EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 September 2025
EMA/CHMP/PRAC/148869/2025

Reflection paper on patient experience data

Draft reviewed by Committee for Human Medicinal Products (CHMP), Pharmacovigilance and Risk Assessment Committee (PRAC), Patients and Consumers Working Party (PCWP), Healthcare Professionals Working Party (HCPWP), Scientific Advice Working Party (SAWP), Methodology Working Party (MWP), Oncology Working Party (ONCWP), Rheumatology/Immunology Working Party (RIWP), Cardiovascular Working Party (CVSWP), Central Nervous System Working Party (CNSWP), Infectious Diseases Working Party (IDWP), Vaccines Working Party (VWP), Network Data Steering Group (NDSG), Committee for Orphan Medicinal Products (COMP), Committee for Advanced Therapies (CAT), Paediatric Committee (PDCO), Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), Emergency Task Force (ETF) and Clinical Trials Coordination Group (CTCG)	31 March 2025
Review by Guideline Consistency Group (GCG)	June – July 2025
Adoption by PRAC and CHMP for release for consultation	18 September 2025
Start of public consultation	29 September 2025
End of consultation (deadline for comments)	31 January 2026
Agreed by <Working Party>	
Adoption by PRAC and CHMP	

Comments should be provided using this form. The completed comments form should be sent by 31 January 2026 to PED_RP@ema.europa.eu

Keywords	***Patient experience data, patient engagement, patient reported outcomes, patient preference studies, patient-generated digital data, clinical trials, real-world data***

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1. Introduction

1.1. Background

The European Medicines Agency (EMA) aims to ensure that medicines deliver optimal treatment outcomes. Successful individualised medical treatment relies on three key factors: 1) an understanding of the disorder and treatment options, 2) comprehensive patient data (e.g., demographic details, medical history, lab results) and 3) consideration of the patient's expectations, preferences and values. Patient experience data (PED) address this third factor and provide a framework for its qualitative and quantitative analysis.

Recent years have seen efforts by regulators internationally[1-3] to steer medicine development towards programmes that not only meet the requirements for quality, safety and efficacy of individual products, but also incorporate the broader perspectives of patients and carers. This is because patients may value different aspects of their disease and available treatments than medicine developers, including the type of relevant outcome measures to be assessed (e.g., quality of life; QoL), populations or stages of disease to be studied or risk tolerability. An optimal patient-relevant medicine development programme incorporates patients' perspectives and documents their experience. Such PED are directly collected from patients or carers experienced in managing the disease and capture their needs and preferences.

These efforts could help to better understand the impact of a medicine on a patient's condition and treatment outcomes, and can allow more informed assessment and decision making by medicine regulators, health technology assessment (HTA) bodies[4], healthcare professionals and patients themselves.

1.2. Problem statement

EMA acknowledges that PED can make an important contribution to the totality of evidence supporting the regulatory assessment of medicines by the Agency. However, PED are not systematically included in all aspects of medicine development (e.g., clinical development programmes, paediatric investigation plans), or in the marketing authorisation application (MAA) or subsequent stages of a medicine's lifecycle such as post-marketing safety monitoring.

A multistakeholder dialogue at the 2022 workshop on PED[5] established consensus on the importance of including PED at all stages of medicines development and regulatory decision making. While some types of PED (such as patient-reported outcomes, PROs) have already been accepted as efficacy endpoints for clinical trials, there is less experience with other PED types such as patient preferences or with qualitative data from patient engagement activities.

Stakeholders also identified potential solutions to address existing hurdles, such as the need for guidance on what methodologies and quality standards are needed for PED to meet regulatory acceptance.[5] While there are some guidelines in the EU[3,6-8], these are either fragmented or outdated. This lack of consolidated guidance creates uncertainties for medicines developers. These uncertainties include whether regulators consider PED useful for regulatory assessment, which standards/requirements should be used to generate validated PED and whether the data generated using valid methods are fit for regulatory assessment and can be submitted. In turn, without more regulatory experience, the scientific knowledge and use of PED cannot mature to a stage that would allow EMA to generate more guidance in the EU.

1.3. Scope

The purpose of this reflection paper is to encourage systematic consideration of PED in medicine development programmes and regulatory submissions.

It also describes general principles on the use of PED across the lifecycle of medicinal products (i.e. during pre-authorisation, benefit-risk evaluation and post-authorisation) and identifies types of PED and main sources of PED.

The target audiences of this document are medicine developers, regulators, researchers and patient groups who generate, collect and review PED.

The scope of this reflection paper does not include detailed methodological guidance.

2. Discussion

2.1. The EU regulatory approach to patient experience data

2.1.1. Patient experience data

In the EU, PED are considered to be data that directly reflect the experience of a patient or carer, without input or interpretation by a healthcare professional, third party or (artificial intelligence [AI]-based) device.[i] These data can be collected from a variety of data sources, including patient engagement activities.

Patient experience can include, but is not limited to, health and functional status, disease symptoms, disease course, treatment preferences, QoL, factors impacting treatment adherence, treatment outcomes and side effects.

PED are generated by patients and can be collected and submitted in support of a regulatory decision-making process by different stakeholders (patient, carer, advocacy group member, researcher, developer such as a marketing authorisation holder [MAH], healthcare professional, etc.). In all cases, it is important for developers to confirm that the data directly reflect the patient's experience and have not been subjected to third party interpretation.

