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<Date of submission>

Submission of comments on Reflection paper on patient experience data (EMA/CHMP/PRAC/148869/2025)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

Indeed while most PED data comes from Phase III trials, we do not recommend discouraging collection of PED from earlier stages. Patients can provide valuable information on their side effects across the product li+[@[Comment and rationale (to go to next line within the same cell use Alt + Enter)]]o more "subjective" than clinician reporting of side effects. For example, t+B10he only way a clinician can report pain as an adverse event is via the report from the patient, however, the clinician is taking that report and filtering it through their experiences.

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All the cells with an asterisk (*) should be filled in prior to completing the columns "Comment and rationale" and/or "Proposed changes / recommendation".
For more details on how to use this template please refer to the tab "Manual for commenter".

Name of organisation or individual*	Line from* (line Nr or 0 for general comment)	Line to* (line Nr or 0 for general comment)	Section number	Comment and rationale (to go to next line within the same cell use Alt + Enter)	Proposed changes / recommendation (if applicable - to be used if you want to propose specific text changes)
-3	74	75	1.2	This is the first instance where there is a note to limited experience with a type of data or method. We appreciate that neither preference data or qualitative data from patient engagement activities may be regularly a part of how EMA evaluates applications, however, the FDA does have guidance on preference studies and greater alignment between EMA and FDA on the use and interpretation of these data sources is critical to: * Promote consistency in regulatory expectations for sponsors. * Enhance efficiency in global drug development and minimize duplication of efforts especially when relevant data already exist that could be used, and A lack of alignment places an unnecessary burden stemming from differing requirements among global regulatory agencies who do not acknowledge relevant guidance from their global colleagues. This issue of claiming limited experiences arises again at lines 241/242	Is the reference to "less experience" essential? This phrasing may not provide meaningful direction to sponsors and may inadvertently imply that these well-established research methods lack credibility. It may be more constructive for the section to outline what the EMA expects from sponsors—specifically, a clear and well-supported rationale, accompanied by appropriate references, to assist the EMA in assessing areas where regulatory experience may be limited.
LUNGevity	107	108	2.1.1	The wording for this notion of third party interpretation should be re-considered. A lot of data can be generated under the heading of "patient experience data" and it will need curating/interpretation from someone, eg the sponsor. The FDA has a similar concept when referring specifically to PROs (https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary), but we believe it touches closer to the heart of what this text is trying to achieve. The FDA have it as "A measurement based on a report that comes directly from the patient (i.e., study subject) about the status of a patient's health condition without interpretation of the patient's response by a clinician or anyone else."	Clarify that data reporting (i.e., patient responses to PRO items, but this can be my broadly expanded to other patient engagement activities for generating patient experience data) is not interpreted by a third party. However, data curation and analysis may involve third-party support. You could also note that patients or caregivers can contribute to aspects of this process to help ensure the results remain patient-focused.
LUNGevity	166	166	2.1.2.2	Further guidelines and methodology for use and interpretation of spontaneously generated online PED are needed. For several reasons, there is concern for selection bias and an inaccurate representation of patients' experience. Compared to the other methods in Table 1, this method is much less rigorous.	
LUNGevity	177	177	2.2	Suggest the addition under "clinical trial design" to refine study design and objectives by providing feedback on the relative burden of the schedule of assessments to support streamlining as appropriate	Suggest additional sub-bullet under "refine study design and objectives" bullet of the "Clinical trial design" section on reviewing the schedule of assessments to ensure the frequency, conduct, and location of assessments are relevant and feasible for patients' adherence

