)	**Yes** n=8, 2009,[1] 2016,[3] 2018,[4] 2019,[5,7] 2020[6] 2021[8]	**No**	**Yes** n=2, 2005,[17] 2016[18]	**No**	**No**	**Yes** n=1, 2021[28]	**No**
General guidance document(s) /initiatives on regulatory submissions and/or clinical trial development including PED-related recommendations	**No**	**No**	**Yes** n=3, 2014,[19] 2019,[20] 2020[21]	**Yes** n=1, 2015[27]	**Yes** n=1, 2021[26]	**Yes** n=3, 2022[29-31]	**Yes** n=1, 2021[36]
Disease-specific guidance document(s) including PED-related recommendations in TAs of interest	**Yes** Alzheimer's Disease, n=1, 2018[9] AD, n=1, 2018[10] Diabetes, n=2, 2020[11,12] Oncology, n=3, 2015,[13] 2018,[13] 2020,[14] SLE, n=1, 2010[15] UC, n=1, 2016[16]	**No**	**Yes** Alzheimer's Disease, n=1, 2018[22] Oncology, n=1, 2016[23] SLE n=1, 2015[24] UC, n=1, 2018[25]	**No**	**No**	**Yes** Diabetes, n=2, 2012[32,33] Oncology, n=1, 2019[34] UC n=1, 2021[35]	Yes Alzheimer's Disease, n=1, 2017[37] Diabetes, n=1, 2010[38] Oncology, n=1, 2021[39]

EMA; European Medicines Agency; FDA, Food and Drug Administration; HC, Health Canada; MHRA, Medicines and Healthcare products Regulatory Agency; PMDA; NMPA, Center for Drug Evaluation of the National Medical Products Administration; PMDA, Pharmaceuticals and Medical Devices Agency; TA, therapy area; TGA, Therapeutic Goods Administration.

Results: PED-related guidance

	FDA (United States)	EMA (Europe)	NMPA-CDE (China)	PMDA (Japan)
Types of PED	COAs, qualitative studies, within-trial interviews, surveys*	COAs	COAs, qualitative studies, social media, surveys†	PROs
Concepts of interest	Signs, symptoms, impact, functioning, HRQoL	Signs, symptoms, impact, functioning, HRQoL (satisfaction in obesity studies)	Signs, symptoms, impact, functioning, HRQoL, satisfaction	Signs, symptoms, impact, functioning, HRQoL
Validation	Specific guidelines on instrument validation	Use validated instruments (no more details)	Language and cultural validation on the local population should be considered	Language and cultural validation on the local population should be considered
Interpretation	MWPC is key; threshold defined from anchor-based analyses	MWPC and between-group difference	MWPC is key; thresholds based on expert consensus, guidelines, and PED	Consider clinical significance of assessment using scale
Missing data	Should be justified and addressed	Should be justified and addressed	Should be justified and addressed	N/A
Trial design	Design considered when COA data analysed	Design considered when COA data analysed. Open study not recommended	Design considered when COA data analysed	Design considered when COA data analysed
Endpoints	Full guidance provided	COAs are acceptable primary, co-primary, secondary, and exploratory endpoints	COAs are acceptable endpoints	COAs to support efficacy and safety endpoints

*Specific guidance on patient preference information provided.
†Patient adherence, persistence, and tolerability are also considered.
COA, clinical outcome assessment; EMA; European Medicines Agency; FDA, Food and Drug Administration; HRQoL, health-related quality of life; MWPC, meaningful within-patient change; N/A, not applicable; NMPA, Center for Drug Evaluation of the National Medical Products Administration; PMDA, Pharmaceuticals and Medical Devices Agency; PED, patient experience data.

Future trends and innovative approaches – North America and Europe

FDA (United States): Set to continue development of guidance to assist drug developers to collect and submit data from patients and caregivers to inform medicinal product development under the agency's 'Patient-Focused Drug Development Initiative,' the PED landscape will keep evolving.

EMA (Europe): Aims to reinforce patient relevance in evidence generation through various initiatives ready for 2025. Wants to explore and deploy additional methodologies to collect and use patient data for benefit-risk assessment.

MHRA (United Kingdom): Kicked off pilot project in March 2022 asking companies to provide evidence on how they involved patients in their drug development process. Intends to deliver its 'Patient Involvement Strategy 2021– 2025' and have supporting processes in place/staff trained by December 2022. Focus will include developing the use of PROs so that they are built into all licensing decisions, and patient involvement in every step of the regulatory process, e.g., published 'Patient Group Consultative Forum' intended to represent the patient and public voice as a key source of information to the agency.

Future trends and innovative approaches – Asia Pacific

TGA (Australia): In 2021, the TGA communicated its plan to focus on the development and adoption of regulatory guidance on data requirements, which will encourage the appropriate inclusion of PROs in submissions.

NMPA (China): A significant amount of content has recently been published related to digital health technology, including electronic PROs. Innovative approaches and technologies are welcomed if appropriate rationale and documentation can be provided to support their use.

PMDA (Japan): PED landscape in Japan is evolving. One of the PMDA's current priorities is the inclusion of the patient's voice in regulatory submissions; however, the focus seems to be more on patient engagement than PED.

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