PED can be collected using quantitative methods (e.g., quantitative surveys exploring relevant clinical outcomes or minimum relevant thresholds for patients; instruments for health-related quality of life [HRQoL] or other patient-reported outcome measures [PROMs]), qualitative methods (e.g., interviews, focus groups or qualitative surveys that reflect the wider perspective of patients' experience) or mixed methods that integrate both quantitative and qualitative approaches.[9]

All PED submitted by applicants are reviewed and can be considered by medicines regulators for decision making. However, high-quality data (according to the EU Data Quality Framework standards[10]) that have been generated and/or appropriately validated and analysed using appropriate and robust methods are more likely to be reliable and fit-for-purpose for regulatory decision making.

[i]Technical validation and aggregation of data by a third party or device during the collection process is not considered third party interpretation.

2.1.2. The Agency's view on patient experience data

EMA's view is that PED should be systematically considered for informing medicines development from the earliest stages (including non-clinical stages) through to post marketing, since PED can be a relevant contributor to the totality of evidence throughout the medicine lifecycle.

For PED to inform or support regulatory benefit-risk assessment and decisions, data should be of high quality and the resulting evidence should be generated using robust and validated methodologies[9] and, where possible, including measures that reflect patients' priorities.

Until more detailed guidance is available in the EU, EMA offers multiple platforms for patient groups, industry and other stakeholders through which they can engage with regulators at an early stage and discuss the best approach to generate, collect and analyse such PED. These platforms include EMA's Innovation Task Force (ITF), scientific advice (SA) and qualification of novel methodologies, all of which offer developers and researchers the opportunity for targeted discussion on their specific development plans or PED methodologies. The ITF briefing meetings provide developers with a forum for early dialogue with EMA on innovative medicines, digital devices and novel methods.[11] Similarly, for developments by academic and not-for-profit entities, the Agency offers academia briefing meetings.[12] Such meetings could also direct developers towards integrating PED in their development programmes from early stages.

2.1.2.1. Scientific advice

Medicine developers are encouraged to liaise early with regulators to seek scientific advice (SA) to discuss the best way to generate and collect PED[13] as developments become more concrete or linked to a specific medicinal product. This means that discussions should be targeted to the specific development plan. Such discussions can cover what type of PED would be most relevant to generate and how PED are generated and collected. Early engagement should be sought as soon as possible, at the earliest possible stage of a medicine's development plans when the key questions have been identified. This ensures that patient perspectives and input can be planned early on to inform potential integration of PED in upcoming clinical trials.

Joint scientific advice with HTAs[14] is strongly encouraged as the preferred route to ensure alignment with downstream decision makers and inclusion of PED that may be pertinent for post-launch evidence generation, relative effectiveness assessments and economic evaluations. Scientific advice, including parallel joint EMA-HTA scientific consultations, can include patient and healthcare professional experts and can also be used to discuss the value of PED throughout the entire lifecycle of the medicine under development.

For orphan medicinal products, although no pre-assessment of actual data can be expected at this stage, sponsors are encouraged to seek protocol assistance to discuss whether their development plans are adequate for generating conclusive evidence to support claims of significant benefit at the time of orphan marketing authorisation. Applicants are also encouraged to do so when they envisage claiming a major therapeutic advantage in the context of conditional marketing authorisation. Where relevant, sponsors or applicants can consider PED as a source of evidence in support of their claim.

2.1.2.2. Qualification of novel methodologies

EMA's qualification procedure for novel methodologies offers a route by which to assess and endorse innovative methods for collecting and using PED.[15] If the novel methodology is accepted, the CHMP issues a qualification opinion, confirming that the proposed method is suitable for use in a defined context of regulatory evidence generation. Once adopted, the opinion is published and can be used by multiple stakeholders.

In earlier stages, CHMP qualification advice is available to help developers understand what evidence is needed to support a future qualification opinion. This allows for targeted refinement and early alignment with regulatory expectations.

Table 1. Examples of methods applicable to PED for which scientific advice and qualification procedures are available

Examples of PED methods
• Clinical outcome assessments (PROs, ePROs, CROs)
• Patient preference studies (PPS)
• Symptom scales
• Digital/AI-based methods (e.g., EORTC CAT core questionnaire)[16]
• Spontaneously generated online patient experience data [ii]

AI, artificial intelligence; CAT, computerised adaptive test; CRO, clinician-reported outcome; EORTC, European Organisation for Research and Treatment of Cancer; ePRO, electronic patient-reported outcome; PROs, patient-reported outcomes.

2.2. Use and value of patient experience data along the medicine's lifecycle

EMA acknowledges the value of PED across all stages of the medicine lifecycle, as the patient's voice is critical to better informing all stages of a medicine's development, from early development through regulatory assessment to post-marketing activities.[1,3]

In addition, PED can inform HTAs and downstream decision making, such as pricing and reimbursement by healthcare systems[17], and can also support more informed and personalised decision making for patients and healthcare professionals in clinical practice (Table 2).

Table 2: Examples of use and potential value of PED in the different stages of the lifecycle of a medicine

Research & development	
Non-clinical research	• Contribute to ensuring that non-clinical research questions address patients' unmet needs; • Help establish the preferred route of administration; • Identify existing products that can be optimised or extended to other indications and populations.[iii]

Clinical trial design	• Formulate trial questions that are most relevant to patients;
	• Refine study design and objectives by:
	  ○ selecting appropriate endpoints, including PRO instruments that reflect how patients feel and function;
	  ○ sharing knowledge on the natural course of the disease and standard of care (this could aid in the selection of the control group, if applicable, and target population);
	  ○ defining entry criteria to ensure that the most appropriate population is enrolled;

[ii] Posts written by individuals on social media platforms are one example of spontaneously generated data in an unstructured from. There is increasing interest among biomedical researchers in developing methods to analyse these large volumes of unstructured data and generate knowledge.

