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Overview of comments received on ICH E22 Guideline on general considerations for patient preference studies (EMA/CHMP/ICH/371537/2025)

Please note that comments will be sent to the ICH E22 EWG for consideration in the context of Step 3 of the ICH process.

1. General comments – overview

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
ACRO	0	0		Digital Study Infrastructure: Patient preference studies are increasingly conducted using electronic data capture systems, decentralized trial platforms, and digital patient engagement tools. While the guideline appropriately focuses on methodological considerations, it could acknowledge the growing role of interoperable digital infrastructure in supporting PPS conduct, improving data quality, and facilitating regulatory transparency. Recognizing the role of modern digital research platforms would help ensure the guideline remains applicable as clinical research continues to evolve.	
ACRO	0	0		Data Standards and Interoperability: The guideline discusses the submission of PPS results within the Common Technical Document but does not address the role of interoperable data standards in enabling integration between PPS data and clinical trial datasets. Encouraging the use of common data standards and structured data formats could facilitate reuse of PPS data across studies, improve transparency of regulatory submissions, and support more efficient integration of patient preference evidence within benefit-risk assessments.	
ACRO	0	0		Integration with Clinical Trial Design: The guideline notes that PPS can inform clinical trial design, endpoint development, and benefit-risk assessment. Additional clarification on how PPS evidence may be integrated into these processes would be valuable for sponsors and regulators. Providing further examples or considerations for how PPS findings should be used to inform endpoint prioritization, trial design decisions, or regulatory submissions could improve consistency in the application of PPS across development programs.	
ACRO	0	0		ACRO thanks EMA for the opportunity to provide this comment. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can answer any questions or provide additional details. Thank you. Karen Noonan, Senior Vice President, Global Regulatory Policy, ACRO.	

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Acute Leukemia Advocates Network	0	0		The entire document is written from the perspective of applicants (pharmaceutical companies) submitting to regulatory authorities. •Section 4.8 repeatedly references the "applicant" as the responsible party •The submission framework (CTD modules) is industry-facing •Quality standards, protocols, and analysis plans are all framed around regulatory submission needs The guideline gives no explicit acknowledgment that PPS conducted by patient organizations, advocacy groups, or disease registries could constitute valid evidence for regulatory submissions — even though such studies often exist and may be of high quality. Different motivations and objectives Patient community-led PPS are often conducted to: •Document unmet needs before industry engagement •Capture preferences outside of a specific drug development context •Represent broader patient populations than sponsor-funded studies typically reach S run by patient communities free from industry sponsorship may carry less bias than sponsor-funded studies, yet the guideline offers no framework for evaluating or crediting this independence. Practical pathway to submission If a patient organization has conducted a rigorous PPS, there is no clear guidance on: •How they could submit it directly •How an applicant could reference it without taking ownership of it •How regulators should weight it relative to sponsor-funded studies Pre-competitive and disease-area studies Patient communities frequently run preference studies across multiple diseases or treatments simultaneously, not tied to a single product. The guideline's framework — oriented entirely around a single drug development program — has no mechanism for this kind of broader, disease-level evidence. The guideline essentially creates a closed loop where: 1.Industry funds PPS 2.Industry submits PPS 3.Regulators evaluate PPS in the context of industry submissions Patient communities are invited in only as participants and consultees, never as originators of evidence. This is a fundamental structural gap that reinforces power imbalances in drug development — particularly problematic given that patient organizations often have deeper, longer, and more trusted relationships with their communities than any sponsor could achieve during a development program.	
Acute Leukemia Advocates Network	0	0		The guideline treats patients primarily as data sources rather than as stakeholders with rights, ongoing relationships with researchers, and a legitimate interest in how their input shapes outcomes. A more patient-centered revision would embed co-production, transparency, and accountability throughout.	
Acute Leukemia Advocates Network	0	0	1.3	Section 1.3 explicitly excludes caregiver preferences, but for conditions where patients cannot self-report (advanced dementia, severe intellectual disabilities, very young children), this exclusion leaves a significant gap with no alternative pathway offered.	
Acute Leukemia Advocates Network	0	0	1.3	Section 1.3 explicitly defers labeling placement to regional authorities. From a patient community perspective, this is a missed opportunity — patients have a strong interest in knowing whether and how their stated preferences actually influenced regulatory decisions, which the guideline doesn't require sponsors or regulators to communicate.	
Acute Leukemia Advocates Network	0	0		The guideline treats preferences as relatively static. For chronic or progressive conditions, patient priorities can shift dramatically over time, and there's no guidance on longitudinal preference research or updating PPS findings as a disease or treatment landscape evolves.	
Acute Leukemia Advocates Network	0	0		While the guideline mentions "demographic diversity" in sampling, it gives no specific guidance on reaching underserved, marginalized, or hard-to-reach populations — groups who are often systematically excluded from preference research yet may have the most distinct preferences and unmet needs.	

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Acute Leukemia Advocates Network	0	0		Currently there is no route for patient communities to submit PPS evidence directly.	The guideline should recommend: •A mechanism allowing patient organizations to submit PPS findings directly to regulatory authorities, independent of any applicant •Guidance on how applicants referencing existing patient community PPS should acknowledge the originating organization and preserve the integrity of the original findings •Protection against industry reframing or reinterpreting community-led data without the originating organization's involvement
Acute Leukemia Advocates Network	0	0			Currently the guideline has no conflict of interest provisions at all. A balanced addition should address: •Industry-sponsored PPS — requiring disclosure of sponsorship and any role the sponsor played in study design or analysis •Patient organization-led PPS — requiring disclosure of any industry funding relationships the organization holds
Acute Leukemia Advocates Network	0	0			The guideline's current language defaults to "applicant" and "researcher" in ways that implicitly exclude patient organizations. A systematic revision should: •Replace "applicant" with "applicant or patient organization" where relevant •Add a definition of "patient community-led PPS" in the terminology •Explicitly state in Section 2.2 that patient input extends to leading PPS, not merely informing them
Acute Leukemia Advocates Network	0	0			The guideline should include a transparency requirement whereby: •Regulators communicate back to patient organizations how their PPS evidence was used in a regulatory decision •Where PPS evidence was discounted or not used, a rationale is provided •This creates accountability and enables patient communities to improve future studies
Acute Leukemia Advocates Network	0	0			When a pharmaceutical company funds or commissions a PPS involving patient communities, the guideline should require: •Prospective agreement on data ownership and access rights for the patient community •Patient community review of the final report before regulatory submission •Disclosure of any divergence between patient community interpretation and sponsor interpretation of the same data •Open access to anonymized datasets where feasible
Breakthrough T1D	0	0		Breakthrough T1D (formerly JDRF) appreciates the opportunity to provide comments to the ICH Guideline on General Considerations for Patient Preference Studies, which was published by the EMA on 12 December 2025.	
Breakthrough T1D	0	0		ABOUT BREAKTHROUGH T1D As the leading global type 1 diabetes (T1D) research and patient advocacy organization, Breakthrough T1D helps make everyday life with type 1 diabetes better while driving toward cures. We do this by investing in the most promising research, advocating for progress by working with governments to address issues that impact the T1D community, and helping educate and empower individuals facing this condition. Since 2015, our organization has invested more than €57 million in European projects. In addition, 30 clinical trials are currently funded by Breakthrough T1D in Europe.	

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Breakthrough T1D	0	0		GENERAL COMMENTS Breakthrough T1D welcomes the ICH's harmonization efforts in developing this guidance, especially given the current absence of such guidance from the EMA. This framework can support developers in designing products and clinical trials that better reflect real-world patient priorities, ultimately leading to therapies that patients are more willing to accept and adhere to. It will also strengthen regulatory and health technology assessment decision-making, enhance clinical trial design, and facilitate shared decision-making in clinical practice.	
Dr Yewande Okuleye:Patient insight, Governance &Health Systems	0	0	0	The draft is a valuable step toward harmonised use of patient preference studies (PPS) in regulatory decision-making. A key remaining gap is the treatment of preferences as if they are necessarily stable and decontextualised. In fluctuating or high-burden conditions, preferences may vary across disease states, decision moments, and prior experiences with care. The guideline would be stronger if it explicitly recognised this at design and interpretation stages.	Add a general principle that, where clinically relevant, PPS should examine whether preferences are context-dependent or time-varying, and should explain the implications for study design, analysis, and interpretation.
EFPIA	0	0	General	The guideline is succient and extremely well written, and much appreciated by EFPIA.	
EFPIA	0	0	General	We suggest updating E22 with specific advice about the circumstances in which preference studies would typically be considered as non-interventional studies and the circumstances in which preference studies would typically be considered market research. This classificaiton has important implications for how a preference study is conducted (and which SOPs apply in an industry setting), so it would be helpful to flag that this is a useful point for industry to consider when planning a preference study.	
EFPIA	0	0		Additional guidance (for example, in Section 3.2 of ICH E22) on how patient preference studies could be positioned alongside existing regulatory guidance —such as FDA PFDD Guidances 3 and 4 on the development and scoring of Clinical Outcome Assessments—would be highly valuable. In particular, further clarification would be helpful regarding the potential role of preference studies in informing outcome or endpoint selection for subsequent clinical trials, supporting interpretation of the relative importance of individual components within multi-component endpoints, and informing the assessment of meaningful change. While these applications are described within FDA PFDD Guidances 3 and 4, those FDA guidances do not explicitly address the use of preference studies. As a result, without additional clarification in E22 on how preference studies can be appropriately integrated with existing PFDD guidance, teams working on COA development may be reluctant to consider preference evidence to support these activities.	
EFPIA	0	0		The guidance would be strengthed by inclusion of clearer messaging on the value of early engagement (where feasible) with regulators on design of patient preference studies intended to inform regulatory decision-making. While not all regulators offer early advice on PPS, greater clarity on when during PPS design, execution, or reporting applicants should seek regulatory input (where feasible), and why, would be helpful. Early engagement can support alignment with regulatory expectations, promote robust PPS design, and help ensure that resulting data are fit for regulatory decision-making	
EFPIA	0	0		The vast majority of the principles, methods, and considerations outlined in E22 are equally applicable to caregiver preference studies. It would add significant value to the guidance to add a brief paragraph or note acknowledging that in cases when patients cannot self-report preferences (e.g. young children, severe neurodegenerative conditions), it is important and appropriate to involve caregivers and stating that these general principles apply when collecting caregiver preferences. It would also be helpful for E22 to clarify that while caregiver preferences can be valuable input to regulatory decision-making, caregiver preferences are not a direct substitute for patient preferences and should focus only on observable signs, behaviours, or events.	
EFPIA	0	0		We would appreciate a comment (either in the guidance or in the training material) about whether there are any specific considerations when planning a preference study in a rare disease, or in a healthy population.	

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EFPIA	0	0		We suggest that it would be helpful for E22 to explain that - unlike clinical studies - preference studies are unlikely to provide yes/no answers. A "negative" answer (e.g. patients view a specific disease concept as not-very-important; only a minority of patients would regard the benefit-risk trade-offs as acceptable) can still inform drug development (e.g. by prompting a re-think on the study endpoints; by identifying an important sub-group of patients for whom this drug could be of value) While this point is well understood by people familiar with patient preference studies, it may be new - and surprising - to people from a clinical trial background, since clinical trials generally provide reasonably clear-cut answers about the effect of a drug.	
EFPIA	0	0	General	The inclusion of PPS as a tool to inform risk management and mitigation strategies is a strong and forward-looking approach. Leveraging PPS to guide the need and design of additional risk minimization measures, such as patient cards or educational materials, can enhance evidence-based decision-making and improve outcomes for HCPs and patients in the post-marketing setting. This represents an important step toward more effective and patient-centered risk management.	
EFPIA	0	0		Overall, the guideline clearly outlines the high-level considerations for the design and conduct of patient preference studies and their inclusion in regulatory submissions to inform decision-making. Furthermore, the guideline's clear, globally harmonized definition of Patient Preference Study is valuable for aligning expectations between Sponsors and regulators. Inclusion of summary of key takeaways and/or a checklist of key components for conducting and/or reviewing a PPS, similar to the COREQ for qualitative research or CHEERS for economic evaluations, would be helpful in further guiding the design and execution of PPS.	
EFPIA	0	0		The guideline focuses on patient preference studies as it relates to medical product development of drugs. Patient preference studies also have an important role in the development of drug/device combination products which is not mentioned in the guideline. For example, patient preference for certain device attributes of the combination products could be of interest. Are combination products in scope of this guideline?	
EFPIA	0	0		While it is noted at the beginning of the document that "characteristics" are also referred to as "attributes," consistent use of one term throughout the document versus switching back and forth would enhance clarity for the reader.	
EFPIA	0	0	2.3	In Section 2.3, specific examples of critical information from preliminary research would be helpful, including key patient-relevant attributes and suggested ranges or effect sizes.	
EFPIA	0	0	2.5	While Section 2.5 effectively discusses rationale for data source selection (global vs. regional), consider adding examples of why regional data may differ, such as cultural or socioeconomic factors impacting PPS.	
EFPIA	0	0		Results interpretation may be one of the most difficult hurdles in communicating findings from PPS. Inclusion of a section on how to interpret some commonly observed results and recommendations for disseminating these to stakeholders would be beneficial to researchers conducting these studies.	
EFPIA	0	0		While the document mentions minimizing patient burden, it also encourages very rigorous qualitative work and large samples. Balancing these two requirements could be challenging in some disease areas.	
EFPIA	0	0	2.7	In Section 2.7, it would be helpful to highlight the need for pretesting/pilot testing with a small number of participants prior to final administration within a larger sample. Pretesting/pilot testing can be important in obtaining initial feedback on the questions and survey to allow for any necessary changes before final administration. While this is noted later in the guidance, it is suggested to clearly state it in this section as well.	
EFPIA	0	0	3.2	In Section 3.2, while it is agreed that PPS should account for pre-specified subgroups, additional context around sample size considerations for each subgroup would be beneficial, particularly as it relates to recruiting larger samples sizes, which have implications for study timelines.	
EFPIA	0	0	4.5	In addition to data from clinical studies, a review of published real world studies may be helpful in informing attribute ranges as these may have more reflective estimates for attributes of interest.	

