EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient experience data in EU medicines development and regulatory decision-making

Outcome of the workshop on 21st September 2022

Patients' perspectives on medicines and their benefits and risks are of great value to the European Medicines Agency (EMA) and the EU Regulatory Network. The Agency has been involving patients in many of its activities for decades, since patients offer valuable insights and perspectives from living with a condition and its treatment, and which outcomes and preferences are important for future treatments. As national healthcare systems are faced with increasing challenges to provide reimbursement for innovative treatments and may need to make informed choices based on robust evidence, users of medicines become instrumental in helping to optimise medicines development and regulatory decision-making. Understanding what matters most to patients will thus also contribute to value assessments by health technology bodies responsible for decisions on reimbursement, ensuring therapies not only get regulatory approval but can reach patients who need them.

Although there has been much progress in the EU in recent years, 'patient experience data' are still not systematically included in all aspects of medicines development and regulation, and they are not always present in the marketing authorisation applications received by the Agency. Reinforcing patient relevance in evidence generation was identified as a key priority for the EU Medicines Regulatory Network to increase patient access to medicines. The European Medicines Agency Network Strategy[1] and the Regulatory Science Strategy[2] thus recommend the advancement of standards for designing, conducting, analysing and reporting relevant studies incorporating robust and meaningful patient experience data for regulatory submission, and to elucidate how such data can best inform regulatory decisions. Patient experience data is also relevant in the context of the implementation of the new Health Technology Assessment (HTA) regulation[3], thus in value assessments by HTAs that inform subsequent decisions by payers.

[1] European Medicines Agencies Network Strategy to 2025:
'Enable access to and analysis of routine healthcare data, analysis of individual patient data from clinical trials, and promote standardisation of targeted data'; 'Pilot the analysis of individual patient data from clinical trials in initial marketing authorisation assessments with a view to a targeted roll out of such analysis'
[2] Regulatory Science Strategy to 2025:
'Advancing patient-centred access to medicines in partnership with healthcare systems'; 'Reinforce patient relevance in evidence generation'
[3] EUR-Lex - 32021R2282 - EN - EUR-Lex (europa.eu)

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Multi-stakeholder dialogue was identified as the best way to progress, and EMA organised a workshop on 21st September 2022, as a starting point to deliver on its commitment to patient experience data. The workshop gathered input from patients, consumers, healthcare professionals, academia, regulators, health technology assessment bodies and industry. The objectives of the workshop included to achieve a common understanding on what constitutes 'patient experience data', including patient engagement, patient preferences and patient reported outcomes; to reflect on current methods and challenges for collecting and incorporating patient data (including real world healthcare data) into medicines development and regulatory assessments, and to agree on priorities to progress ahead.

In this summary, the Agency reflects the main outcomes of the workshop and discusses steps to improve the collection and use of patient experience data to achieve patient-centred medicine development and regulation in the EU.

Key outcomes

Common understanding of Patient Experience Data in the EU

The voice of patients and carers is critical during the whole life cycle of a medicine, from early development to reporting of adverse drug reactions (ADRs) and risk minimisation. Patients' input should become standard at all stages of medicines development and regulatory decision-making. There was broad agreement on the understanding of key concepts:

- **Patient Experience Data (PED)** are data collected via a variety of patient engagement activities and methodologies to collect patients' experience of their health status, symptoms, disease course, treatment preferences, quality of life and impact of health care. For EU regulators, PED does not only involve quantitative sources of evidence (e.g., patient reported outcomes or patient reported experience measures) but also qualitative sources (i.e., any information obtained as part of patient engagement activities that reflect the wider perspective of patients' experience, for example, the outcome of focus groups, surveys or interviews).

  PED ensures that medicines development and approval has taken account of patients' perspectives and experience in living with a particular condition, and ultimately leads to more patient-relevant decisions.

- **Patient Experience Evidence (PEE)** is patient experience data qualified as valid scientific evidence following a scientific assessment. Both PED and PEE are relevant and can complement each other for regulatory purposes; patient data is needed to generate evidence of meaningful outcomes for patients.