[iii] This example may also be relevant during clinical research.

	○ supporting balanced gender participation and a gender-responsive approach that considers different treatment responses for men and women; ○ defining preference and acceptability for comparators (placebo/standard of care) and dose; ○ considering feasibility, relevance and specific aspects of studies for special populations (e.g., children, older and frail people); ○ including QoL and ethical considerations; ○ collecting input on informed consent and assent/agreement form and other documentation; • Increase willingness to participate in a trial, manage expectations and reduce the risk of dropouts from trials, thereby increasing the quality of the data.
Clinical trial conduct	• Report on unexpected emerging effects (beneficial or adverse) of the investigational medicine, as well as on formulation and packaging; • Report suspected adverse reactions to the study investigator; • Collect input on dissemination of results; • Report unforeseen cross-reactions or cross benefits with other medicines that may or may not be reported by participants in the trial.
Evaluation	
Regulatory benefit-risk assessment and decision making	• Potentially define the most relevant clinical outcomes, for both pre- and post-authorisation studies: ○ QoL, burden of disease, clinical meaningfulness of efficacy results, symptom improvement, relevant secondary endpoints, aspects of the clinical trial conduct that may have influenced the results (e.g., exact reasons for dropping out); • Establish the preferred medical device technology and technique; • Describe impact and acceptability of risks and trade-offs (e.g., acceptability of risk minimisation measures) in relation to the documented/plausible benefits and target population; • Provide advice on aspects related to unmet medical needs and identify the most relevant information for patients and carers when developing the product information; • Contribute to identifying relevant gaps in knowledge that could be addressed during post-launch evidence generation.
Assessment of major contribution to patient care	• Establish whether a medicine represents a major contribution to patient care compared with relevant comparator treatments across various regulatory settings, (e.g., for conditional marketing authorisation, granting of data exclusivity and market protection or orphan medicines).
Access and use in clinical practice	
Reimbursement decisions	• Support relative effectiveness assessments and economic evaluations by HTAs at national level to decide whether the medicine will be available in a specific EU Member State and will be reimbursed by national or regional social security schemes:

	○ use as endpoint in comparisons across equivalent therapies or versus the current standard of care, to help establish added value for patients or a more favourable cost-benefit, cost-effectiveness or cost-quality profile.
Routine clinical care/practice	• Support shared decision making during routine clinical practice; • Contribute to clinical guideline development; • Contribute to treatment adherence.
Safety monitoring	
Post marketing	• Provide information on the safety of medicines to support pharmacovigilance and risk minimisation: ○ report suspected adverse reactions, identify risks and inform the assessment of suspected adverse drug reactions; ○ describe impact and acceptability of risks and trade-offs in relation to the benefit; ○ identify relevant patient groups through registries. • Identify preferences for, and acceptability of, risk minimisation measures, support development and dissemination of risk minimisation materials, and adherence to the intended actions for risk minimisation; • Contribute to preventing medication errors; • Contribute to post-authorisation safety studies that identify or investigate risks or evaluate risk minimisation measures; • Identify behaviours leading to shortages.

QoL, quality of life; HTA, health technology assessment body.

2.3. Types of patient experience data

Different types of PED can be defined based on whether they report health outcomes or express patient preferences on treatment trade-offs. The type of PED can also be defined depending on whether data are of a quantitative or more qualitative nature (see sections below and glossary for definitions).

2.3.1. Patient-reported outcomes

Patient-reported outcomes (PROs) are health outcomes that directly report the patient's experience of their health status without amendment or interpretation by a clinician or other party.[3,8] Typically, PROs capture patient-relevant disease and/or treatment outcomes, including symptoms, physical and cognitive capacity and function, symptomatic adverse events and their tolerability[18] and general multidimensional concepts such as health-related QoL.

While objective measures like survival rates, disease progression and clinical outcome measures related to signs, symptoms or pathophysiology are crucial, they might not capture the full scope of a treatment's impact. Including the patient's perspectives provides a more comprehensive picture of the benefits/risks of the treatment under investigation.[19,20] PROs can enrich regulators' understanding of a patient's experience related to symptoms, adverse effects and overall satisfaction,[21] thus contributing additional evidence to support a medicine's approval. Moreover, PROs can strengthen the product labelling by demonstrating improvement in daily functioning.[7,22] In the post-authorisation phase, PROs

collected in registries and other real-world data sources can help monitor the safety of a medicine and inform the benefits and risks of a treatment in the real world from a patient's perspective.

PROs are normally collected through patient-reported outcome measures (PROMs)[8] or proxy-reported outcomes,[23] such as questionnaires and surveys to evaluate the impact of a health condition, treatment or intervention on a patient's life either at a single time point or over time.[24] Other, varying, features of PROMs include their structuring as single- versus multi-item and domain constructs, different scale properties for response elicitation and sum versus separate (domain-, and/or item-) scoring.

PROMs are, by definition, subjective as they are usually generated as self-collected data. Therefore, to ensure they are standardised and valid, it is important to apply psychometric principles, methodological validation concepts and appropriate techniques for questionnaire development and translation.