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EFPIA	0	0	4.5	In Section 4.5, in addition to the importance of engaging patients as partners in PPS, consideration should also be given to obtaining insights from external experts and clinicians, among other stakeholders as this would make the findings more relevant, particularly for attributes related to safety/efficacy and trial endpoints.	
EFPIA	0	0	Training Module	The illustrative example approach is very helpful, and the detailed responses to key questions on the guideline support a deeper understanding of the content and application of the guideline for the conduct of PPS.	
EFPIA	0	0	Training Module	Recommend defining levels on slide 9 for clarity.	
EFPIA	0	0	Training Module	While the module explains why we choose certain methods, details are lacking on technical execution, such as minimum standards for survey programming or data security for preference surveys.	
EFPIA	0	0	Training Module	The FAQ section mentions that we should be careful about throwing out "irrational" responses (like failing a dominance check). However, additional guidance would be helpful on clear thresholds for when a participant's data is "too poor" to include.	
EFPIA	0	0	Training Module	On slide 33, it is recommended to clearly state the timing for when a PPS should be conducted within a clinical trial (baseline vs end of study). Additionally, considerations and limitations of conducting PPS within a clinical trial versus as a standalone study would be helpful.	
EFPIA	0	0	Training Module	As this is a training deck, it would be helpful if an example were included illustrating an inappropriate PPS method used in a regulatory submission, along with a critique and guidance on the preferred approach, to help clarify best practices.	
EORTC	0	0	2.4	It would be helpful for the guideline to encourage making anonymised raw PPS data available through public data repositories to reduce unnecessary patient burden. Public availability of such datasets would enable secondary analyses (such as subgroup exploration or pooled analyses) that might otherwise require conducting new PPS.	
EORTC	0	0	2.5	The term “region” is not defined and could refer to various geographical (e.g., across countries, across continents), cultural, or linguistic areas, creating ambiguity in how the guidance should be interpreted and applied.	
EORTC	0	0	2.5	This paragraph lacks clarity on the specific conditions under which PPS conducted in one region may be considered applicable to another. The guidance does not specify which criteria or key factors should be assessed to justify such transferability (e.g., similarity in healthcare systems, cultural context, therapeutic context) nor does it explain how the applicability of PPS results from other regions should be practically evaluated.	
EORTC	0	0	2.5	The text does not clarify whether any form of adaptation or transformation of results (for example, weighted scoring to approximate the characteristics of the target region) would be considered acceptable for regulatory use.	
EORTC	0	0	4.5	Section 4.5 would benefit from explicitly acknowledging that PROs are an important source for identifying attributes and levels. Patient engagement activities, which the EMA Reflection Paper identifies as one of the main sources of patient experience data together with PROMs and PPS, are already encouraged in identifying attributes and levels. Because both the EMA Reflection Paper on Patient Experience Data and the FDA Patient-Focused Drug Development (PFDD) guidance series describe PROMs, PPS and patient engagement input as complementary components of patient experience data, PRO data should also be mentioned here as an additional relevant source. Additionally, preference-based measures used in health economics are sometimes derived from appropriate PROMs. This is a relevant example of how PRO- and HRQoL-based concepts can form the foundation of meaningful PPS attributes, which are known to be common key considerations for patients in fields such as oncology.	Add: "[…] frequency of dosing, and route of administration). **Patient reported outcome data can help identify symptoms, functional impacts and quality of life concepts that patients consider important, which may inform the selection of relevant attributes and levels where appropriate.**"

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EU EYE	0	0	General Comment	The EU EYE welcomes the development of ICH E22 as understanding patient preferences is a critical factor not only at clinical level when one tailors care plans to be acceptable by patients but also in designing therapies or medical devices: considering patient preferences early on in the development stage will eventually contribute to improved compliance (adherence) with the treatment under development as it provides invaluable insights to which therapy modalities are aligned with individual values, lifestyles, and goals and therefore have the highest potential to increase patient satisfaction. The EU EYE believes that PPS will support not only drug development and regulatory approval but also reimbursement processes, enabling decision making across the medicinal product life cycle that is aligned with the true needs of patients. The current draft guideline can be further strengthened by: acknowledging additional aspects such as the educational aspects (health literacy) which are shaped by age, diseases with racial risk factors, etc https://pmc.ncbi.nlm.nih.gov/articles/PMC4011899/; indicating how PPS change over time or with disease stages, when, how and in which settings caregiver input can be considered; and outlining what other evidence can be used in conjunction with PPS.	
EU EYE	0	0	General comment	Patient preference information is rarely used beyond the purpose of the original study, despite being resource intensive to collect. This guideline can support a more sustainable use of patient preference information along the medical product lifecycle. In order to do this, the guideline must go beyond regulatory utility and draw attention to how culture shapes how people interpret symptoms, express distress, and seek help. It influences whether illnesses are viewed through a medical, social, or spiritual lens, dictating trust in Western medicine versus traditional remedies. Cultural norms, stigmas, and gender roles heavily influence treatment-seeking behaviours and the guidelines should acknowledge this more extensively with a distinct paragraph in relation to the regions that are mentioned in the document.	
EU EYE	0	0	General comment	Research has shown that fifteen factors affect the value of PPS in the medical product lifecycle (MPLC). Some are out of the scope of this guidance such as study design and study conduct. However other aspects should be included and in particularly these with the potential to promote the integration of PPI into decision-making along the(MPLC) e.g.the type of situations (stakeholder acceptance, market situations, and clinical situations) as this affects the use of PPS results and the study organization (expertise, financial resources, study duration, ethics and good practices, patient centeredness). https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2019.01009/full	
EUCOPE	0	0		A complete list of references at the end of the document would be helpful.	
European Alliance for Vision Research and Ophthalmology (EU EYE)	0	0	General comment	It is not clear what the terms regional, region and local region refer to. A footnote is needed when the terms first used e.g. line 49 first mentioning of regional. Are regions correlate to the ICH regions or are they geographic? Is EU considered as one region or not.? Comments below referr to specific sections demonstrating why clarification regarding these terms is needed earlier in the document.	
European Haemophilia Consortium	0	0		**Meaningful acknowledgement of patient input.** Section 2.2 explicitly lists patient involvement at every stage of PPS development — from identifying the need for a study to contextualising findings. This is genuinely progressive and signals that patient engagement is not merely cosmetic.	
European Haemophilia Consortium	0	0		**Recognition of preference heterogeneity.** The guideline acknowledges that patients are not a monolith. Section 3.2 notes that disease severity, prior treatment experience, and subgroup membership can all shape preferences differently. For patient communities — especially those living with rare, progressive, or multifaceted conditions — this recognition matters enormously.	
European Haemophilia Consortium	0	0		**Early planning emphasis.** Section 2.6's insistence on early consideration is welcome. Patients have long criticised being consulted too late in development, when key design decisions are already locked in.	
European Haemophilia Consortium	0	0		**Burden reduction.** Sections 2.4 and 2.5 discourage unnecessary duplication of studies and encourage leveraging existing PPS literature. For patient communities — particularly those with rare diseases — repeated participation in studies is genuinely taxing, and this recognition is appreciated.	

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European Haemophilia Consortium	0	0		**The exclusion of caregiver perspectives appears overly categorical.** Section 1.3 explicitly removes caregiver preferences from the guideline's scope. While it is appropriate to emphasise that caregiver views should not substitute for patient preferences, excluding them entirely may overlook the realities of clinical decision-making. In cases involving cognitive impairment, severe disability, paediatric conditions, or end-of-life care, caregivers often play a central role as decision-making partners. A more nuanced approach acknowledging these contexts could strengthen the guideline, as a blanket exclusion may risk generating preference data that does not fully reflect how treatment decisions are made in practice.	
European Haemophilia Consortium	0	0		**"Representative sample" assumptions may disadvantage marginalised patients.** Section 4.3 stresses that the PPS sample should represent the target population, and correctly flags that advocacy group members or clinical trial participants may not be representative. However, the guideline does not go far enough in requiring proactive inclusion of underserved populations - those with lower health literacy, limited digital access, language barriers, or from under-resourced healthcare systems. Without explicit requirements, the path of least resistance will always be to recruit the most accessible patients, who are rarely the most vulnerable.	
European Haemophilia Consortium	0	0		**Health literacy and numeracy are insufficiently emphasised.** While Section 4.6.2 acknowledges numeracy and readability, these considerations appear as minor points within an extensive checklist. For patients without a scientific background, understanding concepts such as probability, relative risk, or trade-off scenarios can be challenging. The guideline would benefit from a stronger directive requiring plain-language validation of instruments and, where appropriate, incorporating health literacy assessments of recruited participants to ensure data quality and inclusivity.	
European Haemophilia Consortium	0	0		**The discussion of informed consent is currently quite limited.** Section 2.1 references ethical conduct and the protection of personal data; however, it does not provide substantive detail on how patients will be informed about the potential regulatory uses of their preference data. For example, a patient completing a survey on acceptable side-effect trade-offs may not be aware that their responses could ultimately contribute to regulatory benefit–risk determinations. Providing clear information about the possible downstream uses of preference data would therefore strengthen the ethical framework. In addition, patients should be informed about any relevant conflicts of interest, including the role of sponsors or other stakeholders involved in the study. They should also be provided with a clear explanation of what constitutes a conflict of interest and how such conflicts are identified, managed, and taken into account in the conduct and interpretation of the study. Transparency in these areas should be considered an ethical responsibility rather than solely a procedural requirement.	
European Haemophilia Consortium	0	0		**Quality checks risk silently excluding the most authentic responses.** Sections 4.6.3 and 4.7 discuss data quality checks, including removing "illogical" responses. From a patient perspective, there is a real risk that responses labelled as illogical - for instance, a patient accepting a very high-risk threshold because they have exhausted all other options - actually reflect legitimate and coherent preferences shaped by lived experience. The guideline should require that excluded data be examined qualitatively before removal, and that the reasoning be reported transparently.	
European Haemophilia Consortium	0	0		**The translation of patient preference study (PPS) data into regulatory decisions remains unclear.** The guideline notes that PPS data "may be considered together with efficacy and safety information in the benefit–risk assessment," yet provides limited detail on the manner of integration. In cases where both patient and health care professional preference studies are available, it is unclear which perspective takes precedence. From a patient perspective, this lack of clarity can be frustrating. Patients who contribute time and personal insights through preference studies deserve transparency regarding how their input is weighed in regulatory decisions, and under what circumstances it may be superseded by other considerations.	
European Haemophilia Consortium	0	0		**The omission of labelling guidance represents a notable missed opportunity.** Section 1.3 indicates that the inclusion of PPS data in labelling is considered "a regional matter outside the scope of this guideline". This creates a significant gap. Providing patients and prescribers with clear information that the approved benefit-risk profile incorporates documented patient preferences would be highly valuable. Relying solely on regional discretion may result in preference data remaining confined to regulatory files, limiting its accessibility to the very individuals it is intended to inform.	

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European Haemophilia Consortium	0	0		The ICH E22 guideline presents itself as a patient-centred framework designed to strengthen methodological standards for patient preference studies, and it does introduce meaningful improvements, such as encouraging earlier patient involvement, greater diversity in sampling, and more rigorous instrument testing. However, a closer reading suggests that the framework remains fundamentally oriented around industry-driven evidence generation, primarily serving the needs of pharmaceutical sponsors and regulatory decision-making rather than reflecting independently defined patient priorities. In practice, patient preference studies under this framework are typically conceived, designed, and funded by pharmaceutical companies, with research questions aligned to support product development and market access objectives. While the guideline emphasises methods for quantifying patients' willingness to accept risks and uncertainty associated with new treatments, it does not address affordability or access - factors that patients frequently identify as central to treatment decisions. This omission risks shaping evidence generation toward demonstrating acceptance of trade-offs for innovative but potentially costly therapies, often through sponsor-designed and sponsor-funded studies submitted to regulators. As a result, although patient voices may be formally incorporated into the process, the guideline as currently written may not provide sufficient safeguards to ensure that patient preference evidence is interpreted within the broader context of access, affordability, and competing healthcare priorities.	
European Haemophilia Consortium	0	0		EHC does not support the approach outlined in the ICH E22 Guideline on Patient Preference Studies. While acknowledging the importance of patient perspectives, EHC believes that healthcare decisions should prioritise individualized, patient-centered care rather than rely on generalised preference data. In our view, treatment approaches must remain flexible and tailored to the unique needs and circumstances of each patient, rather than be guided by aggregated preference trends.	
European Hematology Association (EHA)	0	0	General Comment	The European Hematology Association (EHA) welcomes the opportunity to comment on the ICH E22 Guideline on general considerations for patient preference studies (EMA/CHMP/ICH/371537/2025). Studies assessing patient preferences hold particular significance in rare blood disorders, as these conditions typically involve small patient populations and limited available evidence. The document provides a solid general framework and our patient community, in particular, sees development of the guideline as an important step towards including patients' needs and priorities in the drug development and evaluation process.	