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LUNGevity	176	178	2.2	Post marketing: This is a very broad list of issues that PED "could in theory" contribute to. However, some of these issues are quite challenging to overcome, regardless of the source of data, for example "Contribute to preventing medication errors" or "Identify behaviours leading to shortages.". It is unrealistic to place this burden on PED at this stage when clinical data have been insufficient to solve these challenges.	Suggest removing the two bullets mentioned
LUNGevity	205	205	2.3.1	It does not help to include patients' voices when the data they report is referred to as being "subjective". When a patient tells their clinician they have been experiencing fatigue and it is reported as an AE we do not refer to those data as "subjective". There have been a number of studies that show that clinicians under-report important symptoms and side effects when compared to patients.	
LUNGevity	209	214	2.3.1	For a guidance that aims to ensure the inclusion of the patient voice leading with the EQ-5D for the PROM section may not be ideal as many patients feel that this instrument does not adequately capture their experiences. While we appreciate that other stakeholders prioritize data from EQ-5D, this has not typically been the stance of the regulators (EMA or FDA and others).	We suggest the EMA reflects this detail for the EQ-5D versus listing it out first in this section and lead with another PRO measure
LUNGevity	269	272	2.3.2.2	Establishing thresholds for what change would classify as minimally important to most patients, we think that this is an interesting approach, though it goes against what is being typically suggested - while IMI Prefer recommend the value of preference studies for determining or understanding patient focused endpoints we would like to avoid a standalone study being conducted for US regulators based on their needs and another preference study to meet EMA needs.	Perhaps soften languages to suggest preference studies as just one avenue and multiple studies should generally be avoided within the same population and context for when defining thresholds.
LUNGevity	275	278	2.3.2.2.	A key factor in selecting methods missing from this text is the patient's position in their disease trajectory. Recruitment can be difficult at certain stages, which may affect the results and should be considered when planning.	Consider the following addition - 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, their efficiency in doing so, as well as the point in their disease trajectory (or e.g. newly diagnosed versus person with cancer versus person facing cancer progression).
LUNGevity	294	294	2.3.3	"EMA has developed several tools for patient engagement," - for ease on the reader it would be useful to reference the specific tools	ideal to have the tools in a foot note or names listed here to cross reference for ease
LUNGevity	333	333	2.3.3.1.1	More guidance is needed methodologically for using surveys, interview and written consultations, including to ensure that there is a diverse population of patients (demographically, clinically, etc.) responding to capture the full patient experience. Patient organisations are mentioned as a conductor, and while they may meet the community, they can be biased in the types of patients they include (e.g., more educated/involved with their disease)	Consider adding clarification on whether data triangulation from multiple patient engagement activities carry more weight than single methods and how quality of the activities can be evaluated.
LUNGevity	403	407	2.4	Within the reasons given for determining the methods and type of data used, one factor not included is plans for how the data is to be leveraged- i.e., to support an application, develop an endpoint, or to generally provide context. The research question may be how drug A impacts frailty or patient experience with frailty, but the level of rigor in methods and data collection for this question will be very different depending on its intended use.	