PROs and PROMs can be generic and not specific to a particular disease, assessing general aspects of health, such as the EuroQoL-5 (EQ-5D) and 36-Item Short Form Health Survey (SF-36). However, there is also a broad range of condition- or population-specific PROMs, for example the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) for heart failure, the Asthma Control Test (ACT) and the Ped PRO CTCAE for cancer.[25]

2.3.2. Patient preference studies

Although not yet fully established nor systematically integrated in drug development, patient preference studies (PPS) can complement evidence from pivotal clinical trials to support decision making.

PPS include any qualitative or quantitative assessment of the relative desirability or acceptability to patients of aspects that differ among alternative health interventions. PPS can, among other things, help with characterising medical need, selecting endpoints and estimating meaningful effect size, as well as identifying subgroups with different preferences.

Thus, PPS assess the desirability or acceptability of a specific option or choice of options over a given health intervention (i.e., medicine, treatment or health device), where individual patients are asked to consider the trade-offs of the benefits and risks of each option, measuring how well they align with patient needs and whether they will provide the benefits patients are seeking. Such information is based on individual beliefs and values regarding the benefits and risks associated with the health intervention, forming a specific type of PED. It varies between individuals and may change over time in the same individual due to changes in individual benefit/risk perception, for example because disease progression is not static. Of note, PROs are also reported directly by patients but are outcome measurements that are based on the status of a patient's health condition.

PPS may be carried out by regulators, developers, patient groups, learned societies/clinicians or any other relevant stakeholder. In special circumstances (e.g., young children and other vulnerable populations such as adults who are unable to provide consent, including those with dementia), preferences can also be collected from parents or carers. However, it is important to distinguish these from formal PPSs.

PPS can be especially informative when different opinions coexist in sensitive situations (e.g., when a treatment is not clearly superior to another as in a registrational comparative trial, or when factors other than solely the objective data play a role for the patient).[26] Nonetheless, PPS have not been extensively used in regulatory decision making to date. Reasons for this may be that these studies are

complex to perform and there are limited standardised methods to elicit and capture patients' preferences.

To enhance the understanding of patient perspectives in the context of medicine development and regulation, EMA considers it valuable to encourage the conduct of well-designed and reliable PPS and the use of PPS data. To this end, it is important to continue developing the foundational standards for PPS planning and conduct, as well as guidance on how to integrate PPS results into decision making. Moreover, it is also crucial to identify situations where PPS may have the greatest value and address possible methodological limitations of study design and conduct.

The regulatory interest in PPS is stressed in the '*Qualification of the IMI PREFER framework*' adopted by the CHMP in 2022.[27] The research framework[28] and the document entitled "*Points to consider on method selection*", proposed by the public-private EU/US PREFER project, provide a reference for a case-by-case approach to planning and conducting PPS. In addition, a draft ICH guidance document on PPS is also expected to be released for public consultation in 2026.[29]

2.3.2.1. Qualitative patient preference studies

Qualitative PPS comprise individual or group methods, including in-depth or semi-structured interviews or focus groups. The data generated can be analysed in different ways, including direct coding from audio recording or mind mapping. In the regulatory setting, these methods can explore in-depth knowledge and expectations about the disease or treatments, and the relevance of the different clinical outcomes or attributes of a medicine. Examples of questions suitable for qualitative PPS include questions where participants can enter open comments, for example: 'how would you describe the impact of your disease on your daily activities?'. The explorative nature of qualitative input makes these PPS most suitable for situations where knowledge is still limited, such as the early phases of a medicine's lifecycle, or for diseases where clinical outcomes endpoints are not yet well defined or are of debatable relevance. Qualitative PPS may be also useful to inform the design of a subsequent quantitative PPS.

2.3.2.2. Quantitative patient preference studies

PPS can also be conducted using quantitative methods. These studies result in quantifiable data and are usually more suitable when more is known about the disease or treatment, when sensitive decisions are to be made or when there is large variability in individual views. An example may be establishing the threshold of what is considered clinically relevant, which may differ between individual patients, or among patients, clinicians and regulators, but in all cases is essential for the evaluation of the benefit/risk balance.

There are numerous methods by which to elicit quantitative patient preferences, including discrete choice experiment, best-worst scaling, rating-based conjoint analysis, probabilistic threshold technique, or swing weighting. While most quantitative PPS research has been conducted using discrete choice experiments, the selection of the most adequate method depends on multiple factors, such as the complexity of the method based on the study population and their capacity to answer the research question as well as their efficiency in doing so.

Current literature on patient preferences encourages the use of mixed methods, starting studies with a qualitative phase and continuing with a quantitative one. It is important that PPS are relevant for the target population and address outcomes meaningful to patients, complementing the information gathered through outcomes measures in traditional trials.

2.3.3. Data obtained through patient engagement activities

Although prospectively planned studies such as PPS or studies including PROs are more established ways to collect PED during medicines development, data obtained through patient engagement activities should also be considered as an important contributor to the totality of evidence.

The 2022 EMA workshop on PED defined patient engagement as interactions with patients to gather their experience with a disease and their preferences regarding treatments and outcomes.[5] Patient engagement activities may be initiated by regulators and medicine developers, or by patients and patient organisations themselves. In this context, patients include family, carers and legal representatives of vulnerable individuals (for example, in paediatric or cognitive conditions where patients are not able to represent themselves).

A variety of methodologies can be used by medicine developers, regulators and other stakeholders to seek patients' input. EMA has developed several tools for patient engagement that are applied at various points during EMA's regulatory processes to provide insights into how patients experience their condition, symptoms, burden of disease, burden of treatment, quality of life and treatment preferences. PED collected through EMA patient engagement activities are included in the assessment and reflected in the assessment report, alongside any PED that may be submitted as part of a marketing authorisation application.