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European Hematology Association (EHA)	0	0	General Comment	Overall, the guideline is well written and informative. It provides a comprehensive overview of the relevance, design, implementation, and application of patient preference studies (PPS), with a clear scope and aim and useful recommendations for this rapidly evolving field. As a generic tool, it does not appear to omit key elements. However, it may be too high-level for certain specialty settings, particularly hematology, where decisions span indolent chronic diseases to rapidly fatal acute leukemias, and treatment options range from chemotherapies with predictable toxicities to novel immunotherapies with unique and uncertain long-term risks (e.g., CRS, neurotoxicity, prolonged cytopenias). The guideline could be strengthened by adding disease-severity and/or therapy-class specific considerations, including how to weigh attributes such as uncertain long-term sequelae and potential for cure versus quality of remaining life. In addition, it would be helpful to more explicitly acknowledge the value of PPS in rare diseases and the practical challenges of conducting these studies in small, geographically scattered patient communities, including cross-country differences in access to diagnosis and treatment that may influence patient preferences. Whilst participant diversity is briefly mentioned under section 4.3, EHA considers that there needs to be far more consideration of this aspect, which is critical for patient preference studies. Demographics such as age, sex, socio-economic group, country of origin, type of healthcare system, severity of disease to name but a few will all impact PPS. Therefore, there needs to be very careful consideration of study design to include diverse participants, potentially with enrichment for some subgroups where a difference in PPS may be seen in initial participant samples. A brief discussion of practical feasibility would also be valuable, noting that many centers lack dedicated infrastructure (personnel, funding) to routinely conduct PPS, and offering suggestions on who should perform these studies and how to implement them in a workable way.	
European Hematology Association (EHA)	0	0	General Comment	Whilst EHA's patient community welcomes the guideline as an important step toward stronger methodological standards for PPS, they find that the guideline needs to go further to make PPS evidence genuinely decision-relevant and patient-centered. First, PPS should not be treated as a parallel, supplementary exercise; the guideline should set clearer expectations for integrating preference elicitation into evidence generation (e.g., embedding preference modules in pivotal trials and explicitly linking preferences to the clinical outcomes and safety attributes patients experience), so that PPS can be interpreted alongside efficacy and safety in benefit–risk assessments. Second, the draft is framed predominantly around “the applicant” and sponsor submissions. Our patient community warn that, as written, the guideline risks positioning patients primarily as data sources rather than stakeholders with an ongoing interest in how their input is governed, interpreted, and used. A more patient-centered approach would embed co-production, transparency, and accountability throughout. In practical terms, it should explicitly recognize high-quality PPS conducted independently by patient organizations, advocacy groups, and disease registries, and provide pathways for how such evidence can be submitted directly or referenced by applicants without transferring ownership. Third, to avoid tokenistic collection of preferences, the guideline should provide clearer direction on interpretation and weighting—how regulators/HTA bodies should appraise PPS (including independence and potential bias), how PPS findings should be used alongside other evidence, and what constitutes an actionable contribution to decision-making.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	0	0	General Comment	In addition, EHA's patient community considers that the guideline does not adequately address the role patient organizations can play in the design and interpretation of PPS. This is particularly important for rare diseases, where patient organizations, which can connect small and dispersed patient communities, can ensure that PPS reflect patient priorities. Furthermore our patient community notes that the guideline does not sufficiently acknowledge that patient preferences can change over time and disease course. This is particularly true for chronic or progressive diseases, such as many hematological conditions. The impact and relevance of the guideline would be enhanced by strengthening these aspects.	
European Hematology Association (EHA)	0	0	General Comment	EHA’s patient community requests that the guideline include clearer transparency and feedback expectations on how PPS evidence is integrated and weighed in regulatory decisions, including when other perspectives (e.g., healthcare professionals) take precedence. There should be a requirement to communicate back to participants and patient communities how PPS informed the decision—and, where it did not, why—not only to build trust and accountability but also to help improve future studies. The current deferral of labelling to regional processes is a missed opportunity, as it may keep PPS impact confined to regulatory files rather than visible to patients and healthcare professionals.	
European Patients' Forum	0	0	General	The European Patients’ Forum (EPF) welcomes the development of the ICH E22 guideline as an important step toward strengthening the systematic use of patient preference studies (PPS) across the medicine lifecycle. The guideline provides a solid foundation for improving the methodological and regulatory relevance of PPS. As a general comment, EPF would recommend strengthening meaningful patient involvement throughout the PPS development phases, from initiation to study design and analysis of results. In addition, including specific methodological considerations on how to involve patients, and leveraging the role and knowledge of patient organisations in study design, recruitment, dissemination, and interpretation, would strengthen the guidance. Transparency on the use of PPS, and encouraging sponsors to communicate results to patients as well as to publis studies in the scientific literature, should also be mentioned more specifically in the guidance.	
European Patients’ Academy on Therapeutic Innovation (EUPATI)	0	0	General	The guideline is a clear and concise resource that empowers stakeholders to advance the science in this area, marking an important first for Pharmaceutical R&D in healthcare. Its success will depend on effective implementation and continued learning from experience, while recognizing the significant effort made to achieve a harmonized approach across diverse global healthcare systems.	
European Patients’ Academy on Therapeutic Innovation (EUPATI)	0	0	General	EUPATI believes training is a valuable tool to address the need for enhancing capacity and adequate knowledge for all stakeholders. This includes Patients', Developers' and Regulators' training on Patient Preference Studies, including methodologies to gather such data, interpretation of such data and use of such data during the drug development process as well as in Regulatory and HTA decision making. Those trainings should comprise tailored content considering the type of involvement in PP investigations: As study participants, as partners in developing the research, as PP study sponsor, as user in healthcare decision making.	Add: To foster the quality and relevance tof this research, training will be needed for Patients', Developers' and Regulators' on Patient Preference Studies including methodologies to gather such data, interpretation of such data and use of such data during the drug development process as well as in Regulatory and HTA decision making.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EURORDIS	0	0	General	Some general information on the typical participant numbers and duration of patient-preference (PP) studies, from study design to publication, may be useful. Based on published studies (e.g., Bridges, A Roadmap for Increasing the Usefulness and Impact of Patient-Preference Studies in Decision Making in Health: A Good Practices Report of an ISPOR Task Force, Value in Health, 2023, and references therein), the number of participants usually ranges from dozens to several hundred. Qualitative studies often include approximately 50-100 participants for exploratory purposes. Quantitative studies, such as discrete choice experiments or best–worst scaling, typically involve 200–500 or more participants to support robust statistical analysis and capture preference heterogeneity across subgroups. Regarding the duration from study conception to publication, the process generally includes: Defining the research question and study design: 1-3 months Developing and piloting the study instrument: 1-2 months Recruiting participants and collecting data: 1-6 months (depending on target population and recruitment strategy) Analyzing data and reporting results: 1-3 months Communicating findings to stakeholders and integrating feedback: 1-2 months Total estimated duration: 5-16 months	
Eurordis - François Houÿez	0	0		Some general informationon the average numbers of participants and the average duration of PP study from the design to the result publication phase would be welcome. From published studies (Bridges,A Roadmap for Increasing the Usefulness and Impact of Patient-Preference Studies in Decision Making in Health: A Good Practices Report of an ISPOR Task Force, Value in Health, 2023 and references included), it seems the number of participants typically ranges from dozens to several hundred. Some studies use around 50–100 participants for qualitative exploration, while quantitative studies (such as discrete choice experiments or best-worst scaling) may involve 200–500 or more participants to ensure robust statistical analysis and to capture preference heterogeneity among subgroups. Regarding the typical duration such studies require, from design to the publication of findings, the process can include: - Defining the research question and study design (1–3 months) - Developing and piloting the study instrument (1–2 months) - Recruiting participants and collecting data (1–6 months, depending on the target population and recruitment strategy) - Analysing the data and reporting results (1–3 months) - Communicating findings to stakeholders and integrating feedback (1–2 months) Total: 5 to 16 months. The total duration is highly dependent on the complexity of the study, the availability of participants, and the need for ethical approvals or iterative feedback from stakeholders	
Eurordis - François Houÿez	0	0		There could be situations where patients don't elicite any preference. Their responses could be evenly distributed among different attributes and levels, not being able to prioritise treatments, or not informing on endpoint selection, or not able to provide useful information on the acceptability of benefit-risk trade-offs. They could be divided, global response could be 50/50. Would that be due to a poorly designed PP study, or truly reflecting patients facing questions where they cannot express a clear preference? In this case, should the study findings be shared with regulators,would they still be value in submitting them? My opinion is yes, but industry might diverge. Was this discuss among ICH E22 guideline developers?	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Lymphoma Coalition	0	0	General Comment	Lymphoma Coalition welcomes the development of ICH E22 and supports the recognition of patient preference studies (PPS) as a meaningful component of evidence generation in drug development and evaluation. Drawing on our experience generating and applying patient experience data in lymphoma and CLL, we consider this guideline an important step forward. At the same time, we see opportunities to further strengthen the draft to ensure that PPS are not only methodologically rigorous, but also genuinely patient-centred, inclusive, and actionable for decision-making. In particular, the guideline would benefit from stronger expectations regarding representativeness and inclusion, the role of health literacy and decisional context, the appropriate integration of caregiver input in relevant settings, recognition of preference heterogeneity over time and along the disease journey, and greater clarity on how PPS findings should be interpreted and used alongside other evidence. Strengthening these elements would help ensure that PPS more accurately reflect the lived realities, decisional contexts, and diversity of patient populations, ultimately improving the relevance and impact of the guideline.	
Lymphoma Coalition	0	0	General Comment	The guideline is heavily regulatory-centric, with minimal explicit mention of HTA bodies, reimbursement decisions or value frameworks. PPS is often more directly used in HTA than in regulatory decisions.	
Lymphoma Coalition	0	0	General Comment	The guideline does not address how PPS findings can be used in clinical practice, particularly in shared decision-making between patients and clinicians.	It could benefit from adding a subsection describing how PPS can inform clinical guidelines, decision aids, and patient-clinician discussions, supporting alignment of treatment decisions with patient values.
Patient Engagement Professional Society (PEPS)	0	0	General / Section 4	The cumulative rigour requirements across E22—study design documentation, pre-registration, sample justification, instrument pretesting and piloting, quality checks, analysis plan pre-specification, and Common Technical Document (CTD) module reporting—represent a substantial investment feasible primarily for large organisations with dedicated health economics, outcomes research, and regulatory affairs functions. Taken together, they risk creating a two-tier system in which PPS is a practical option for well-resourced sponsors but structurally inaccessible for small and medium-sized enterprises (SMEs), start-ups, and the patient advocacy organisations that generate some of the most relevant and independent preference evidence in the field. This is not an argument for reduced scientific rigour, but for proportionate rigour calibrated to the intended use of the study.	Make the proportionality of requirements explicit in the guideline, clarifying that the level of documentation and validation required should be calibrated to the intended regulatory use of the study rather than applied uniformly across all PPS contexts. A PPS conducted early in development to inform attribute selection does not require the same validation standards as one submitted in support of a marketing authorisation benefit-risk assessment.
Patient Engagement Professional Society (PEPS)	0	0	General / Section 4	Without a minimum methodological floor distinguishing regulatory-grade PPS from commercial market research, the cumulative burden creates a perverse incentive: smaller organisations may default to market research approaches that fall below any regulatory standard precisely because the bar for regulatory-grade PPS has been set beyond their reach.	Establish a minimum methodological floor that distinguishes regulatory- or HTA-grade PPS from commercial market insight work, defined at a level that is accessible to SMEs, start-ups, and patient advocacy organisations while preserving the scientific integrity of the evidence base.
Patient Engagement Professional Society (PEPS)	0	0	General / Section 4	The guideline does not provide sponsors with a practical tool for identifying which requirements apply to their specific study context, increasing the risk that the most demanding standards are treated as the universal default.	Provide a tiered framework or decision aid that helps sponsors identify which requirements apply to their specific study context—based on intended use, study phase, and population—reducing the risk that the most demanding standards are treated as the universal default.
Patient Engagement Professional Society (PEPS)	0	0	General	E22 uses terminology that maps differently across regional frameworks (EMA Patient Experience Data framework, FDA Patient-Focused Drug Development guidance series, NIHR Learning for Involvement, EUPATI). Without cross-referencing these frameworks, the guideline contributes to terminological fragmentation rather than resolving it. The qualitative/quantitative framing in Section 3.1, discussed above, constitutes a further inconsistency with regional positions.	Reference established terminology frameworks (EMA Patient Experience Data, FDA PFDD Guidance 1 and 2, NIHR Learning for Involvement, EUPATI) to identify where guideline terminology aligns with or diverges from existing regional usage, and to support consistent interpretation across the guideline's target audience. Resolve the qualitative/quantitative framing in Section 3.1 to ensure consistency with EMA and FDA positions.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Patient Focused Medicines Development (PFMD)	0	0	1.1–1.3	Sponsors and patient organisations engaged with both this guideline and the recent EMA Reflection Paper on Patient Experience Data (EMA/CHMP/PRAC/148869/2025) will encounter a terminological landscape that does not fully cohere. This guideline employs 'patient input' to describe the collaborative dimension of PPS development; the Reflection Paper organises around 'Patient Engagement' and 'Patient Experience Data' as structuring concepts. The relationship between PPS as defined in this guideline and the broader PED category and patient engagement activities described in the Reflection Paper is not articulated in either document, creating unnecessary interpretive complexity for stakeholders seeking to develop an integrated approach to patient evidence generation.	Include an orienting note in the introduction or scope section of this guideline clarifying the relationship between PPS as defined here and the broader concepts of Patient Experience Data and Patient Engagement addressed in the parallel EMA Reflection Paper on Patient Experience Data (EMA/CHMP/PRAC/148869/2025), reducing interpretive complexity for stakeholders working across both frameworks.
Patient Focused Medicines Development (PFMD)	0	0	General	The guideline frames the utility of PPS almost exclusively within the regulatory submission context. PPS evidence also informs health technology assessment, reimbursement decisions, and clinical guidelines, and is an increasingly consequential input across the full health policy decision-making landscape. Limiting the framing of PPS utility to the regulatory domain undersells its relevance and risks discouraging investment in the methodological quality of preference research across contexts where it matters equally.	Explicitly acknowledge within the guideline that PPS evidence has broader applicability beyond the regulatory submission context — informing health technology assessment, reimbursement decisions, and clinical guidelines — and that its utility extends across the full health policy decision-making landscape.
PSI	0	0	2.2	It may be important to elaborate more on ethical considerations, including informed consent, data privacy, and managing potential conflicts of interest when engaging patients in PPS. Are there recommendations on ethical standards and patient engagement best practices?	
PSI	0	0	3.2	The guideline emphasizes the importance of Patient preference studies in drug development and regulatory decision-making. it would benefit from clearer guidance on the applicability of PPS across different therapeutic areas, especially in rare diseases or pediatric populations where patient engagement may be challenging.	
TEDDY	0	0	n.a.	Children and adolescents participation in decision-making process remains inconsistent due to the complexity of interactions between clinicians, parents, and paediatric subjects; existing interventions—largely focused on information provision and engagement—show some positive effects but are limited by heterogeneous and methodologically weak evidence, underscoring the need for more tailored, age-appropriate, and rigorously developed approaches to enable meaningful and sustained participation in clinical practice (https://doi.org/10.1038/s41390-024-03509-5). It is important to explicitly consider paediatric subjects when discussing Patient Preference Studies (PPS), as paediatrics represents a heterogeneous population that differs from adults in terms of developmental stage, maturity, and ability to understand and communicate health-related choices. PPS are particularly valuable in this context because they can capture factors such as treatment adherence, acceptability, and the impact of therapies on everyday aspects of life like play and school, while also incorporating caregiver perspectives when needed. By integrating the preferences of both paediatric subjects and their caregivers, researchers and clinicians can better balance benefits and risks, design more acceptable interventions, and improve adherence, ultimately supporting more ethical and patient-centered decision-making that gives young patients a voice appropriate to their level of maturity.	
ACRO	0	0		Founded in 2002, the Association of Clinical Research Organizations (ACRO) is non-profit trade association representing the world’s leading clinical research and technology organizations, which provide specialized services that are integral to the development of drugs, biologics and medical devices that enable patients to live longer, healthier, and more productive lives. ACRO members provide a wide range of specialized services across the entire spectrum of development - from preclinical, proof of concept, and first in human studies through post-approval, pharmacovigilance, and health data research. ACRO member companies employ nearly 400,000 people worldwide and conduct research in every global region.	
ACRO	0	0		ACRO supports the development of this harmonized approach on the use, design, conduct, analysis and submission of patient preference studies (PPS). ACRO agrees with the importance of generating qualitative and quantitative insights about the relative importance of characteristics that are considered by patients when making decisions about drugs.	
Faculty of Pharmaceutical Medicine	0	0		A key stakeholder in the application of PPS data is HTA bodies. While reference is made to engaging regulatory bodies, no reference is made to HTA bodies. Given that there are now joint regulatory and HTA body meetings at which scientific advice is obtained by industry, consideration could be given to including HTA bodies as stakeholders in this Guideline.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Faculty of Pharmaceutical Medicine	0	0		While the value of PPS is increasingly accepted they are still not widely conducted. Could a subsection on 'Barriers' to conducting and applying the findings from these studies be included in Section 4 and also how to overcome these.	
Faculty of Pharmaceutical Medicine	0	0		Suggest including that consideration be given to how data from PPS should be shared with all relevant stakeholders in order to avoid duplication of effort and possible patient fatigue	
PSI	0	0	4.8	Detail guidance on how to present PPS results effectively to regulators, may be including interpretation of results and dealing with conflicting data is missing	examples of templates or examples for reporting PPS findings in regulatory dossiers
PSI	0	0	4.7	Focus is more on traditional statiscal methods. Guidance on use of AI, advanced machine learning techniques are not discussed	the guidance may encourage use of innovative analytical techniques to enhance robustness or atleast comment on use of AI for analysis.
PSI	0	0	General	No mention of longitudinal PPS designs. It could be valuable for capturing evolving patient preferences over time or in response to a treatment. However, since no agreement is achieved in the literature, maybe the guideline could include it as future research needed on this?	
Acute Leukemia Advocates Network			2.4		The guideline should create a framework for PPS that are: •Disease-level rather than product-level — capturing what patients value across a therapeutic area before any specific drug is in development •Pre-competitive — conducted collaboratively, potentially by consortia of patient organizations, academic researchers, and multiple sponsors •Reusable — with explicit guidance on how such studies can be referenced across multiple regulatory submissions, reducing cumulative burden on patient communities
Acute Leukemia Advocates Network			1,2 or 3,1		Suggested addition to Section 1.2 or 3.1: The guideline should explicitly state that PPS conducted by patient organizations, disease registries, or advocacy groups constitute a recognized category of evidence. This would require: •A dedicated section describing patient community-led PPS as a distinct study type •Criteria for evaluating their quality on their own terms, not solely against industry-submission frameworks •Guidance for regulators on how to weight independently conducted PPS
Faculty of Pharmaceutical Medicine			1.3	There is potential for formal PPS research to be conflated with Patient Involvement and/or Engagement activities. It may be useful to confirm in the scope section that this guidance is not guidance on how to involve or engage patients and the public, nor should formal PPS be used as a replacement for PPI.	
Faculty of Pharmaceutical Medicine			2.2	I welcome the inclusion of guidance on how patients can be involved in the development of PPS and the interpretation/contextualisation of PPS findings.	