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LUNGevity	412	416	2.4.1	Meaningful PED and PRO data are valuable across all stages of clinical development. While Phase III trials typically generate the largest body of PED evidence, earlier-phase studies provide an important opportunity to identify and refine the concepts most relevant for later assessment. Patient reports of side effects are no more “subjective” than clinician assessments, which often depend on information provided directly by patients. For example, the only way a clinician can report pain as an adverse event is via the report from the patient, however, the clinician is taking that report and filtering it through their experiences. Ensuring that patient perspectives are captured directly can strengthen the interpretation of tolerability, support dose-finding activities, which has been encouraged by the FDA, and enhance the relevance of outcomes used in pivotal studies.	Consider removing the statement "as it has a number of advantages over collecting them in early phase studies" since early-phase PRO data can help define tolerability standards.
LUNGevity	418	421	2.4.1	This sentence about "regulators, have been working on developing patient-focused guidelines on using PED" should include any countries efforts to put out guidances that cover PED and what goes under that umbrella term. In general this paragraph includes too many ideas to follow, the start of the paragraph is about PED, then PROs are discussed with mention of any other types of COAs falling under PED and then there is a return to PED.	The FDA PFDD guidance docs are already included as a part of the reference list for this document, we recommend, at minimum adding these references to this section. Restructure paragraph to improved flow of ideas.
LUNGevity	428	433	2.4.2	Further clarification and guidance is needed on what it means to "meet quality standards equivalent to trial-based PED" for primary data collection outside of a clinical trial for regulatory assessment. Recognizing that there are important differences between RWD and trial-based data and this may be an unobtainable bar that will hinder use of these data.	Consider adding text on what exactly quality standards are needed as well considering including an example where PED from say a registry could compliment clinical trial data.
LUNGevity	432	436	2.4.4	A device may or may not be less burdensome, as a device requiring charging and connections to upload data and it may or may not be faster - it depends on what is being measured. We see the nuance of interpreting data from wearables like pedometers in the lung cancer community, when patients may have a similar number of steps in a day, but there can be large differences within those steps for their energy levels at the end of the day that impact their quality of life (e.g., having energy to eat dinner with family vs going to be early), which would not be captured by step count alone.	We recommend removing subjective language and just stick to what EMA is looking for from wearables
LUNGevity	443	449	2.4.2	Consider adding clarification on using data that has associated patient or carer consent. Insurance claims data often does not have patient consent for use. Also consider adding confidentiality and privacy considerations.	
LUNGevity	464	466	2.4.4	On wearables: Clarity is needed on what would constitute PED - for example, its unclear how measuring adherence to medications constitutes PED as its not data directly from the patient on their experience, as we haven't considered readings from blood pressure devices as a part of PED. Second wearables have their own "burdens" for patients that are different from filling in surveys. Also, the perceived burden of all trial activities (not just PED/PROMs) should be considered/reviewed by patients/patient representatives to help aid in trial recruitment and retention.	Remove text suggesting wearables may be less burdensome and re-consider example around medication adherence.
LUNGevity	503	509	2.5.2	The statement “Making PED representative can be difficult, as patients often have different values and expectations” risks unintentionally downplaying the evidentiary value of patient experience data. Differences in values, expectations, and lived experience are inherent to all forms of human-generated evidence—clinicians also operate with differing assumptions and perspectives, and therapeutic misconception remains a challenge across stakeholder groups. Variation in patient experience should therefore be recognised as a core strength of PED, not a limitation. When PED are collected using rigorous, transparent, and well-defined methodologies, they can be sufficiently robust to inform regulatory and HTA decision-making, even if individual experiences vary. While representation is an important issue, this section, as written, does not clearly articulate how different PED methodologies could be used to meaningfully reach and reflect diverse patient communities. Nor does it clarify what constitutes sufficient representativeness for EMA decision-making, particularly given that clinical trials are global endeavours and routinely rely on evidence drawn from heterogeneous populations.	Remove the commentary on the difficulties associated with representation, focus on presenting solutions on how we work with the community and how different methodologies could be leveraged to broaden whose voices are included.
LUNGevity	518	519	2.5.3	The sentence regarding preferences differing across geographical areas does not seem to fit with the current paragraph on timing. This may better fit under 2.5.2 Representativeness	Suggest moving text to 2.5.2

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LUNGevity	521	523	2.5.3	The issues being flagged for selection bias are problematic for all studies, not just PPS. We appreciate impact can vary, but it's not clear what pointing these specific issues out do to encourage and help people navigate this issues in their studies	Offer solutions for PPS specifically, otherwise suggest acknowledging these issues are **not** exclusively a problem for PPS and researchers should just keep these in mind when recruiting as well as analyzing data
LUNGevity	526	526	2.5.4	The examples given for the data source used are confusing and suggest further editing. A clinical trial could use a wearable to gather data, surveys, etc. such that clinical trials as a data source separate from the other examples seems confusing and connotating mutual exclusivity	
LUNGevity	534	536	2.5.5.1	Other regulatory agencies have spent a lot of resources on this issue around the idea of validation - there is no need to completely ignore that work because the expectation should not be that sponsors need to look at psychometric properties of scales/measures using different methodology for the different agencies, that is not a good use of patients and caregivers time.	We suggest adding the sound scientific rationale presented to support validation of a measure/scale/tool within a population and context will be considered versus the current text
LUNGevity	548	556	2.5.6	Participant burden has been extensively addressed in a recent international Delphi survey that proposes 19 recommendations - one of the key recommendations that we strongly support is the inclusion of patients and caregivers and other relevant stakeholders in the selection of items/measures.	Reference Aiyegbusi et al 2024 Nature Medicine. And include the importance of discussing with all stakeholders how to reduce burden
LUNGevity	614	617	3	In light of other comments made, the it would be wonderful to use the conclusion to unite all stakeholders, global regulatory, HTA/payers and other stakeholders of which EMA is just one. Such alignment would help minimise divergence in quality expectations and acceptance criteria across regions within Europe and globally	