This chapter covers patient engagement activities relevant to medicines regulatory work. Other patient engagement methodologies may be used by medicine developers during medicines development and by other stakeholders in various research projects.

2.3.3.1. Patient engagement in medicines development and regulation

Early patient engagement by medicines developers in research and development can contribute to establishing the right research questions, providing insights into patients' preferred outcomes and selection of appropriate measures (such as PROs), medicine characteristics and their views on the balance between risks and benefits. It can also improve the design of trials to ensure they are ethical and feasible, with good enrolment and retention of participants.[30]

There is scope for expanding patient engagement activities within medicines development.[3,31] For example, patient engagement has been shown to result in research that is more tailored to patients' needs, improved study relevance and quality and regulatory benefits.[32] The value of early patient input on clinical trial design has been demonstrated particularly in the field of HIV, where, for example, patients have advised on how to mitigate the burden of trial participation, thereby improving the quality of the trial results.

From the outset, EMA has been engaging with patients as part of its regulatory activities to capture their experiences with living with a condition and its treatment. These interactions have evolved over time, and various methodologies have been developed according to the specific activities, supported by a dedicated framework.[6] An overview of engagement with patients and patient organisations across a medicine's regulatory lifecycle is provided on EMA's website and in stakeholder engagement reports.[33]

Different levels and methodologies for engagement exist, such as surveys, written consultations, focus groups and interviews, patient input into EMA scientific advice or scientific advisory groups (SAGs), committee consultations, public hearings, and patients' participation in technical expert groups. A single method of engagement (e.g., one individual bringing their personal experience) brings added value on its own, though several methods can be used in parallel to complement each other, offering more diverse perspectives and enriching the data collected.

Information obtained through patient engagement activities can complement PED obtained from other sources/methodologies and can be used to inform the overall benefit-risk assessment and regulatory decisions on topics such as labelling, risk management plans or post-marketing surveillance. The choice of patient engagement methodology/activity will be determined by the research question/objective, or to complement the evidence obtained with other methods. Although patient engagement activities do not always generate data in a structured way, critical insights from patients are valuable (for example, at EMA they are used to inform ongoing procedures).

2.3.3.1.1. Surveys, interviews and written consultations

Input from individual patients and organisations can be obtained through surveys and written consultations in various contexts. For example, EMA scientific committees such as the Paediatric Committee (PDCO) regularly survey paediatric patients and/or their families when evaluating a paediatric investigation plan (PIP) and the feedback they receive informs the committee of the patient perspective. Similarly, the Committee for Orphan Medicinal Products (COMP), in addition to inviting individual patients, has used surveys to gather input from a larger number of patients when evaluating elements such as significant benefit. In addition, patient organisations often conduct interviews or focus groups among their members to respond to EMA consultations. Lastly, where possible, individual experts might collect information from their community to support the patient perspective.

Input from written consultations and surveys can be useful to identify patient preferences for treatment-related aspects, such as oral versus injectable medicines, concerns/awareness about potential side effects or long-term effects or patients' willingness to accept side effects in a trade-off for benefits. Patients may also share their experience with previous treatments.

CHMP early dialogue was adopted following a successful pilot in 2021, where patient organisations were consulted on orphan medicines. This was then extended to other products and to healthcare professional organisations. At the start of a CHMP evaluation, organisations are invited to provide input on aspects of the condition that are important for the evaluation, such as the condition's impact on patients, acceptability of current treatment and unmet needs and concerns, as well as expectations for future treatments such as the outcomes that matter most and views on the acceptability of side effects. The organisations use various methods for collecting input.[34] The feedback is then shared with rapporteurs and the company and is reflected in the assessment report.[35]

2.3.3.1.2. Stakeholder meetings and workshops

Patients and patient organisation representatives participate in meetings ranging from focus groups and targeted meetings on specific topics to multistakeholder workshops, according to the objective. When there is an important regulatory or scientific advance in a therapeutic area or specific disease, thematic workshops may be organised to elicit the perspectives and priorities of stakeholders, in particular patients. Workshops can sometimes be co-organised with patient organisations, for example the joint stakeholder workshop by EMA, SMA Europe and TREAT-NMD on spinal muscular atrophy, where patient perspectives were heard on the impact of the disease, standards of care, clinical benefits and outcome measures.[36] In referral procedures, stakeholder meetings have yielded information on awareness and communication of risks, including the quality and effectiveness of risk communication, and patient views on options to improve risk management and risk communication.

2.3.3.1.3. EMA scientific advice, scientific advisory groups, committee consultations and public hearings

Several EMA scientific committees have patient representatives as members: COMP (orphan medicines), PDCO (paediatric medicines), CAT (advanced therapies) and PRAC (pharmacovigilance).

These patient representatives have full voting rights and participate in the usual work of the committee, contributing a patient perspective to the committee's activities.[37] Patients are also members of various task forces within the Agency, such as the Emergency Task Force.

Patients are engaged as individual external experts when they are invited to contribute to scientific committee activities related to the evaluation of specific medicines, such as scientific advice/protocol assistance[iv], SAGs, ad hoc expert groups or committee consultations. Individual patient experience can point out issues that are difficult to identify via other sources, such as the persistence of an adverse reaction or its impact on quality of life during the safety monitoring phase.