2. Specific comments on text

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	2	23		Given that this is the first ICH guideline focused on a type of patient experience data, it would be helpful to include a harmonized definition of patient experience data and its various types to ensure broader understanding to the audience.	We recommend inclusion of a definition of patient experience data, which may be adopting the FDA definition or harmonizing the FDA and EMA definitions.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	3	4	1.1	The phrasing of the definition of PPS "Patient preference studies (PPS) aim to assess the relative desirability or acceptability of actual or potential health interventions, or their characteristics and outcomes." is awkward, because of the switch between treatments and characteristics. A slight edit helps.	Patient preference studies (PPS) aim to assess the relative desirability or acceptability of actual or potential health interventions, or <u>of</u> their characteristics and outcomes.
Lymphoma Coalition	3	8	1.1	The text defines attributes mainly as characteristics of interventions and gives efficacy/safety as examples. This is correct, but from a patient perspective it risks underemphasising the broader set of treatment-related factors that often drive decisions in real life (such as quality of life). In lymphoma and other cancers, treatment choices are shaped not only by efficacy and safety, but also by uncertainty, monitoring burden, logistical burden, caregiver dependence, route and setting of administration, disruption to work/family life, cognitive load, financial burden, and effects on identity, autonomy and daily functioning.	Amend text to include: efficacy, safety outcomes, quality of life, or any other potentially relevant characteristics. In addition, after line 8, add wording such as: Relevant attributes may also include treatment burden, route and setting of administration, frequency of monitoring, impact on daily functioning, emotional and social consequences, caregiver dependence, uncertainty, and other factors that affect patients' lived experience and decision-making.
PSI	3	4	1.1	The meaning of "the relative desirability or acceptability of actual or potential health interventions, or their characteristics and outcomes" is not clear, especially as a starting sentence.	Patient preference studies (PPS) are designed to systematically elicit how patients value different health interventions or specific characteristics and outcomes of those interventions. In particular, PPS provide structured insights into the relative importance of characteristics—commonly referred to as attributes—that patients consider when making decisions about drugs. Such attributes may include, for example, efficacy- or safety-related outcomes, as well as any other potentially relevant characteristics.
Chiesi Farmaceutici	4	8	1.1	Definition of health intervention should be broadened to Digital Health Solutions or Medical Devices, since the foot note one this is not defined either.	
Thermo Fisher Scientific	4	6	1.1	The guideline uses the term "drug" to indicate interventions that are in scope for the document and then gives additional detail in Footnote 1 that this term is used to cover many medicinal products. Suggest acknowledging in the sentence drugs are not the only type of intervention for which PPS can generate insights, and then refer to the footnote. We assume vaccines are in scope and would suggest explicitly stating this in the footnote (as an example of a preventive medicinal product).	PPS can generate structured insights about the relative importance of characteristics, also referred to as attributes, that are considered by patients when making decisions about drugs <u>(or other medicinal products)</u>[1]. Suggest stating vaccine as an example of a preventive medicinal treatment in the footnote.
EU EYE	6	8	1.1	It is not clear whether " any other potentially relevant characteristic" includes those factors which often drive decisions of eye patients in real life such as less frequent medication regimes, outdoor mobility, travelling distance during follow-ups, and treatment-associated symptoms https://www.ispor.org/heor-resources/presentations-database/presentation/ispor-europe-2018/identifying-patient-preferences-for-glaucoma-treatment-evidence-from-literature-review.	Rephrase to: "any other potentially relevant characteristic such as treatment burden, impact on daily functioning, and other factors that affect patients' decision-making in real life.
European Heart Network (EHN)	6	8	1	Proposing addition to ensure the guideline reflects the average patient experience, not only clinical outcomes. Patients often weigh practical burdens very heavily.	propose addition: "Relevant characteristics may also include treatment burden, mode and frequency of administration, financial burden, access to care, impact on daily activities, work, education, and caregiving responsibilities."
European Hematology Association (EHA)	6	8	1.1	Apart from efficacy and safety outcomes, quality of life considerations as well as route and setting of administration constitute particularly important attributes in PPS. Suggestion to mention these in the introduction as well.	"These attributes may include, for example, efficacy or safety outcomes<u>, quality of life, administration aspects,</u> or any other potentially relevant characteristics."
Thermo Fisher Scientific	6	8	1.1	Suggest including administration characteristics as an example, as these are relevant in some regulatory contexts e.g. to evidence a major contribution to patient care for orphan drug designation.	"These attributes may include, for example, efficacy or safety outcomes, aspects of <u>administration (if relevant to regulatory decision-making)</u>, or any other potentially relevant characteristics."
Acute Leukemia Advocates Network	7	8			Efficacy, safety outcomes, quality of life or any other potentially relevant characteristics.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	9	11	1.1	It is not clear what is meant by 'these'; recommend that 'insights' is not used, given insights implies less robustness/suitability for regulatory submission vs. the term evidence	Modify: Using qualitative and quantitative preference methods to understand the patient perspective on health interventions is important for various aspects of drug development, such as identifying unmet needs, designing clinical studies, and interpreting results.
Lymphoma Coalition	9	27	1.2	The guideline positions PPS primarily in relation to drug development, regulatory submission, benefit-risk assessment, and approvals, without adequately acknowledging the broader ecosystem in which PPS evidence is used. In practice, PPS also inform HTA, reimbursement, and clinical decision-making. In addition, the guideline does not recognise the role of PPS in supporting shared decision-making, patient information, and communication between patients and healthcare professionals. For patient organisations, the value of preference data extends beyond development into clinical care. This narrow framing risks limiting the applicability of the guideline and reinforcing a regulatory-centric view, rather than supporting the integration of patient preferences across the full healthcare lifecycle.	Expand the purpose to add: In addition to informing drug development and regulatory decision-making, patient preference studies may also contribute to health technology assessment, reimbursement decisions, and clinical practice. PPS can support shared decision-making between patients and healthcare professionals, inform patient-facing materials, and enhance communication regarding treatment options, thereby supporting the integration of patient preferences across the medical product lifecycle.
Thermo Fisher Scientific	9	11	1.1	This brief paragraph provides a statement, but it would be helpful to provide some context and clarification as to how understanding these insights is important for drug development, perhaps giving some examples of potential impact.	
European Heart Network (EHN)	12	14	1	Proposing an addition that makes heterogeneity explicit and brings in equity and inclusion, including transgender patients and patients facing social or geographic disadvantage.	propose addition: "Patient perspectives and preferences may differ across groups, including by sex, gender, gender identity, age, socioeconomic status, geographic location, health literacy, disability, and access to healthcare."
Eurordis - François Houÿez	12	14	1.1	People frequently believe PP studies can best inform in situations where important benefits could be outweighed by severe risks (informationshowing a subset of patients willing to take the high risk for the significant benefit), However, other situations are equally important: low benefit and low risk, showing a subset of patients who are still interested by the limited benefit; and low benefit and high risk, where the product can be authorised for a small group of patients if significant evidence that that at least a subset of patients would take the risks for the benefit.	PPS may be particularly valuable when seeking to understand how patients perceive and prioritise potential treatment outcomes and other characteristics, and their views on different aspects of their condition: different situations should be explored, with high benefit / high risk, or low benefit/low risk, low benefit/high risk, and explore whether a subgroup of patients would be interested by these different situations.
Thermo Fisher Scientific	12	14	1.1	This brief paragraph provides a statement, but it would be helpful to provide some context and clarification as to why PPS may be particularly valuable in these contexts, perhaps giving some examples. In addition, PPS are not commonly used to understand patients' views on different aspects of their condition, but are valuable when seeking to understand patients' views on different aspects of treatment for their condition. Suggest amend accordingly.	PPS may be particularly valuable when seeking to understand how patients perceive and prioritise potential treatment outcomes and other characteristics, and their views on different aspects of <u>treatment for</u> their condition.
Avicenna Alliance Public and Patient Involvement Task Force	15	18	1.1	We appreciate the inclusion of a diverse range of relevant actors, including patients, healthy individuals, and those at risk, who may contribute to PPS. We also suggest including carers as relevant actors, as they may share and witness important aspects of PPS and can provide valuable perspectives on how different interventions affect their role in disease management. This consideration is particularly relevant in paediatric conditions.	
Cancer Patients Europe	15	18	1.1	The guideline recognises that patients provide "relevant perspectives," but does not sufficiently emphasise that patient input reflects lived experience, which is distinct from clinical or caregiver perspectives and cannot be substituted.	Strengthen wording to explicitly state that patient preferences capture lived experience and should be considered a unique and indispensable source of evidence, not interchangeable with other inputs.
EFPIA	15	15	1.1	The phrasing "use drugs" can often be understood (to a native-English-speaker) as "using illegal drugs". This can be easily addressed by rephrasing the sentence to say "use medicinal products".	Patients who eperience a disease or use **medicinal products** can provide relevant perspectives....

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Heart Network (EHN)	15	18	1	Revising wording to anchor the diversity point in the main introductory definition.	Proposed revised wording: "Patients who experience a disease or use drugs can provide relevant perspectives on the disease outcomes and effects of drugs and other health interventions. For diagnostic or preventive interventions, or possible future treatments, healthy and at-risk individuals may also contribute informative perspectives. These perspectives may differ depending on lived experience and personal circumstances, including gender identity, socioeconomic conditions, geographic context, and barriers to care."
Breakthrough T1D	24	27	1.2	This section states that the purpose of this guidance is to provide general considerations for "PPS aimed at informing drug development, regulatory submission and evaluation, drug approvals, and maintenance of such approvals." While not explicitly stated, this implies that the guideline is targeted primarily toward sponsors and product developers. However, patient advocacy organizations often fund PPS with the intent of informing regulatory decisions. For example, Breakthrough T1D has funded patient preference research on which outcomes are most meaningful to people living with T1D and assessing the risk tolerance of novel T1D therapies. To ensure the broadest possible use of this guideline, we suggest that ICH add language to this section explicitly stating that the considerations within the guideline are relevant to all stakeholders undertaking patient preference research, including non-sponsor organizations and researchers.	
EFPIA	25	27	1.2	The draft guideline states, "This harmonised guideline outlines general considerations about the use, design, conduct, analysis, and submission of PPS aimed …" We believe that "Considerations" understates the wealth of ideas in the guidance and suggest stressing "principles" as well.	"This harmonised guideline outlines general principles and considerations about the use …."
PSI	25	25	1.2	align first sentence with the headlines of the following sections	This harmonised guideline **outlines general principles and practical considerations** about the use, design, …
Breakthrough T1D	28	59	1.3	It may be beneficial to provide a brief explanation of the distinction between patient preference studies (PPS) and other patient-focused measures, such as patient-reported outcome measures, including the different roles that different types of studies, data, and instruments can play in informing regulatory decisions.	
Chiesi Farmaceutici	28	59	1.3	The guideline would benefit from clearer articulation of the types of regulatory questions for which stated-preference methods	Clarify in the guideline the regulatory questions for which stated-preference methods are uniquely informative, including benefit–risk trade-offs, threshold acceptability, and prioritisation of attributes under constraint, and distinguish these from questions that can be adequately addressed using standard survey instruments.
Chiesi Farmaceutici	28	59	1.3	More information is also needed regarding how sponsors should document and justify their methodological choice.	Provide best practices on how sponsors should document and justify the choice of method, ensuring that a well-reasoned decision to use a standard survey rather than a PPS is transparently described and does not result in an unexplained evidential gap.
Chiesi Farmaceutici	28	59	1.3	The guideline would benefit from more information on the rationale for excluding caregiver preferences. In its current form, it is not always clear whether this exclusion reflects methodological scope limitations or considerations related to evidential weight. Explicitly distinguishing between these aspects would improve transparency and avoid misinterpretation of the role of caregiver input in regulatory decision-making.	Clarify the rationale for excluding caregiver preferences by explicitly distinguishing between methodological scope limitations and considerations related to evidential weight.
Chiesi Farmaceutici	28	59	1.3	While the primary focus of the guideline is on direct patient PPS, there are regulatory contexts in which caregiver or proxy preferences may be informative, particularly when patients are unable to directly express preferences. The absence of information on this point may limit appropriate use of such evidence.	Include information on when caregiver or proxy preferences may be informative in regulatory contexts, and specify which quality standards should apply in those circumstances, while maintaining the primary focus on direct patient PPS.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Chiesi Farmaceutici	28	59	1.3	The guideline currently provides limited information on PPS methodology for special populations, such as paediatric patients, cognitively impaired individuals, or patients at end of life. Given the distinct ethical and methodological considerations in these groups, greater clarity on future expectations would be helpful.	Signal the intent to address PPS methodology for special populations—including paediatric, cognitively impaired, and end-of-life populations—through supplementary guidance or a future guideline annex.
EUCOPE	28	28	1.3	The guideline states that revealed-preference methods are outside the scope of this guideline. However, we recommend the guideline should cover all preference methods	
Lymphoma Coalition	29	35	1.3	Terms such as “region”, “regional”, and “local region” are used without definition, creating ambiguity and limiting interpretability, particularly in a global guideline.	Add a footnote or definition clarifying these terms.
Thermo Fisher Scientific	29	59	1.3	We assume these guidelines are not intended to cover health state valuation (i.e. utility studies) using time trade-off or standard gamble with patients. As such we propose this is explicitly called out as 'outside the scope of this guideline' as there would be different considerations required for this type of study.	
Thermo Fisher Scientific	29	32	1.3	The document discusses "acceptable trade-offs" and acceptability of benefits and risks, but does not explicitly acknowledge commonly used quantitative preference outputs (e.g. marginal rates of substitution, maximum acceptable risk, minimum acceptable benefit, preference weights). The absence of explicit terminology and expectations on metrics to be presented may reduce alignment between preference studies.	Suggest adding a footnote next to trade-offs listing commonly used trade-off outputs e.g. maximum acceptable risk and minimum acceptable benefit
EFPIA	30	30	1.3	it can be both interviews and survey	[collecting preference data] New text: through interviews, survey or both.
EUCOPE	35	35	1.3	The footnote at the end of this line could be avoided. A short description of revealed-preference methods (which is almost given in lines 32-33 already) could be pulled into the main text.	Remove footnote and transfer information into main body if necessary
EU EYE	36	46	1.3	Lines 36-46 effectively provide a definition of what is not considered ‘a patient’ for the PPS. Given that there are a few definitions of what constitutes a ‘patient’, this guidance should answer the following question in order to increase its applicability and relevance: “Should clinical and economic decision makers consider patient preference data exclusively or should the views of other stakeholders be considered?” e.g. for some technologies, such as cancer screening or genetic testing, individuals without the condition may become a patient after consumption. In other instances, the patient may not be able to reliably state their preferences, such as young children or those with significant cognitive impairments. For many decisions, even individuals with the disease may not have consumed the technology unless they were in the treatment arm of a trial. Instead of defining who is not a patient, it will be more beneficial if this guidance provides a clear definition of what a patient is for the purpose of the PPS.	
Lymphoma Coalition	36	46	1.3	The section focuses on defining what is not considered a patient, rather than clearly defining who is a patient in the context of PPS. This creates ambiguity, particularly in cases such as at-risk populations, screening contexts, or individuals without prior treatment experience.	Provide a clear and inclusive definition of “patient” for PPS purposes.
Patient Engagement Professional Society (PEPS)	36	39	1.3	Section 1.3 states that E22 applies to drugs intended for prevention or diagnosis, but the guidance that follows is developed almost exclusively in the context of treatment settings. Prevention and diagnostic contexts present materially distinct challenges for PPS design: preferences about the probability of developing a future condition differ structurally from preferences about managing an existing one; the significance of false positives and false negatives in screening programmes requires specific attribute framing; and the relevant patient population may include healthy or at-risk individuals whose relationship to the disease is prospective rather than lived.	Include a dedicated sub-section or annex addressing PPS design considerations for prevention and diagnostic settings, covering attribute framing for probabilistic risk, population definition for at-risk or healthy individuals, and the structural differences between prospective and lived disease experience.
Patient Engagement Professional Society (PEPS)	36	39	1.3	Sponsors and patient organisations working in prevention and diagnostic contexts are left without practical guidance for adapting the general principles of ICH E22 to their specific situation.	Provide worked examples or illustrative scenarios for prevention and diagnostic use cases, sufficient to give sponsors and patient organisations a practical reference point when adapting the guideline's general principles to these contexts.
Avicenna Alliance Public and Patient Involvement Task Force	40	42	1.3	We acknowledge the statement on caregivers, particularly in relation to our comment above. However, we consider it important that caregivers are actively consulted, especially in the context of managing paediatric conditions.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	40	42	1.3	While caregiver preferences should not be treated as a substitute for patient preferences, completely excluding caregiver input creates a major gap for populations who cannot reliably self-report (e.g., young children, advanced dementia, severe cognitive or psychiatric impairment, end-of-life contexts, frail/high-dependence patients). In these settings, caregivers often play a central role in treatment decisions and bear substantial lived burden, so guidance should offer a clear pathway for incorporating caregiver perspectives when patient input is not feasible.	Include a statement recognizing that there are contexts (such as those described) in which caregiver input may offer relevant perspectives and complementarity to patient preferences.
LEO Pharma	40	42	1.3	Although the guideline excludes caregiver preferences, in certain contexts such as paediatric populations or patients with severe cognitive impairment, caregivers may act as primary decision makers or treatment administrators. In these situations, caregiver input may be critical to understanding treatment acceptability and feasibility, while recognising that caregiver preferences are not a replacement for patient preferences where direct elicitation is possible.	Consider acknowledging that, in specific populations where patients cannot reliably provide preferences or where caregivers are the primary decision makers with regards to patients' treatment, PPS methodologies may be adapted to include caregiver input acting as a proxy, with appropriate justification.
Lymphoma Coalition	40	42	1.3	The statement that caregiver preferences are different from and not a replacement for patient preferences is valid, but the current wording is too dismissive and does not reflect important realities in paediatric, cognitively impaired, highly dependent, or severely ill populations. In haematologic malignancies, particularly among children, adolescents, frail patients, or those with intense care dependence, caregivers often play a central role in treatment decisions and lived burden. Their perspectives should not replace patient preferences, but can be highly relevant and sometimes essential.	Caregiver preferences are distinct from patient preferences and should not be considered a substitute for direct patient input where patient input can be obtained. However, caregiver perspectives may be complementary and particularly informative in contexts such as paediatric care, cognitive impairment, severe dependency, or where caregivers are substantially involved in treatment decision-making and care burden.
Marieke Heisen, Patvocates	40	42	1.3	Caregiver preferenes may be informative for the regulatory assessment, but not addressed further. This leaves unclear in which cases regulators would be receptive. This guideline is an opportunity to clarify common confusion concerning caregiver preferences vs. proxy reporting of patient preferences by caregivers; for instance in the pediatric setting, or when the patient cannot cognitively process the questions being asked (e.g. advanced dementia). I think it is important to explain the difference and to acknowledge the appropriateness of proxy reporting.	
Patient Engagement Professional Society (PEPS)	40	42	1.3	Section 1.3 notes that caregiver preferences are informative but are not further addressed. For paediatric populations, patients with cognitive impairment, and those in late-stage or end-of-life settings, this exclusion removes from the guideline's framework precisely the populations where PPS is most difficult to conduct and where the regulatory and ethical stakes are highest. It is unclear whether the exclusion is methodological (proxy PPS requires different study designs outside stated-preference scope) or principled (caregiver preferences carry different evidential weight). The two rationales carry different implications for practice.	Clarify the rationale for excluding caregiver preferences, distinguishing between methodological scope limitations and evidential weight considerations. This distinction is necessary for sponsors to understand whether proxy approaches may be used or whether separate methodological guidance is required.
Patient Engagement Professional Society (PEPS)	40	42	1.3	The absence of guidance on caregiver and proxy preferences leaves sponsors without a methodological or regulatory pathway for generating patient-centred preference evidence for paediatric, cognitively impaired, and end-of-life populations.	Include guidance on when caregiver or proxy preferences may be informative in regulatory contexts, and which quality standards apply in those circumstances, even if the primary focus of the guideline remains on direct patient PPS.
Patient Engagement Professional Society (PEPS)	40	42	1.3	No signal is given in the guideline on whether future guidance will address PPS methodology for populations unable to self-report.	Signal the intent to address PPS methodology for special populations—paediatric, cognitively impaired, end-of-life—in supplementary guidance or a future guideline annex.
Patient Focused Medicines Development (PFMD)	40	46	1.3	The unconditional exclusion of caregiver preferences in the scope section does not acknowledge the patient populations for whom direct stated-preference elicitation using the methods addressed in this guideline is not feasible: those with advanced dementia, severe cognitive or intellectual disability, young children, and those in late stages of life-limiting illness. For these populations, proxy or caregiver preference evidence is not a methodological approximation — it may represent the only available and ethically appropriate means of capturing the perspectives of the people most directly affected by regulatory decisions. An exclusion that provides no indication of how preference evidence for these populations should be handled creates a regulatory gap that will disproportionately affect the most vulnerable patient communities.	Qualify the exclusion of caregiver preferences to acknowledge the patient populations for whom direct stated-preference elicitation is not feasible, and to clarify that caregiver or proxy preference evidence may nonetheless be informative to regulatory assessment in those contexts, without implying equivalence with directly elicited patient data. Signal within the scope section an intention to develop supplementary guidance on proxy preference methods for populations where direct preference elicitation is not feasible.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Thermo Fisher Scientific	40	42	1.3	We acknowledge that caregiver preferences are different from, and not a replacement for, patient preferences; however, in instances when it is may be inappropriate or unethical to directly elicit the preferences of the patients themselves or in instances when the caregiver is the decision-maker, it seems that the guidelines presented in this document would be applicable. As a specific example, in instances when the drug is indicated for paediatric patients, the parent or legal guardian is the treatment decision-maker. This would also be relevant for patients with a severe cognitive impairment who may not be able to complete a PPS. In these contexts understanding caregiver preferences related to choice of drug for treatment of the patient is useful as the caregiver plays a role in treatment decision-making. Scoping caregiver preference studies out leads to a lack of guidance on undertaking preference studies to inform the relative desirability of treatments in these contexts, which is potentially inequitable. Suggest including a more nuanced discussion on this and including caregiver studies in scope when caregiver preferences are relevant to treatment decisions.	We agree that caregiver preferences should not be used in lieu of patient preferences when the patient is able to make their own treatment decisions and it is feasible to elicit their preferences. However, we suggest broadening the scope of the guideline to include caregivers when the caregiver plays a key role in treatment decisions (e.g. paediatrics, patients with severe cognitive impairments etc.) and where it would be inappropriate/infeasible to elicit individual the patients' preferences.
Avicenna Alliance Public and Patient Involvement Task Force	43	46	1.3	Reflecting on the statements relating to caregivers and healthcare professionals, you may wish to include a note of caution regarding potential conflicts of interest.	
EFPIA	47	48	1.3	this document misses a description of the variety of efficacy and safety endpoints and to highlight that patient reported outcome measures may be used as attributes	We recommend inclusion of examples of variety of endpoints including patient reported outcome mesaures in section 4.5
EFPIA	47	48	1.3	Scope clarification: PPS and PROs distinction may be misunderstood without practical guidance on complementarity.	While PPS differ from pateint reported outcomes (PROs), they are complementary: PROs meansure outcomes, PPS assess the relevative importance of those outcomes and acceptable trade-offs. Joint planning can improve endpoint selection, interpretation, and weighting of multi-item measures.
EFPIA	47	48		Suggest to include COA's as the overarching category to PRO's	Suggest to replace "...patient reported outcome measures" with "….Clinical Outcome Assessments, including patient reported outcome measures"
EORTC	47	48	1.3	The sentence "It does not focus on patient reported outcome measures." may unintentionally suggest that patient reported outcomes (PROs) are not considered drug characteristics, because it directly follows a sentence stating that the guideline "addresses PPS and the value that patients place on characteristics of drugs". Earlier sections (e.g., lines 6–8) explicitly list clinical outcomes such as efficacy and safety as examples of drug characteristics that matter to patients. PRO-derived outcomes are also clinical outcomes and therefore logically fall within this broader category.The current placement and phrasing risk creating confusion: readers may interpret the statement as excluding PROs from drug characteristics, rather than understanding that PROM methodology is simply outside the scope. If the intention is to differentiate PPS from PROMs, the explanation provided in the ICH E22 training materials achieves this more clearly and avoids misinterpretation.	Revise: "[…] value that patients place on characteristics of drugs. **Patient-reported outcomes (PROs) may themselves represent important drug outcomes, but the methods for developing and validating PRO measures are not covered here.**"
European Hematology Association (EHA)	47	48	1.3	While the guideline does not focus on PROs, it may strengthen the document to include mention of the complementarity between PPS and PROs, seeing as in practice the two are interconnected.	Add acknowledgement that PPs and PROs are complementary and can inform each other.
European Patients' Academy on Therapeutic Innovation (EUPATI)	47	48	1.3	This guideline addresses patient-preference studies, and the value patients place on drug characteristics, including efficacy and safety-related attributes. It does not focus on the development or validation of patient-reported outcome measures as clinical endpoints.	Add: For clarity of the reader, a delineation from and overlaps with the terminology of PRO concepts would be helpful
LEO Pharma	47	48	1.3	The guideline notes that it does not focus on Patient Reported Outcome Measures (PROMs). While scientifically distinct, there is a risk of regulatory misalignment if the attributes in a PPS (e.g., "reduction in itch") do not map to the concepts measured by PROMs in Phase 3 trials. Ensuring conceptual alignment allows the "value" identified in preference studies to be directly applied to the "benefit" measured in clinical trials.	Suggest adding a recommendation for "conceptual alignment" between PPS attributes and clinical trial endpoints to facilitate the integration of preference data into the Benefit-Risk Conclusion (CTD Module 2.5.6).