- **Patient Engagement**[4] **(PE)** refers to all activities involving interaction with patients to gather their experience on disease, preferences, outcomes and treatments.

- **Patient Preferences (PPs)** refer to how desirable or acceptable is to patients a given alternative or choice among all the outcomes of a given medicine.

- **Patient Reported Outcomes (PROs)** refer to a health/treatment outcome reported directly by the patient without the interpretation of a clinician or another person.

[4] Legal basis, Reg No. 726/2004 - article 78 i) and ii) ; EMA framework for engagement with patients and consumers

Current methodologies

Collection methods and analyses of PED must be fit-for-purpose and produce reliable data. Some methodologies have been developed for collecting and analysing PED, including quantitative and qualitative methodologies based on engagement, but more is needed.

Patient preference studies have not been used much to date in decision-making, because these studies are rather complex to perform, time consuming, with few standardised methods to elicit and capture patients' preferences and they can pose significant resource for companies. It is important to continue building the foundational standards and guidance for integrating PPs in decision-making. There is a need for more discussions on methodology, guidance for requirements, effective research design and global harmonisation across the entire medicinal product life cycle, including upstream interested parties/stakeholders and downstream regulators/policymakers. Equally, it is important to ensure that guidance is developed based on practical experience with the use of PP tools and methodologies, so that it is proportionate and does not add unnecessary rigidity that would prevent incorporating the outcomes of the ongoing learning process.

A robust methodology is also needed to develop PROs, validate and evaluate them in study settings (trials or Real World Data). As a principle, PROs should be sensitive to measure the effects of the medicines and simultaneously be meaningful to patients. For this, it is important to consider heterogeneous settings (acute versus chronic conditions) and different patient populations (e.g., cognitive impairment, paediatric, elderly). It is important to define what is the expected PRO data quality for inclusion in the Summary of Product Characteristics (SmPC), because based on the experience to date with cases where PROs are collected, only a fraction have sufficient quality to be included in the Product Information. Adequate planning, collection during the entire study duration and the use of proper statistical analysis is also essential.

Challenges and actions

The workshop served to identify the main challenges faced by stakeholders on PED and to agree actions to address those challenges, thus improving the current status quo.

Alignment among decision-makers needed

Industry stakeholders reported the results of a survey showing that one of the main reasons developers did not include PED as part of the data package submitted in support of marketing authorisation applications was the belief that EU regulators either did not welcome PED or did not consider it of value. The workshop served to clarify and convey a clear and strong message that EU regulators welcome and want PED to be part of marketing authorisation applications.

All stakeholders raised the need for early dialogue to address requirements and expectations in a timely manner. Developers should systematically involve patients in the early stages of medicine development and their input at this stage would ultimately support and guide the planning and generation of PED.

The value of EMA's scientific advice (or protocol assistance for orphan medicines) was highlighted and acknowledged as a cornerstone of the successful generation, collection and use of PED in medicines development and regulatory decision-making. In addition to scientific advice in the context of the development of a specific medicinal product, EMA supports the qualification of new methodologies by

issuing and publishing "qualification opinions", which endorse the use of a methodology in a specific context of use for the generation of evidence for regulatory decision-making.

Furthermore, stakeholders made additional calls to explore other methodologies that would allow for more exploratory joint discussions with regulators and policymakers, such as focus groups or stakeholder platforms to discuss case studies.

> ***Action:*** In general, most challenges identified at the workshop can be addressed through effective research design, collaboration and dialogue between different stakeholders and early patient involvement. Therefore, it was agreed to continue multilateral stakeholder cooperation to obtain the best regulatory outcomes, and to explore additional engagement opportunities (e.g. focus groups) for key topics. In particular, when generating PED, it is key to ensure from early stages that, in addition for regulatory purposes, it needs to be useful for other decision makers such as health technology assessment bodies.

Need for regulatory guidance

All stakeholders raised the need for guidance on what criteria and minimum PED requirements are needed for regulatory decision-making, and ultimately to ensure medicines are fit-for-purpose.