Direct interaction also allows clarification of questions and further contextualisation of the patient's input. An individual's personal experience can trigger larger and more structured investigation and can therefore benefit from being supported by other sources of information (e.g., PED collected using other methodologies such as surveys or PROMs, or a joint position developed by a patient organisation).

Engagement in scientific advice procedures takes place early in the regulatory process. Patients usually comment on clinical aspects such as the trial design and feasibility, population and selection of endpoints or comparators/standard of care to ensure these are relevant and acceptable to patients. Patients' input in scientific advice has been shown to have an added value and impact.[38] Engaging patients, during scientific advice, in reviewing developers' plans for the collection of PED is an area for future exploration.

At later stages, patients are invited as experts to SAGs or ad hoc expert group meetings, and they can also be invited to the final deliberations during the applicant's oral explanation at the CHMP plenary meeting. In these roles, they provide additional comments and context that is taken into account in the committee's decision-making process.

Following the 2010 revision of the EU pharmacovigilance legislation, public hearings were introduced as an engagement tool in 2017 and can be convened by the PRAC on a case-by-case basis. The main aim is to hear the public's views (including those of patients) on the risks associated with a medicine, particularly in relation to the therapeutic effects, available alternatives and the feasibility and acceptability of proposed measures to manage or minimise risks. Contributions at public hearings inform the committee's decision making.[39] At the 2017 public hearing on valproate-containing medicines patients, carers and families comprised half of the invited speakers and submitted a number of written interventions. The input received helped identify issues that would not otherwise have been highlighted, informed the agendas of subsequent PRAC meetings and meetings with stakeholders and was instrumental in the recommendation of new measures to avoid foetal exposure to valproate.[40]

2.4. Sources of patient experience data

PED can be collected from different sources, broadly distinguished by the type of setting and context in which the data is generated or collected, as well as the methodologies and tool(s) used. The methods to be used and the type of data to be collected will depend on the research question, the target population (including special populations such as older, frail or paediatric patients or other vulnerable populations) and the clinical context (e.g., chronic versus acute conditions).

[iv]Protocol assistance is scientific advice for products with orphan designation; hereafter the term scientific advice is used to refer to both types of advice.

2.4.1. Patient experience data collected in clinical trials

The most common types of PED, such as PROs, have traditionally been collected in clinical trials (more often phase III studies) to support decision making in regulatory settings, HTA/reimbursement decisions and clinical care.

Collection of PED within phase III studies is encouraged as it has a number of advantages over collecting them in early phase studies. Such advantages include the possibility of using confirmatory studies with sufficiently large samples and linking the observed safety and efficacy data with PROs and patient preferences, for example so that minimally clinically relevant changes for the PRO (from the patient perspective) can be defined and validated. It is important to note that the validation of a PRO is expected to be conducted in a study that is separate from the study used to collect confirmatory data based on that particular PRO. To support researchers and medicines developers on how to robustly and systematically collect, analyse, report and submit PED, stakeholders, including regulators, have been working on developing patient-focused guidelines on using PED in medicines development and regulatory decision making.[21,41]

2.4.2. Real-world data as a source of patient experience data

In the real-world clinical care setting, PED collection has added value in providing information on patients' healthcare needs and preferences and increasing knowledge on the benefit-risk profile of treatments. For example, PROs have provided useful information for safety signals as each adverse event reported by a patient is a PRO. In addition, PPS outcomes have provided information on patients' acceptance of a therapy in routine care and the possible trade-off of its effectiveness and toxicity.[42,43]

To support regulatory assessment, data collected outside clinical trials must meet quality standards equivalent to trial-based PED. In this real-world clinical care setting, PED are often collected in non-interventional studies (including surveys) through primary data collection that follows a pre-specified research protocol or other instruments. When available, PED can be extracted from existing sources of healthcare data, for example from patient registries (then considered as secondary healthcare data use).

Using a primary data collection approach in non-interventional studies, researchers or patient groups design and pre-plan research protocols that allow them to ask tailored questions and collect insights from patients. These can include aspects of the natural history or burden of the disease, QoL for patients and their caregivers, their preferences and trade-offs and their unmet needs. Such PED can subsequently support the planned clinical trials, for example by informing the selection of the most suitable patient-relevant endpoints. This can be included as part of the pre-authorisation evidence package or as part of post-authorisation studies.[44] The same primary data collection approach can be applied to gather useful information on treatments and outcomes from the patient's perspective in early access or compassionate use contexts.

Healthcare data sources for secondary use, such as electronic health records databases, insurance claims databases, administrative data sources and existing patient registries do not always capture the patient perspective and tend to focus on collecting traditional clinical outcomes and endpoints. However, as the routine collection of PED, together with other health data (e.g., laboratory and clinic records), has the potential to enhance several downstream activities such as individual patient management, quality of care evaluations and study planning, a growing number of initiatives are attempting to integrate PED collection within these existing sources of health data.[45]

2.4.3. Safety surveillance systems

In the context of post-marketing safety monitoring, reporting of suspected adverse drug reactions (ADRs) by patients themselves is an important type of PED, and existing safety surveillance databases and repositories such as EudraVigilance are an important source for collecting and analysing them. In this context, detailed guidelines are available to support the collection as well as patient reporting of suspected ADRs.[46,47]

2.4.4. Other potential sources of patient experience data

Other sources of PED, less conventional and yet to be established, include mobile health technologies and social media data.