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Lymphoma Coalition	47	48	1.3	The guideline explicitly says it does not focus on PROs, but PPS and PROs are deeply interconnected in practice. The guideline should clarify the important complementarity between PPS and PROs in practice.	Add clarifying language acknowledging that PPS and PROs are complementar and can inform each other. For example by explaining that PPS can help identify which outcomes matter most to patients and inform interpretation of meaningful change in PROs.
Marieke Heisen, Patvocates	47	47	1.3	What I really find commendable of this guideline is that it describes a wide angle of purposes of PPS witin the regulatory context (see section 3.2). This line here "This guideline addresses PPS and the value that patients place on characteristics of drugs" doesn't do right to what the guideline is covering in reality. It is in my opinion too narrow.	Suggestion: "This guideline addresses PPS and how it can inform drug development and evaluation, including treatment priority setting, outcome selection, and acceptability of benefit-risk trade-offs."
Chiesi Farmaceutici	48	48	1.3	Very brief mention to the difference between PPS and PRO measures can be useful. The brief phrase in column G could be added	PPS assess patient values and trade-offs, whereas PROs quantify patient-experienced outcomes such as symptoms, daily functioning, or quality of life
EFPIA	49	50		Suggest to be more specific about labelling being a matter relevant to the applicable Health Authority	"The placement of PPS data in medicine labelling is considered a matter relevant to the corresponding Health Authority and outside of the scope of this guideline".
EFPIA	49	49		On line 49, it is stated that placement of PPS data in labelling is outside the scope of the guidance. Suggest clarifying what is meant by placement (i.e., the location of PPS in a label vs. inclusion of PPS in labeling in general).	
EUCOPE	49	50	1.3	There is a missed opportunity here to agree on harmonised principles around when PPS data are suitable and informative for the label.	
Marieke Heisen, Patvocates	49	50	1.3	"The placement of PPS data in labelling is considered a regional matter outside the scope of this guideline." While this line is understandable based on the fact that ICH is a global body, many readers may view the guideline as directly applicable to EMA procedures: - The relationship/adoption of guidance between ICH and EMA is not explained in the guideline itself. - The ICH E22 document is offered for review on the EMA website and carries the EMA logo. What will be the route for EMA, other than this guideline, to share with the readers how they will consider PPS in labelling? If a reader interprets the guideline as an EMA guideline, the sentence is confusion; 'regional' might be understood as at a lower level than EMA, e.g. country-specific. This statement therefore leaves a lot unclear.	
EU EYE	51	53	1.3 Scope and Direction	The guidance is an opportunity to highlight the need for researchers to significantly reduce inherent bias in stated preference studies so that stated choice responses replicate real behaviour more directly - the hypothetical scenarios of such studies are non-binding and often lack real-world consequences. A reference to calibrating models could illustrate this aspect e.g. jointly estimating choice and choice certainty https://www.sciencedirect.com/science/article/abs/pii/S0191261516301709 Biased results may guide drug development towards a direction that does not reflect real world. For example patient preference studies in USA have found that most respondents are willing to receive IVT therapy indefinitely if it means adequate preservation of their vision. https://www.nature.com/articles/s41598-021-98568-7 However RWD have shown loss to follow-up (LTFU) or non-persistence to treatment among patients correlated to factors such as age, race, ethnicity, and insurance status. https://www.aao.org/education/editors-choice/barriers-to-neovascular-amd-treatment-compliance-a The bias issue with the stated preference studies can be addressed in various places. We provide the phrasing for consideration either in lines 51-53 or Section 2.3 Preliminary Research lines 75-79 to draw attention to the bias issue	Proposed phrasing: Many methods are available for designing PPS. Recommendations about choice of method and consequently how to conduct the PPS, beyond the general principles outlined below, are outside the scope of this guideline. This guideline assumes that researchers will familiarise themselves with the inherent biases in stated preference studies as a result of the hypothetical scenarios and will address them effectively.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Thermo Fisher Scientific	51	59	1.3	Suggest part of footnote 3 is brought into the main body, for clarity, and a slight re-ordering of text.	Suggestion below: Preference research is a large and evolving field. As such, this guideline provides general considerations and scientific principles rather than detailed technical instructions. Many methods are available for designing PPS. Recommendations about choice of method and consequently how to conduct the PPS, beyond the general principles outlined below, are outside the scope of this guideline. While not formally endorsed or qualified within this guideline, there are external resources that may offer relevant insights and supplementary information.[3] When technical topics are described as examples, these reflect possible options based on current practice, but newer or alternative methods may also be appropriate. When available, interaction early in the process with regulatory authorities can be useful to ensure that the PPS meets regulatory expectations and scientific standards. Footnote 3 would then list the relevant materials.
Patient Focused Medicines Development (PFMD)	53	58	1.3	The guideline acknowledges IMI-PREFER, ISPOR, and other methodological frameworks only in a footnote with a qualifying disclaimer that they are not formally endorsed. IMI-PREFER was developed through a major European public-private partnership and received a positive Qualification Opinion from EMA's CHMP in April 2022 (EMA/CHMP/SAWP/850803/2021); it generated guidance across attribute selection, sampling design, qualitative research standards, and reporting that is closely aligned with the principles of this guideline. ISPOR's Good Practices Task Force reports have shaped how patient preference studies are designed, conducted, and reported across jurisdictions. A footnoted disclaimer understates their relevance and risks discouraging practitioners from drawing on a well-developed evidence base.	Strengthen the treatment of IMI-PREFER, ISPOR, and other relevant frameworks from a footnoted disclaimer to a substantive cross-reference that acknowledges their contribution to the evidence base and methodological principles underlying this guideline, supporting more consistent implementation across therapeutic areas. Recognise that the conditions under which patient involvement in preference research is genuine and capable of generating decision-relevant evidence are themselves a subject of accumulated multi-stakeholder guidance — including PFMD's Quality Criteria for Patient Engagement, IMI-PREFER's recommendations on patient involvement in study design, and related frameworks from PCORI, EUPATI, and HTAi.
EFPIA	54	59	1.3	The evolving nature of the preference field and its impact on the guidance should be introduced much earlier. Consider moving this paragraph to the beginning of section 1.3. Additionally, the current lines 51 - 53 make for a much stronger ending to the Scope and Direction section.	An example for starting Section 1.3 is: “Preference research is a large and evolving field. As such, this guideline provides…and scientific standards. This guideline focuses on methods called stated-preference methods. Stated-preference methods involve collecting preference data through…”
Thermo Fisher Scientific	57	57	1.3	Suggest change "available" to "feasible"	Suggest change to: "When feasible, interaction early in the process with regulatory authorities can be useful to ensure that the PPS meets regulatory expectations and scientific standards."
Avicenna Alliance Public and Patient Involvement Task Force	60	74	2	We recommend providing greater clarity on the terminology used to describe the degree of patient participation. For example, our organisation distinguishes between patient outreach, engagement, and involvement, recognising different levels of participation, from information provision to consultation and co-creation (https://zenodo.org/records/14696578). While some organisations may use these terms interchangeably, this can lead to differences in interpretation. Clear and consistent terminology throughout the document would support alignment and implementation. For example, we consider patient involvement to be particularly relevant here, as there is scope for patients to participate in a co-creation process when designing the PPS, rather than contributing passively through interviews, which represent a one-way form of communication.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
PSI	61	61	2.1	suggest to replace header “2.1 Protection of Study Participants”	2.1 Protection of PPS Participants
European Heart Network (EHN)	64	65	2	Protection should include practical accessibility, not just formal ethics and privacy.	Proposed addition: “Researchers should also consider and minimise avoidable barriers to participation, including barriers related to literacy, language, disability, digital access, time, cost, and other socioeconomic constraints.”
Acute Leukemia Advocates Network	66	73		The guideline mentions patient input but frames it largely as a tool to improve study design rather than genuine co-creation. There's no requirement for patients to be involved as equal partners or co-investigators, nor any standards for *how* that involvement should be structured or compensated	
Cancer Patients Europe	66	74	2.2	Patient input is described as supportive rather than as active partnership. This underestimates meaningful patient engagement.	Strengthen language to reflect co-creation
Chiesi Farmaceutici	66	74	2.2	The guideline does not clearly differentiate between patient involvement in the design of PPS vs patient participation	Clarify the distinction between patient involvement in PPS design and patient participation as study subjects, and provide separate, role-specific guidance on expectations for each.
Chiesi Farmaceutici	66	74	2.2	Current guidance focuses primarily on whether patient involvement has taken place, with limited attention to its substantive impact on study design. Greater transparency regarding how patient input informed design decisions would enhance scientific credibility and interpretability of PPS	Propose that sponsors describe not only that patient involvement occurred, but how patient input informed and shaped PPS design decisions, including the rationale for any resulting changes.
EFPIA	66	66	2.2	Please include a definition of "patient input" which may be pulled from the FDA PFDD glossary. Given that stakeholders use many terms, such as patient voice, patient experience, patient experience data, patient perspective, it would be helpful to clarify how the guideline is defining "patient input"	
EFPIA	66	68		Most of the time, the guideline is discssing patients as participants in a preference study. However in section 2.2, the terminology 'patient' is referring to patients as collaborators in a preference study design. It would be helpful to add a sentence to clarify this difference.	
European Hematology Association (EHA)	66	74	2.2	EHA's patient community suggests expanding this section to a) explicitly mention the role of patient organizations, particularly for rare diseases, and b) recognize patients as equal partners in the design, development and interpretation of these studies.	"Patients should be involved, where feasible, as partners in defining objectives, selecting attributes, reviewing materials, and interpreting findings. The involvement of patient organizations and patient advocates is particularly important in rare diseases where they can help represent small and disperse patient communities."
European Patients' Forum	66	74	2.2 Patient Input in the Development of PPS	Clarify that patient input should occur early and iteratively. Engaging patients at the earliest stages, such as during research question formulation, attribute identification, and study design, ensures that the evidence generated reflects outcomes and trade-offs that matter most to patients in real-world decision contexts. This early input helps avoid misalignment between researcher assumptions and patient priorities. Maintaining iterative engagement throughout the research lifecycle is crucial. Repeated consultation, through methods such as cognitive interviews, pilot testing, and feedback loops allows researchers to refine attributes, validate instrument design, and ensure that preference elicitation tasks remain understandable and meaningful. This iterative process enhances both the methodological robustness and the validity of PPS findings, improving their credibility and usability in regulatory, clinical, and policy decision-making.This approach aligns with the goals of the IHI-UNIFIED project, which aims to establish a harmonised, evidence-based framework for integrating patient preference information (PPI), clinical outcome assessments (COAs), and digital health technology (DHT)-derived measures into healthcare decision-making. Embedding early and ongoing patient input within this framework supports the development of patient-centred endpoints and robust standards, contributing to more consistent and internationally aligned guidance.	ADD: “Patient input should be sought early and iteratively throughout PPS development to ensure study objectives and design reflect patient priorities.”