As clinical trials become increasingly global, it is essential to work on harmonisation and international collaboration. Common considerations are needed for all clinical outcome assessments (COAs), which would need to be complemented by specific guidance on established types of COAs other than PROs, such as observer-reported outcomes (ObsROs), clinician-reported outcomes (ClinROs) measures and performance outcomes (PerfOs).

The ongoing harmonisation work at ICH was acknowledged, however it was mentioned that this would still take some time and stakeholders need prompt guidance on the process and regulatory requirements, to be able to systematically include PED in regulatory submissions.

Currently the Agency favours a case-by-case discussion on companies' specific development plans through scientific advice and qualification of new methodologies. Thus, it is very important to maximise the existing support mechanisms for developers at EMA, including the qualification of novel methodologies, regulatory/HTA parallel scientific advice and EMA's Innovation Task Force (ITF) discussions. The learnings from the IMI PREFER project should also be incorporated.

> ***Action:*** The Agency will elaborate a position paper (reflection paper) to provide advice on the best EU approach to generate and collect PED. This will help provide clarity on the process and support mechanisms at EMA, while further collaboration at ICH level continues.

Need for further transparency on decision-making

Stakeholders highlighted that the criteria for deciding whether PED can be considered valid evidence for decision-making are not always clear and accessible. The Agency acknowledged that, at present, there is room for improvement in the way PED's assessment is explained in the assessment report.

> ***Action:*** EU regulators will explore how to better reflect in the assessment report the way PED is assessed as well as the rationale for acceptance/exclusion for Benefit/Risk decision-making in the AR. Further consideration to the way PED is reflected in the product information should be paid. For orphan medicines, PED is also important for discussing significant benefit at time of reviewing the maintenance of the status at time of marketing authorisation application, and

it can also be explored how to best reflect PED in the orphan maintenance assessment report. Stakeholders will also look at how to increase transparency using modern channels.

Digitalisation of patient-generated health data

All stakeholders agreed that the ongoing digital transformation offer enormous opportunities for PED collection and analysis. In particular, mobile health tools could allow real time monitoring and remote participation of patients in observational studies or clinical trials. However, they also imply the use of novel endpoints which will need to be validated and pose further data collection challenges. It is important to ensure appropriate control and security of data, underpinned by an ethical common data governance in the EU. This would create trust and enable patients' willingness to share their personal data. Some innovative ideas, such as the personal data locker proposed by patient organisations are being explored; however, these pose some challenges such as the need for interoperable data given the heterogeneous IT and health systems across Europe.

> ***Action:*** Integration with ongoing activities in the European Health Data Space and the Big Data work plan 2022-2025 are ongoing, and the patient voice will continue to be gathered and used in these forums. In particular, recommendation 3 on data discoverability includes a review on the utility of eHealth data in Q4 2023.

Need for resources and technical expertise

The workshop helped consolidate the notion of PED as a new scientific discipline that has tremendous potential for medicines development and regulation. However, progressing in this area will require adequate resourcing (human and financial) and technical expertise, both for regulators, developers, and patients.

> ***Action:*** As part of the overall strategic plan to advance PED generation, the Agency will look into different options to increase capacity and adequate training. This includes training in areas relating to digital data included in the Big Data work plan 2022-2025, specifically in the recommendation 4 on strengthening the EU Network skills by offering training modules to patients, healthcare professionals & academics in Q4 2023.

Overall strategy on PED

Challenges remain and should continue to be addressed with regard to understandability for patients because some methodologies are not patient-friendly, and those which are easier for patients may not always be the optimal. It is also very important to look at data interpretability, variability and applicability of results. It is also key to establish clear responsibilities, as part of an overall strategy of PED in the EU.

> **Action:** Encourage collaboration and dialogue between different stakeholders and early involvement of patients. It is recognised that EMA is in the optimal position to facilitate stakeholder discussion and progress in this area and, on the basis of the workshop's outcomes, EMA will enable discussions within the Network on current status, next steps and how to monitor progress.