Mobile health technologies are considered an increasingly important source of PED that can inform different stages of product development, evaluation and clinical management.[48] Such technologies allow for collection of larger amounts of data from patients when compared with more traditional methods (e.g., paper questionnaires). Data collection can be done in a faster and less burdensome manner for all stakeholders involved, especially when recorded by a worn device, although not all data from wearables are PED (such as vital signs). Wearables specifically designed to measure disease symptoms and adherence to treatment provide quantifiable information on the quality of life of the patient. Nonetheless, more experience is needed in this area to develop standards and to qualify methods for data collection by mobile health technologies as valid data sources that can then generate more effective feedback to patient users.

Social media, such as general purpose platforms as well as virtual patient organisations and patient communities, forums and health/support networks, have the potential to be a source of PED, as they can bring together many people interested in sharing and discovering more about their conditions, ADRs, etc.[49,50] However, these sources are prone to bias, in particular systematic bias and other important limitations in terms of data quality (e.g., missing data, limited representativeness, lack of medical validation), which currently limit their reliability as a PED source. As with other sources of PED, compliance with data protection regulation should apply. Previous research has highlighted some unique use cases in which data from social media, especially when combined with other more established sources of data on medicines use and safety monitoring, could provide insights useful in the regulatory context, for example to inform stakeholders about abuse and misuse of medicines, patient tolerance and reasons for stopping medication.[48,51,52]

2.5. Considerations for systematic implementation of patient experience data

The successful incorporation of PED in medicines research and development and in supporting scientific evaluation by regulators faces some challenges. Several of these challenges have been highlighted to EMA by stakeholders. Potential strategies to overcome these challenges have been reviewed in the literature[9] and are briefly discussed below.

The following considerations do not constitute formal regulatory guidance, and developers are advised to engage early with EMA on their specific development plans (see Section 2.1.2).

2.5.1. Data quality

In terms of data quality, PED are often prone to missing, incomplete, or poor-quality data, which may impact data reliability and relevance for the specific research question.[10]

Missing data in PED can lead to significant gaps and biases in understanding patient outcomes. Therefore, addressing and accounting for missing data is essential to ensure reliable and interpretable results. Missing data, and the lack of understanding of the underlying reasons and mechanisms are well recognised challenges in PED, especially for PRO analysis. Therefore, the study protocol should describe how missing data will be accounted for in the analysis and whether sensitivity analyses will be done to assess deviations from the method used. The proportion of missing values and the reasons why they are missing (e.g. disease progression, death, treatment toxicity, or patient/clinician decision) should also be reported.

To avoid missing data and improve completion rates and data quality, the scientific literature recommends several strategies, such as simplifying data collection tools, minimising participant burden, and using reminders, electronic capturing of PED or follow up.[53]

2.5.2. Representativeness

Making PED representative can be difficult, as patients often have different values and expectations. This can be improved by involving a wider range of patients, using varied methods of data collection, working with patient organisations, and supporting health and digital literacy. While broader input may make agreement harder to achieve, this is usually outweighed by the benefit of more representative and nuanced insights. Using different ways of involving patients—such as interviews, surveys, or workshops—and involving patient experts who can consult with other patients or experienced peers can further strengthen the quality of the data.

2.5.3. Study design

When PED are generated and collected through clinical studies, the choice of the study design can also lead to additional complexities and limitations. A further challenge is defining the optimal timing and frequency of assessments, which will depend on the natural course of the disease. If the recall period is too long, some important events may be missed because the respondent may not be able to accurately recall the information, thereby introducing bias. Shorter recall periods can reduce recall bias but may not be appropriate for assessing infrequent activities. Their use should be carefully balanced against the risk of overburdening participants and study administrators or unnecessarily increasing resource use. In addition, patients' perceptions on disease burden and treatment preferences may differ across geographical areas.

Regarding quantitative PPS (see Section 2.3.2.2), it is important to consider aspects on study design such as potential selection bias in interviews or focus group meetings. For example, factors such as disease severity, functional capability, gender, financial status and accessibility of in-person meetings may lead to skewed patient representation and unreliable PPS.

2.5.4. Data collection methods and tools

The quality of PED can vary depending on the method of collection (qualitative, quantitative or mixed) and the data source used (e.g. clinical trials, registries, surveys, wearables). This variability may impact the robustness of the data, their accessibility and the types of questions they can reliably address.

2.5.5. Challenges related to the use of PROs

2.5.5.1. Validation of PRO instruments

It is crucial to use validated PRO instruments to ensure that any differences in patient responses are based on robust and clinically meaningful differences in patients' experiences, instead of variations in study design or biases.[21] PRO instrument validation should ideally take place prior to their use in clinical trials supporting the MAA.[7] However, an unequivocal definition of a 'validated' PRO instrument remains challenging. In particular, there is a lack of consensus on adequacy of methods and evidence standards for PRO instrument validation for pharmaceuticals (e.g., language of questionnaire). In this respect, EMA's qualification of novel methodologies can be used to support the validation of PROs and PROMs.

2.5.5.2. Selection of PRO instruments and items

Selection of appropriate PRO instruments is key for their intended use. Marketing authorisation applications that include PROs frequently struggle to identify an appropriate core set of items or PROMs.[54] The selection of a PROM should reflect the purpose and objectives of the study, as well as the PRO domains most appropriate and relevant for the patient population and the disease or treatment being assessed. Overall, while selecting core items to make a PROM more practical or focused for certain applications, it is important to carefully consider how this selection might affect the measure's effectiveness and the interpretation of its results.