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Patients' Forum	66	74	2.2 Patient Input in the Development of PPS	Include reference to patient understanding of the objectives and context for the PPS. The guideline recognises the value of patient input but does not explicitly address the importance of ensuring patients understand how PPS contribute to drug development, regulatory submission and evaluation, drug approvals and post-market surveillance. Without adequate understanding, participation may be less meaningful and expectations about the impact of PPS may be unrealistic. Supporting patient understanding can improve data quality, transparency and trust in regulatory science. At the same time, one of the challenges may be the number of patients required for the PP study. Patients and their organisations can play a key role not only in discussing this and other challenges, but also as active partners in identifying individuals who can participate in the study. This more active role should be properly acknowledged.	ADD: “Patients should be supported through appropriate educational materials to understand the decision-making context in which PPS may be used, including how preference evidence may contribute to benefit-risk assessment and regulatory evaluation. Providing accessible information about the potential role and limitations of PPS in decision-making can support meaningful participation and improve the interpretability of results.” ADD (line 71): Identifying feasibility challenges in conducting a PPS, proposing solutions, and actively contributing to disseminating the study to reach the target number of participants.
European Patients’ Academy on Therapeutic Innovation (EUPATI)	66	66	2.2	Patient input into development of PPS - We welcome the clear message that patients need to be involved in the development of PPS and in which areas they can best contribute. Add a general statement that The involvement of patients and other stakeholders as collaborators in the design of qualitative and quantitative studies to capture patient experience data can also enhance the quality and relevance of study design.	Add: Patient input into PPI studies should be conducted with strong scientific rigor through co-creation between patient organizations, academia, and industry, with patients involved early in the design process. Early engagement helps address key considerations such as literacy, burden, and representativeness.
European Patients’ Academy on Therapeutic Innovation (EUPATI)	66	66	2.2	The section 2.2 could emphasize more clearly that patients or patient organisations can also act as sponsors of such studies.	Add: "patients or patient organisations can also act as sponsors of such studies."
Lymphoma Coalition	66	74	2.2	Patient input is described primarily as a means to improve study design, rather than as a fundamental component of evidence generation. There is no expectation for patients to be involved as equal partners or co-investigators.	Expand this section to include co-creation, co-investigation, and co-interpretation, and specify levels of patient involvement (e.g., consultation, collaboration, co-design). Patients should be involved, where feasible, as partners in defining objectives, selecting attributes, reviewing materials, and interpreting findings, with attention to diversity, representativeness, and appropriate support.
Patient Focused Medicines Development (PFMD)	66	74	2.2	Section 2.2 frames patient input as a contribution that 'supports' a set of applicant-led activities, positioning patients as contributors to processes implicitly owned and led by others. This framing is inconsistent with the partnership models adopted by other regulatory bodies: the MHRA's Patient Involvement Strategy names partnership as a strategic pillar; the NIHR defines patient and public involvement as research carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them; and the FDA's Patient-Focused Drug Development programme embeds patient input from earliest development through to regulatory submission. The distinction matters in practice: evidence from PREFER demonstrates that attribute sets developed collaboratively with patients who have lived experience of the condition under study are less prone to the misspecification errors that most frequently limit the interpretability and credibility of PPS results.	Revise the framing of Section 2.2 to reflect patient engagement as a collaborative, ongoing process throughout the PPS lifecycle, using language consistent with the partnership models adopted by the MHRA and NIHR, rather than positioning patient input primarily as a contribution to applicant-led activities.
Patient Focused Medicines Development (PFMD)	66	74	2.2	The enumeration of activities in Section 2.2 implies that patient involvement is limited to discrete, defined functions rather than being an expectation spanning the full arc of a PPS. This risks being interpreted narrowly in implementation, excluding, for instance, patient involvement in the dissemination and contextualisation of results — a phase explicitly listed in the guideline but framed as a patient contribution rather than a joint activity.	Clarify that the expectation of patient involvement extends across the full arc of a PPS — from initial scoping of the research question through to contextualisation and dissemination of results — and is not limited to the discrete activities enumerated in Section 2.2.
Patient Focused Medicines Development (PFMD)	66	74	2.2	The guideline provides no basis against which applicants can assess or demonstrate the quality of patient involvement in PPS design and conduct, leaving this assessment to unspecified good practice. Established multi-stakeholder quality criteria exist for this purpose and are well-recognised within the field.	Reference established multi-stakeholder quality criteria for patient engagement in research as a practical basis against which applicants can assess and demonstrate the quality of patient partnership in PPS design and conduct. Relevant frameworks include IMI-PREFER's guidance on the conditions for credible patient involvement in preference studies, PFMD's Quality Criteria for Patient Engagement, PCORI's Engagement Rubric, EUPATI's guidance on patient engagement in medicines development, and HTAi's good practice guidance on patient and citizen involvement.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	67	74	2.2	Perhaps, patients' input as way to enhance trustworthiness of findings is missing: sharing results and getting participants' feedback is a well accepted technic to enhance trustworthiness and robustness of results	add a bullet point: - reviewing and providing feedback on results
EFPIA	67	74		Suggest including encouraging obtaining patient perspective. Currently phrased very neutral.	include words like "patient input is highly valuable to support activities,…"
Patient Engagement Professional Society (PEPS)	67	74	2.2	Section 2.2 describes patient input in PPS design using consistently permissive language: involvement 'can support' attribute selection, instrument development, contextualisation of findings, and other activities. When regulatory guidance uses 'can,' organisations working under resource and time pressure will read it as permission to omit. Patient involvement in attribute selection and findings contextualisation is not optional if the resulting PPS is to be considered fit-for-purpose; it is a validity condition. This framing is self-undermining given the scientific rationale for patient involvement articulated elsewhere in the guideline.	Strengthen the language in Section 2.2 from permissive to directive for those aspects of PPS design where patient involvement is a validity condition rather than a quality enhancement—particularly attribute selection and contextualisation of findings.
Patient Engagement Professional Society (PEPS)	67	74	2.2	Section 2.2 conflates two functionally distinct roles without distinguishing between them: patient involvement in study design as co-designers, advisors, or protocol reviewers, and patient participation as data providers (study subjects completing the preference elicitation instrument). These roles require different competencies, different governance arrangements, and carry different implications for study validity. Conflating them creates ambiguity and leaves open the possibility that organisations will meet the letter of the guidance by enrolling patients as study participants while treating involvement in study design as discretionary.	Explicitly distinguish between patient involvement in PPS design as co-designers, advisors, or protocol reviewers, and patient participation as study subjects, with separate guidance on expectations for each role.
Patient Engagement Professional Society (PEPS)	67	74	2.2	The guideline does not require sponsors to document what patient involvement changed and why. Without this requirement, involvement risks being treated as a procedural checkbox rather than a substantive contribution to study validity.	Require sponsors to document not only that patient involvement occurred, but what it changed and why—specifically, how patient input shaped design decisions—rather than treating involvement as a procedural checkbox.
Patient Engagement Professional Society (PEPS)	67	74	2.2	Provide indicative guidance on the depth and timing of involvement appropriate at different stages of PPS development, sufficient to prevent the guideline from inadvertently normalising superficial engagement as compliant practice.	Include indicative guidance on the depth and timing of patient involvement appropriate at different stages of PPS development (exploratory, instrument development, finalisation and contextualisation), sufficient to prevent superficial engagement from being treated as compliant practice.
Patient Engagement Professional Society (PEPS)	67	74	2.2	ICH E22 introduces the term 'patient input' in Section 2.2 without defining it. The FDA defines 'patient input' broadly to encompass data or information provided by patients in any form (FDA PFDD Guidance 1, October 2020). E22 appears to use the term in the narrower sense of co-design involvement. The EMA does not use the term at all. The National Institute for Health and Care Research (NIHR) draws a methodologically significant distinction, reserving 'involvement' for the co-design of research and 'engagement' for communication and dissemination (NIHR Learning for Involvement, updated 2024). Introducing undefined terminology that maps differently onto existing regional frameworks works against the harmonisation objective of the ICH process.	Add a glossary section defining 'patient input' as used in the guideline, explicitly distinguishing it from patient participation as study subjects. Reference established terminology frameworks (EMA Patient Experience Data, FDA PFDD Guidance series, NIHR Learning for Involvement, EUPATI) to identify where the guideline terminology aligns with or diverges from regional usage.
EFPIA	68	74		Patient input is also recommended to ensure language used in the PPS is accessible and understandable	Add "Reviewing language accessibility"
Marieke Heisen, Patvocates	68	74	2.2	Good examples are provided here of what patients bring to the table, e.g., they can identify the use for a PPS, and be part of designing a PPS, including selecting on attributes and levels. However, the interaction is referred to as 'patient input'. It is important to call this patient involvement and/or co-creation, as being part of the design of a PPS is true patient involvement. 'Patient input' does not imply any involvement in the decision making, it is rather unidirectional. Linked to comment lines 264-267. There, the term engagement is used when actually study participation is meant.	
EFPIA	69	69	2.2	The term ‘use’ is too vague, suggest rephrasing the sentence.	Identifying the <u>need</u> or <u>value</u> ~~use~~ for a PPS

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Eurordis - François Houÿez	69	69	2.2	Patient input on identifying the use for a PPS: this input should be seeked early during the R&D phase, to inform the developer on how patients perceive early efficacy / safety data, or for the selection of the dose in confirmatory trials, when there is a dose effect... For example when deciding to stop the development of a drug, assuming the risks won't be accepted by patients, it is important to verify such an assumption via a PP study. Generally speaking, at all important decision steps, it is important to verify if patients and the decison-maker are aligned. The identification of the need (or the use?) for a PPS could also happen when patients are part of a Scientific Advice procedure, or when consulted for the marketing authorisation, or the post-authorisation phase.	Identifying the **need** for a PPS at important decision steps, from early clinical phase to authorisation and post-authorisation
PSI	69	69	2.2	replace “use for” by “use of”. This is how it is stated later (L134)	use of
Thermo Fisher Scientific	69	74	2.2	We agree that patient input is incredibly valuable throughout a PPS. However, protocols are often long and have technical information that is mandatory and not necessarily patient or lay friendly. We suggest patient advisors/partners input into key areas of the protocol to use their time effectively, particularly any patient facing materials, but we would advise against recommending patient advisors review the full protocol, unless they particularly wish to. Identifying feasibility challenges in the conduct of a PPS - this could be expanded to say 'identifying and providing input to resolve feasibility challenges (e.g. best approaches to support recruitment and data collection) in hard to reach populations or in populations who may have difficulty participating in a PPS (e.g. those with visual impairment)	Suggest adjusting 'developing PPS protocols' to 'inputting into key aspects of the PPS protocol and appendices i.e. all patient facing materials, including input on introductory text, the decision context and attributes and levels (and definitions) presented in the PPS to ensure that participant-facing materials are presented in a way that is patient-friendly and easily understood.
Eurordis - François Houÿez	71	71	2.2	One of the challenges could be the numbers of patients needed for the PP study. Patients and their organisations can help not only discussing this and other challenges, but can be active partners for the identification of patients who willtake part in the study. This more active role should be acknowledged.	Identifying feasibility challenges in the conduct of a PPS, proposing solutions and play an active role in disseminating the study to the desired number of participants
EFPIA	73	73		Current: Selecting attributes and levels	Proposed changes: Identifying and selecting attributes and levels In addition, suggest defining “levels” as this appears to be the first mention of this term.
European Hematology Association (EHA)	73	73	2.2	This is the first time the concept of “levels” is mentioned in the guideline. Suggestion to introduce and explain this term in the introduction.	Add a definition of the term "levels".
European Heart Network (EHN)	74	74	2	without a clarification "patient input" risks meaning only highly engaged, highly educated, well-connected, or easy-to-reach patients. Patients should be selected according to the likelihood that they will require the respective medicinal products. Medicines that are exclusively intended for specific target groups should only be considered for those patient populations. However, it should be taken into account that medicines are also used off-label, particularly in children and adolescents when no approved treatment is yet available for these groups.	add points: • Ensuring that patient input reflects the diversity of the population affected by the condition, including populations that may be underserved or under-represented in research; • Considering diversity in sex, gender, gender identity (including transgender and non-binary individuals), age, socioeconomic background, health literacy, disability, and geographic setting when seeking patient input.
Eurordis - François Houÿez	74	74	2.2	This role is particularly important. A group of patients should always be consulted to help interpret and contextutalise the PP study results.	Contextualising the PPS findings and highlighting their practical implications. Same findings can be discussed in different contexts (with the developer, with regulators, with other patients…)
Dr Yewande Okuleye	75	79	2.3	Section 2.3 refers to literature reviews, expert consultations and patient interviews, but it could more explicitly state what preliminary work should uncover. For conditions marked by episodic crises or major shifts between stable and acute states (for example sickle cell disease), preliminary qualitative work should explore contextual and temporal drivers of preference, including prior treatment history, prior experiences of care, and trust in services. Otherwise a later quantitative PPS may be built on attributes that are incomplete or falsely stabilised.	After 'all relevant information is identified and included in the PPS design', add wording such as: 'This should include contextual and temporal drivers of preference, including disease-state variation, prior treatment experience, and prior experiences of care where relevant to the research objective.'

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EFPIA	75	79		Important to position qualitative research as part of the PPS development, not just preliminary research. Need to clearly discriminate between preliminary research, and research that is part of the PPS (e.g. qualitative phase).	
European Heart Network (EHN)	76	78	2	Revising wording to capture experiences that may not surface through standard expert-led approaches.	Proposed revision: "Typically, it will be important to conduct thorough preliminary research (e.g., literature reviews, expert consultations, patient interviews, and engagement with patient organisations and community representatives) to ensure that all relevant information is identified and included in the PPS design."
European Hematology Association (EHA)	76	79	2.3	This section could be strengthened in two ways: a) including consultation with patient organizations and patient advocates, and b) mentioning the importance of gaining an understanding of the treatment journey and decision context.	"Typically, it will be important to conduct thorough preliminary research (e.g., literature reviews, expert consultations, interviews with patients, patient organizations and/or patient advocates) to ensure that all relevant information is identified and included in the PPS design. Preliminary research should consider the patient journey, timing of decisions, prior treatment experience, and the practical and emotional context in which trade-offs are made."
Lymphoma Coalition	76	79	2.3	Preliminary research is described in general terms, but it should explicitly include understanding the treatment journey and the real-life decision context.	Preliminary research should also consider the patient journey, timing of decisions, prior treatment experience, and the practical and emotional context in which trade-offs are made.
Syneos Health CRO	76	77	2.3 Preliminary Research	The section provides a helpful overview of preliminary research and illustrative examples; however, it is missing a key component that can further strengthen understanding of patient sentiment within a disease area.	Specifically, it would be valuable to expand the scope to include patient experience mapping, which complements many of the preliminary research approaches already outlined. Patient experience mapping can be developed through literature reviews alone or in combination with primary research, such as patient interviews. In addition, relevant methodologies may incorporate social listening, which is increasingly used to capture real-time perspectives and sentiments directly from affected communities.
Acute Leukemia Advocates Network	80	84		There's no mechanism to actually *limit* cumulative burden — no registry requirement, no patient community consultation before launching a new study, and no feedback loop returning results to participants.	
Alexander G. Mathioudakis, European Respiratory Society	80	84	2.4	The guideline notes that de novo PPS may not always be justified, but does not explicitly encourage sponsors to assess existing patient preference studies when planning new trials or PPS. As a result, relevant existing evidence on patient priorities, trade-offs or outcome relevance may be overlooked, leading to unnecessary duplication or suboptimal study design.	Consider explicitly encouraging sponsors to systematically assess available, relevant patient preference studies as part of early trial and PPS planning, in a proportionate manner. This may support more efficient study design, reduce unnecessary burden on patients, and improve alignment of trials with patient priorities.
EU EYE	80	84	2.4	The guideline should mention the parameters one can use to decide when meta-regression is possible e.g. diseases with high study volume, consistency in the used elicitation methods, similarities in studied attributes, and reported preference parameters. https://www.sciencedirect.com/science/article/pii/S1098301525024088	
EU EYE	80	84	2.4 De Novo Work may not always be justified	Clarify whether the paragraph on De Novo Work May Not Always be justified refers to the same region or it refers to cross region work. This is another case demonstrating the need to clarify the terms related to region (see General Comment above). The following section 2.5 Global Applicability addresses perhaps this but the phrasing is very confusing without clarifications as to what local region, region, etc are.	

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EUCOPE	80	80	2.4 De Novo Work may not always be justified	We suggest avoid giving principles in the section titles.	Title could be rephrased to "De Novo Work vs Use of Existing Information".
Eurordis - François Houÿez	80	84	2.4 De Novo Work may not always be justified	Another situation where de novo work is not justified, is when a developer conducted a PP study at an early R&D stage, and during the marketing authorisation evaluation, regulators consider different attributes, or different levels should be tested, not based on hypothetical results, but on results from clinical trials.	Although most studies are designed for a specific set of attributes and therapeutic context, there may be existing relevant PPS literature that can address the intended research objective and question(s). Ongoing and future studies should take existing relevant literature of sufficient quality into consideration to avoid unnecessary burden on the patient community. When a PP study has been done to inform the developer during the R&D phase, part of the framework could be re-used / adapted to answer questions at the rgulatory evaluation phase, with different atributes and levels, based on the Effects Table.
Lymphoma Coalition	80	84	2.4 De Novo Work may not always be justified	The concept is right, but the wording could be stronger regarding repetitive, extractive research practices. Patient communities are repeatedly asked to contribute to studies with limited visibility on impact. Good PPS practice should include justification of added value and avoidance of engagement that consumes patient time without clear purpose.	Add: This includes avoiding repetitive or extractive use of patient communities where the anticipated added value of new data collection is limited.
Lymphoma Coalition	80	84	2.4 De Novo Work may not always be justified	The concept of "sufficient quality" is not defined, limiting its operational value and potentially leading to inconsistent interpretation.	Provide criteria for assessing quality, including methodological rigor, relevance, and alignment with research objectives.
Patient Focused Medicines Development (PFMD)	80	84	2.4 De Novo Work may not always be justified	Section 2.4 establishes the principle that existing relevant PPS literature should be considered before commissioning de novo work, yet does not acknowledge that a significant body of patient preference evidence is generated outside sponsor-led programmes — particularly by patient organisations. This creates a disconnect between the formal regulatory framework and the reality of how patient insight is generated and mobilised across the ecosystem. When relevant evidence exists but is not systematically recognised, stakeholders may default to commissioning de novo studies, increasing burden on patient communities and delaying integration of patient perspectives into decision-making.	Acknowledge within the guideline that patient organisations, disease research foundations, and other non-applicant entities may generate PPS that is relevant to regulatory assessment, and that this evidence may constitute the existing literature that applicants are expected to consider under Section 2.4.
Patient Focused Medicines Development (PFMD)	80	84	2.4 De Novo Work may not always be justified	Applicants are not currently encouraged to seek out patient organisation-generated preference evidence before commissioning de novo work. The absence of this expectation may perpetuate unnecessary duplication and impose avoidable burden on patient communities, contrary to the spirit of Section 2.4.	Encourage applicants explicitly to identify and engage with patient organisation-generated preference evidence before commissioning de novo work, and early in the study design process, recognising that this evidence may address research questions relevant to their submissions while reducing unnecessary burden on patient communities.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Patient Focused Medicines Development (PFMD)	80	84	2.4 De Novo Work may not always be justified	No guidance is provided on how the quality and regulatory applicability of patient organisation-generated PPS might be assessed, nor on the pathway by which such evidence can be referenced or incorporated within a regulatory submission. Without this, the absence of a formal mechanism may itself become a barrier to use of evidence that exists and is relevant.	Provide initial guidance on how the quality and regulatory applicability of patient organisation-generated PPS might be assessed, in a manner proportionate to the research context and not imposing submission-equivalent methodological requirements on independent community-generated research. Clarify the pathway by which patient organisation-generated preference evidence can be referenced or incorporated within a regulatory submission.
European Hematology Association (EHA)	81	81	2.4 De Novo Work may not always be justified	In addition to a specific set of attributes and therapeutic context, it is important to consider the target patient population of an existing PPS as well as the health care system, before translating results to the specific research question. EHA suggests adding this consideration.	"Although most studies are designed for a specific patient population, health care setting, set of attributes, and therapeutic context, …."
European Hematology Association (EHA)	81	84	2.4 De Novo Work may not always be justified	Our patient community welcomes this section, discouraging duplication of studies. They note that repeatedly contributing to studies with limited added value is a burden for patients and patient communities, particularly in rare diseases. However they find that the section could be strengthened, in its wording and by defining "sufficient quality".	Add the text: "This includes avoiding repetitive use of patient communities where the anticipated added value of new data collection is limited." Provide criteria for assessing quality, including methodological rigor, relevance, and alignment with research objectives.
EFPIA	83	84	2.4 De Novo Work may not always be justified	Not clear what is meant by taking existing literature of sufficient quality 'into consideration' when evaluating whether a PPS is required to address research objectives.	Provide more clarity as to what consistutes sufficient quality (e.g. PICO assessment, targeted literature review, systematic review; patient-focused data, product labeling) and how it is to be considered (e.g. identification of treatment attributes/outcomes that are meaningful to patients)
EU EYE	83	84	2.4 De Novo Work may not always be justified	It is not clear how one can decide what sufficient quality is. Please consider adding some broad criteria to guide decision of what sufficient quality is.	
European Heart Network (EHN)	83	84	2.4 De Novo Work may not always be justified	While it is important to minimise unnecessary burden on patients participating in preference studies, it is equally important to account for national and regional differences when interpreting and applying study findings. Patient preferences are shaped by variations in healthcare systems, cultural contexts, socioeconomic conditions, and daily living environments. As a result, findings that are applicable in one country (e.g. Portugal) may not be directly transferable to another (e.g. Estonia). Consideration of these differences is essential to ensure the appropriate interpretation and transposability of patient preference study results.	propose adding: However, it should be checked if national findings can be applied to a different regional context or if additional demographic aspects can be of added value.

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Syneos Health CRO	83	84	2.4 De Novo Work may not always be justified	The current reference to using literature that is “relevant” and of “sufficient quality” lacks specificity and would benefit from clearer guidance. Given the wide variability in available sources, additional criteria are needed to distinguish high-quality, appropriate evidence. For example, some materials may be outdated or derived from non–peer-reviewed sources, which can limit their applicability. At the same time, in areas with limited research, older or non-traditional sources may still provide value. These considerations should be more explicitly addressed.	To improve clarity, it is recommended to define both relevance and quality more concretely. Literature should generally be limited to publications from the past five years. Older sources may be included only when more recent evidence is unavailable, and in such cases should be used to inform baseline understanding rather than serve as primary evidence, with validation through additional methods (e.g., primary patient research). Regarding quality, priority should be given to peer-reviewed publications. Non-traditional sources (e.g., blogs or community websites) may be considered if the author can be credibly verified, e.g.,as part of the relevant patient community.
Cancer Patients Europe	85	92	2.4 De Novo Work may not always be justified	Using PPS from other regions may obscure regional disparities in access and healthcare systems, which are highly relevant for cancer patients in Europe.	Include a requirement to assess health system differences, access inequalities, and socio-economic factors
Chiesi Farmaceutici	85	92	2.4 De Novo Work may not always be justified	Section 2.5 recognises that PPS generated in one region may inform regulatory assessment in another, but provides limited information on how sponsors should assess and document cross-regional applicability. For global programmes, this is increasingly important as expectations for population relevance continue to evolve	In Section 2.5 provide minimum acceptability on cross-regional transferability.
Chiesi Farmaceutici	85	92	2.4 De Novo Work may not always be justified	Differences across regions—such as cultural perceptions of treatment, disease experience, health literacy, and healthcare system context—may materially influence patient preferences and therefore warrant explicit consideration.	Identify the factors that should be considered when assessing cross-regional applicability, including cultural, disease-related, health literacy, and healthcare system differences.

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EU EYE	85	92	2.4 De Novo Work may not always be justified	it appears that the term local region refers to the region that development of drug takes place and the term region refers to anywhere else and where development may have taken place at a different time but it is still not clear whether by region one refers to ICH regions e.g. EU, USA,Japan, Canada, Switzerland, China, Brazil, Singapore, and UK. The distinction between a local region when compared to a region must be made clear. If the term region refers to the ICH regions, the need for robust justification for using studies from one region to another (under Global application) should also apply for using studies from one MS of EU to another MS as although both MSs belong to the same ICH region, there are documented differences between EU member states. For example a Multinational European Study of Patient Preferences for Novel Diagnostics to Manage Antimicrobial Resistance has demonstrated that patients in different European countries do not have the same preferences for the attributes of diagnostic tests to manage AMR in primary care. Failure to account for such differences during test development could reduce test uptake, result in continued overuse of antibiotics, and hamper marketisation. https://pmc.ncbi.nlm.nih.gov/articles/PMC6978300/ Global application section acknowledges interregional differences but intra-regional differences should also be acknowledged . e.g. Patient preference studies (PPS) in drug development generally focus on UK-wide perspectives, but subtle differences in preferences, health attitudes, and access exist between the Welsh and English populations, often driven by demographic and policy disparities. While core preferences for treatment efficacy are similar, differences arise in health needs, language requirements for trial participation, and access to new medicines Regional disparities may introduce undetectable bias as a result of which region has more participants in a study e.g. Patient preference studies (PPS) in Belgium, spanning both Flanders and Wallonia, are increasingly vital for integrating patient perspectives into drug development via initiatives such as PREFER. However research on inflammatory and chronic diseases has showed high involvement from Flemish regions rather than Wallonia.	
Eurordis - François Houÿez	85	92	2.4 De Novo Work may not always be justified	When designing a PP study, developers are encouraged to request SA. SA should be seeked for in different regions, to discuss the applicability and possible the numbers of patients for subgroup analysis. Alternatively, when presenting findings, provisions for the extension to more participants should be discussed, if justified.	
Lymphoma Coalition	85	92	2.4 De Novo Work may not always be justified	The concept of global applicability is introduced, but lacks practical guidance on how to assess transferability of PPS results across regions. The text mentions culture and healthcare similarity, but this is not enough. Preferences can be shaped by access constraints, legislation, cultural context, reimbursement rules, health literacy, trust in the system, social protections, travel burden, and local standards of care. A PPS conducted in one setting may not travel well if patient choices are shaped by what is realistically available or affordable.	Add criteria or considerations for evaluating transferability, such as legislative frameworks, cultural differences, healthcare system context, and variability in risk tolerance. Suggest the use of bridging qualitative research where appropriate. Expand the section content to add: …including consideration of differences in standards of care, access to treatments and diagnostics, financial and travel burden, health system organisation, health literacy, and cultural norms that may influence treatment preferences.
Patient Focused Medicines Development (PFMD)	85	92	2.4 De Novo Work may not always be justified	The global applicability provisions in Section 2.5 create a risk of compounding representativeness gaps: if the available body of preference evidence is concentrated in the most accessible and well-resourced patient communities, cross-regional use of that evidence will propagate those biases into regulatory decisions across multiple markets. Conceptual equivalence in instrument translation, referenced briefly in Section 4.6.2, is a necessary but insufficient condition for ensuring that cross-regional application is scientifically defensible; cultural validity — encompassing the extent to which the constructs, trade-off contexts, and risk framings embedded in a PPS instrument are meaningful to patients in a different cultural setting — requires substantially more than translation alone.	Strengthen the guidance on cross-regional applicability under Section 2.5 to address the equity implications of applying preference evidence across regions with different patient populations, disease experiences, and healthcare contexts, and to clarify that cultural validity requires a more systematic assessment than conceptual equivalence in translation alone.