2.5.6. Participant burden

Participant burden can pose challenges to PED collection. For example, an excessive respondent burden may lead to unwillingness to complete the questionnaires and will ultimately result in missing data and inaccurate information. Therefore, several factors should be considered before selecting a methodology to avoid extensive and lengthy methodologies and minimise the burden. These factors include the frequency and timing of assessment, study duration, length and/or formatting of the instrument, mode of administration (paper, telephone or web-based), participant's health and digital literacy level, complexity of instructions and disease severity and/or treatment toxicity. Adequate and timely feedback to participants, as well as responsiveness to any queries that may arise, will further support engagement and participation and is considered good practice.

2.5.7. Training and capacity building

Training is a valuable tool to address the need for enhanced capacity and adequate knowledge for all relevant stakeholders, including regulators. To this end, EMA provides training for patient organisations and patients who participate as individual experts in medicine-related activities, for example through annual training sessions and a range of online materials.[55,56] This training covers activities such as providing input during scientific advice and SAGs. In addition, patients gain knowledge through practical experience, for instance through mentoring by more experienced patients. This has proved beneficial and is being further explored.

2.5.8. Language

Another important challenge is language, both in terms of the terminology pertaining to medicines development and regulation, and the lack of translation into languages other than English. Making materials more accessible by providing them in easy-to-read language and in multiple languages would enable broader engagement of patients and increase representativeness. EMA is working to simplify

and improve the user friendliness of the documents used for patient input into regulatory activities, such as scientific advice, and also invites patients to give feedback on their experience to help improve the process.

2.5.9. Perceived lack of value

One barrier to the use of PED is lack of alignment between stakeholders and decision makers on the value of PED as a measurement. This may be due to a lack of medical validation of PED by healthcare professionals,[57] although this should not automatically be a reason to reject assessment of the patient experience. In this regard, it is very important to ensure methodological rigor in data collection, analysis, and reporting, for example by addressing these points in a scientific advice procedure.

In the clinical setting, trust in patients' perspectives can also help maximise the use of PED, for example to increase adherence to treatment and help detect the causes of non-adherence.

The value of PED may be seen as limited if a conflict of interest is perceived (e.g., an expert acting as consultant to both to regulators and industry). However, conflicts of interest are not unique to PED and should be seen as a broader issue within the entire healthcare assessment ecosystem. For this reason, robust regulatory safeguards are necessary to mitigate potential risks. Safeguards should include fully transparent processes and disclosure of financial and non-financial ties, clear guidelines, rigorous peer review, and independent oversight to ensure that the data used in regulatory decision making are free from undue influence.[5]

2.5.10. Transparency on the use of PED in regulatory assessment

Patient organisations, industry and other decision makers have requested more transparency on how PED are evaluated and the grounds on which they may or may not be accepted as evidence when establishing the benefit/risk balance of a medicine. Since not all PED submitted by companies as part of MAAs are requested or approved for inclusion in the EU product information, any specific shortcomings of those data that prevent the inclusion of PED in product information should be adequately explained in the public assessment reports.

If applicants wish to include PED in regulatory documents such as the EU product information, and providing such data are relevant in supporting the conditions of use of the medicine, it is important that they consult applicable guidelines.[58] It is also recommended that developers seek scientific advice on their proposals. Ultimately, inclusion of PED in the EU product information will depend on the scientific assessment by the CHMP.

2.5.11. Global alignment on patient experience data

Global alignment on how to collect and assess PED is important to optimise the development of medicines and to ensure that the medicines reach patients promptly. The ICH Reflection Paper on Patient Focused Drug Development[1] details areas where harmonisation of methodological guidance is needed, in particular for PROs and PPS. The Agency is collaborating on the development of such ICH guidance on patient-focused drug development and also exchanges best practices for patient involvement in regulatory processes with other regulators.

Once adopted, ICH guidelines should be considered by stakeholders when planning inclusion of PED in medicines development and regulatory submissions.

3. Conclusions

This reflection paper discusses types and sources of PED, general principles and elaborates on the use and value of PED across the medicine lifecycle. From EMA's point of view, PED can inform medicine development and regulatory submissions, by providing patient insights that can be valuable for the assessment of marketing authorisation applications, as well as in the post marketing setting.

Stakeholders are therefore encouraged to embed PED across all stages of medicine development. This can be achieved by liaising early with EMA through scientific advice/qualification of novel methodologies, in order to enable case-by-case discussions on specific development plans and regulatory submissions.

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5. Glossary

Carers are persons who provide care to someone with a chronic illness, disability or other long-lasting health or care need, outside a professional or formal framework.

Patients are persons with personal experience of living with a disease. They may or may not have technical knowledge in medicine development or regulatory processes (differently from patient experts), but their main role is to contribute based on their subjective disease and treatment experience.

Patient engagement activities include all activities involving interaction with patients to gather their experience on disease, preferences, outcomes and treatments.

Patient experts are patients who, in addition to having disease-specific expertise, have the technical knowledge in medicine development and/or regulatory affairs through training programmes provided by specific organisations.

Patient organisation representatives are persons who are mandated to represent and express the collective views of a patient organisation on a specific issue or disease area.

Patient preference studies (PPS) are studies that include any qualitative or quantitative assessment of the relative desirability or acceptability to patients of aspects that differ among alternative health interventions. PPS can, among other things, help with characterisation of medical need, selection of endpoints and estimation of meaningful effect size, as well as identification of subgroups with different preferences.

Patient reported outcomes (PROs) are health/treatment outcomes reported directly by the patient about their health condition or treatment outcome, without the interpretation of a clinician or another person or a device.