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LEO Pharma	86	92	2.4 De Novo Work may not always be justified	The guideline allows for PPS data from one region to be used in another but requires "justification." To support global development efficiency and avoid duplicative, costly studies, industry would benefit from clearer criteria on what constitutes a scientifically robust justification for portability of preference data across regions. As PPS are increasingly used to inform regulatory benefit–risk assessment, clarification on whether, and in which circumstances, applicants may consider seeking scientific advice from Health Authorities on PPS design would be valuable. Early dialogue could be particularly useful when PPS are expected to play a meaningful role in the benefit–risk narrative, while remaining optional to avoid creating an unintended expectation of prior signoff.	We suggest providing examples of acceptable justifications, such as demonstrating a similar Standard of Care (SoC), comparable disease burden, or qualitative evidence showing that fundamental patient priorities for a specific condition are consistent across the relevant ICH regions.
Patient Engagement Professional Society (PEPS)	86	92	2.4 De Novo Work may not always be justified	Section 2.5 establishes the principle that PPS conducted in one region may inform regulatory assessment in another and that applicants should justify why such PPS is informative to the local region. However, it provides limited practical guidance on which factors require specific assessment and what documentation is expected. Regulators and HTA bodies increasingly expect patient preference evidence to reflect the specific population under consideration, and the bar for demonstrating cross-regional applicability is rising.	Provide more detailed guidance on which factors—including cultural differences in treatment perception, disease experience, health literacy, and healthcare system context—require specific assessment when applying PPS findings across regions.
Patient Engagement Professional Society (PEPS)	86	92	2.4 De Novo Work may not always be justified	Sponsors running global clinical programmes need a consistent standard for documenting cross-regional applicability of PPS data.	Clarify what documentation of cross-regional applicability assessment is expected in regulatory submissions, to give sponsors running global programmes a consistent standard to work to.
Breakthrough T1D	89	90	2.4 De Novo Work may not always be justified	We agree that "the degree of applicability of PPS results from other region(s) to the local region should be evaluated." Even within a region like Europe, there are considerable differences in languages, cultures, and preferences among patients across member states, which might affect how they view benefit-risk trade-offs. It would be helpful to include additional information in the guideline on which specific aspects are most important to consider when evaluating a study's relevance across different regions.	
Thermo Fisher Scientific	89	90	2.4 De Novo Work may not always be justified	In this section it states 'the degree of applicability of PPS results from other region(s) to the local region should be evaluated' without any insight as to how to do this. In Section 4.3. additional detail is given. Suggest either referring to section 4.3. or moving that information up here: From Section 4.3: When data are used across regions, the similarity of culture and health care of a local region to other region(s) should also be carefully considered if they impact preferences. Having some indication (e.g., qualitative preference information) from the local region to support the use of quantitative results from other region(s) studied is helpful.	Add this text to section 2.5: Having some indication (e.g., qualitative preference information) from the local region to support the use of quantitative results from other region(s) studied is helpful.
European Heart Network (EHN)	91	92	2.4 De Novo Work may not always be justified	Regional transferability is not only about culture; it is also about whether people actually face the same real-world care context.	Proposed addition: "In assessing applicability across regions, consideration should also be given to differences in healthcare access, affordability, infrastructure, language, health literacy, social context, and other factors that may influence patient preferences."
Avicenna Alliance Public and Patient Involvement Task Force	93	116	2.4 De Novo Work may not always be justified	We understand that the overall considerations are deliberately general. However, it may be helpful to specify which elements are required versus "nice to have", to support appropriate scoping of PPS study efforts (and corresponding budgeting) at an early stage. There is otherwise a risk that such studies may be deprioritised or considered unnecessary due to the additional effort within the standard drug development pipeline.	

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EUCOPE	93	93	2.4 De Novo Work may not always be justified	Same comment as for line 80, we suggest avoiding giving principles in the section titles.	Title could be rephrased to "Early consideration and planning".
Lymphoma Coalition	93	98	2.4 De Novo Work may not always be justified	The guideline recommends early interaction with regulators, but does not similarly encourage early engagement with patients and patient organisations. If patients are brought in late, key assumptions, attributes, language, and feasibility choices may already be fixed.	Suggest to add: ...Early engagement with patients and patient organisations, alongside regulatory dialogue where relevant, can improve the relevance, feasibility, and interpretability of PPS.
Patient Engagement Professional Society (PEPS)	93	98	2.4 De Novo Work may not always be justified	There is currently no decision trigger or pathway that tells sponsors when a PPS should or must be conducted. Predictability on this question, even if framed as indicative rather than prescriptive, would increase uptake among organisations with constrained resources who need a clear rationale to invest in a PPS at all.	Include indicative guidance on when a PPS should be considered across the development lifecycle, framed as a decision aid rather than a prescriptive requirement, to support organisations with constrained resources in making the case for early investment.
EFPIA	94	95	2.4 De Novo Work may not always be justified	We agree with the emphasis on systematic consideration of the usefulness of PPS throughout drug development, and suggest linking this explicitly to drug development planning activities. This proposed edit is intended to add more emphasis on consideration of preference studies in drug development planning documents (such as a Clinical Development Plan) and to encourage discussion of preference study considerations with regulators (when such discussion is feasible). We also suggest providing some examples (either within E22 or within the FAQ) of the when different types of preference studies could fit into a typical drug development program, as a way of providing additional context to readers less familiar with the topic.	Beginning as early as possible, the usefulness of PPS should be considered systematically throughout drug development, and can usefully be considered as part of overall drug development planning (as discussed further in ICH E8(R1)). This would allow the discussion of the usefulness of the proposed preference studies with the regulator (when feasible) at a suitable timepoint. While detailed discussion about the timing of a PPS is specific to a development program, the timing of th esutdy typically will be influenced by the objective of the PPS, when enough information is available to design the PPS to support the objective, and when the results from the PPS are anticipated to be used. E.g. a preference study intended to inform the choice of study endpoints would typically need to provide results prior to the planning of a pivotal submission study; a preference study intended to provide information on the acceptability of benefit-risk trade-offs could need to provide results in parallel with the results of the corresponding clinical trial (so that the preference and clinical results could be combined to provide quantitative benefit-risk information).
EFPIA	95	98	2.4 De Novo Work may not always be justified	Consider adding a few clarifying examples to situations that impact timing of a PPS	While Detailed discussion about the timing of PPS is specific to a each development program. The timing of the study typically will be influenced by multiple factors including the objective of the PPS, potential challenges with recruitment, availability of data to inform PPS design, and when the results from the PPS are anticipated to be used.

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Alexander G. Mathioudakis, European Respiratory Society	99	113	2.4 De Novo Work may not always be justified	Participant training or preparation is not explicitly addressed as a determinant of PPS data quality. This is particularly relevant for qualitative studies and stated-preference methods such as discrete choice experiments, where insufficient preparation may result in non-informative responses, while excessive or inappropriate training may introduce bias through framing or anchoring effects.	Consider explicitly recognising proportionate, method-appropriate participant preparation or training as a quality consideration in PPS design and conduct, alongside existing measures to minimise bias.
Alexander G. Mathioudakis, European Respiratory Society	99	113	2.4 De Novo Work may not always be justified	The guideline emphasises the importance of selecting outcomes that are meaningful to patients, but does not explicitly acknowledge core outcome sets (COS) as an established, independent methodology for identifying outcomes that matter to patients and other key stakeholders. As a result, opportunities may be missed to use existing, consensus-based outcome frameworks when designing trials or PPS.	Consider explicitly recognising COS as a gold-standard, multi-stakeholder methodology for outcome selection. Where a relevant COS exists, encouraging alignment with the COS, or transparent justification when deviations are necessary, may support more patient-centred, consistent and comparable outcome selection across studies.
European Hematology Association (EHA)	99	113	2.4 De Novo Work may not always be justified	The quality standards section focus only on methodological rigour and do not explicitly include patient-relevant validity (e.g., whether attributes truly reflect what matters to patients).	Include explicit reference to content validity and face validity from the patient perspective, ensuring that study design reflects outcomes and attributes meaningful to patients.
European Patients' Forum	99	113	2.4 De Novo Work may not always be justified	Recognising limitations such as bias, small sample sizes or lack of representativeness strengthens transparency and scientific robustness of PPS design. Early identification of methodological limitations helps mitigate risks affecting validity of results.	ADD: “Limitations, such as potential bias, small sample sizes, or non-representativeness, should be considered and mitigated where possible.”
European Patients’ Academy on Therapeutic Innovation (EUPATI)	99	113	2.4 De Novo Work may not always be justified	In section 2.7 Quality Standards reference is made to proportionality, aliging with research objective, principles of good studyy design and conduct, pre-registration and quality by design. This is setting a high hurdle of expectations. The paper could be even more clear about the proportionality of qualtiy to the different contexts of use. If "context of use" as used in EMA´s guielines on Qualification and "research question " as defined in 4.1 are interchangeable both terms may be added here.	Add: The level of quality should always consider the context of use as not all PPS is directed towards Regulatory and HTA decision making. The expectations on quality of patient preference research and the need for co-creation and alignment will depend on the context of use / research question - who are the relevant stakeholders and what decisions will be informed by the PPS in question.
Eurordis - François Houÿez	99	102	2.4 De Novo Work may not always be justified	In case the study would aim at answering several questions all at once, the research team should consider dividing the study in different substudies. This would help prevent participants of being confused, not understanding clearly where all these questions are leading to.	The research question(s) should align with the research objective, which drive the methods chosen, protocol, analysis plan, data management, and a report that is informative for the given purpose. In case the study would pursue several objectives, it may be more efficient to consider dividing the study into several ones, not to confuse the participants.
Lymphoma Coalition	99	113	2.4 De Novo Work may not always be justified	Quality standards focus on methodological rigour but do not explicitly include patient-relevant validity (e.g., whether attributes truly reflect what matters to patients).	Include explicit reference to content validity and face validity from the patient perspective, ensuring that study design reflects outcomes and attributes meaningful to patients.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	100	113	2.4 De Novo Work may not always be justified	Should ethical review / IRB be added? Also consider adding the supervision by a steering committee comprising patients/patients representative/ clinicians / other healthcare practitioners (such as nurse, physiotherapists, occupational therapists...) relevant expert in PPS qualitative and quantitative (e.g. in the field of social sciences)	add a bullet point: - review by an IRB/ethic committee add a bullet point: - involvment of a steering committee comprising patients or their representatives, healthcare practitioners and relevant experts in qualitative or quantitative research
EUCOPE	100	100	2.4 De Novo Work may not always be justified	Editorial	The research question(s) should align with the research objective, which drive**s** the..
EFPIA	103	107	2.4 De Novo Work may not always be justified	Consider revising the phrase 'good study design' to 'best research practices' to suggest a more holistic and overarching framework.	PPS are expected to follow the principles of best research practices ~~good study design~~ and conduct.
Eurordis - François Houÿez	103	107	2.4 De Novo Work may not always be justified	Another important principle should be not only to generate a study report, if applicable, but also to inform study participants on the findings.	PPS are expected to follow the principles of good study design and conduct. This includes generation of study documents such as informed consent forms, protocol, interview guide, analysis plan, (final) survey instrument, when applicable, and study report. It also includes ensuring that the study design and statistical analysis approaches are pre-specified and well-documented. Equally important, patients who took part in the PP study should be kept informed of the findings.
European Heart Network (EHN)	105	106	2.4 De Novo Work may not always be justified		Add : as well as a short summary in lay-language for the patients as form of acknowledgement of their input.
EFPIA	106	107	2.4 De Novo Work may not always be justified	Consider reworking for clarity	statistical analysis ~~approache~~s <u>plan</u>
Breakthrough T1D	108	109	2.4 De Novo Work may not always be justified	ICH states that "it may be useful to pre-register protocols using a registry, a comparable platform, or other formal mechanisms to enhance research credibility and transparency." Further, ICH notes that de novo work may not always be justified, as "ongoing and future studies should take existing relevant literature of sufficient quality into consideration to avoid unnecessary burden on the patient community" (section 2.4). Thus, registry entries can be a source of such information to aid developers and researchers in refining their protocols. We recommend strengthening the recommendation in lines 108–109 to state that researchers, investigators, or developers are "highly encouraged" to pre-register their PPS protocols.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	108	109	2.4 De Novo Work may not always be justified	this section refers only to pre-register protocol and does not mention the usefulness to share or publish the results	we recommend to make this statement more broad to cover the publication and sharing the results when appropriate
Thermo Fisher Scientific	108	109	2.4 De Novo Work may not always be justified	Suggest removing the following from quality standards as there is currently no functioning registry for PPS: It may be useful to pre-register protocols using a registry, a comparable platform, or other formal mechanisms to enhance research credibility and transparency.	
Breakthrough T1D	110	111	2.4 De Novo Work may not always be justified	ICH refers developers to ICH E8 to use a risk-proportionate approach to align critical quality factors using a "quality-by-design" (QbD) approach. It would be helpful if ICH could expand upon the critical quality factors that are most important to patient preference studies, as the list is wide-ranging (e.g., scientific validity (minimization of bias), operational feasibility and execution (site capability and training), etc.). A QbD approach entails creating a design space and a control strategy. While this is more feasible and understandable in other areas of drug development (e.g., manufacturing or bioanalysis of samples), it is not clear how QbD applies to PPS.	
Cancer Patients Europe	114	116	2.4 De Novo Work may not always be justified	The guideline refers to multidisciplinary teams but does not explicitly include patient representatives or patient organisations.	Add explicit reference to inclusion of patient representatives as part of the PPS team
EUCOPE	114	114	2.4 De Novo Work may not always be justified	Same comment as for line 80, we suggest avoiding giving principles in the section titles.	Title could be rephrased to "Expertise in the PPS Team".
European Hematology Association (EHA)	114	114	2.4 De Novo Work may not always be justified	As mentioned in Paragraph 2.2, patient input is essential in the design and development of PPS. It might be worth mentioning this in Paragraph 2.8 as well when discussing the composition of the study team.	"Whenever possible, the design, conduct, analysis, and submission of a PPS should be undertaken by a cross functional study team with the relevant PPS methodology, clinical expertise, and patient representation."
European Patients' Forum	114	116	2.4 De Novo Work may not always be justified	Consider including patient representatives as part of the multidisciplinary team. Patients provide lived experience of disease and treatment which may improve relevance of attributes, feasibility of instruments and interpretation of results. Patient organisations convey the collective voice of patients and are experts in chanelling insights from their communities. In addition, the EMA's Patient Experience Data (PED) reflection paper highlights the importance of ensuring that patients understand what patient preference studies are and how they can contribute, both as study participants and as research partners. Co-creation approaches are increasingly recognised as good practice in patient engagement.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Eurordis - François Houÿez	114	115	2.4 De Novo Work may not always be justified	These guideline is primarly intended for developers of pharmaceuticals, academics, and regulators. Patients and their organisations are mentioned as providers of input in the design and conduct phase of PP studies (paragraph 2.2). Yet, this paragraph does not specifically address whether patient organisations should or could conduct such studies themselves. It is likely that some organisations might consider conducting patient preference studies during a medicine life-cycle themselves. Even though the document does not prevent a patients' organisation from designing and conducting such a study, this can only be done by applying international scientific standards and practical recommendations (4. Line 176). Therefore, Paragraph 2.8 should maybe be reinforced to call for partnerships when a patient organisation envisages to conduct a PP study.	The design, conduct, analysis, and submission of a PPS should be undertaken by a cross-functional study team with the relevant PPS methodology and clinical expertise. Teams which do not have in-house experience or competence to design and conduct PP studies (eg SMEs, patient organisations) are encouraged to partner with academics or research organisationswith experience in this domain.
Lymphoma Coalition	114	116	2.4 De Novo Work may not always be justified	For high-quality PPS, teams need more than methodologists and clinicians. They also need patient partners and expertise in communication, accessibility, and literacy.	Suggest to add: …including, where feasible, patient partners and expertise in health literacy, communication, behavioural science, and ethics.
Patient Focused Medicines Development (PFMD)	114	116	2.4 De Novo Work may not always be justified	The requirement for a cross-functional team with 'relevant PPS methodology and clinical expertise' in Section 2.8 does not reference patient representatives as members of that team. For an evidence type whose entire rationale rests on capturing the perspectives of people living with disease, the absence of patients and patient advocates from the defined team composition is an inconsistency that warrants correction. Embedding patient representatives within the team — not only as study participants but as contributors to design, oversight, and interpretation — is one of the most operationally straightforward means of improving the relevance and credibility of PPS outputs across the development lifecycle.	Amend Section 2.8 to include patient representatives explicitly within the expected composition of the multidisciplinary PPS team, recognising their role not only as study participants but as co-contributors to study design, oversight, and interpretation of findings.
EFPIA	115	116	2.4 De Novo Work may not always be justified	Given the importance of patient input into preference study work, it would be helpful to have a cross-reference to the earlier discussion of the role of patients in the work on a preference study.	The design, conduct, analysis and submission of a PPS should be undertaken by a cross-functional study team with the relevant PPS methodology and clinical expertise. **As mentioned in section 2.6, input from patient research partners is also valuable.**
PSI	115	116	2.4 De Novo Work may not always be justified	This is essential for study rigor, but it would be stronger if statistical expertise is explicitly mentioned. A skilled statistician is critical for designing robust surveys, determining sample size, and conducting appropriate analyses in patient preference studies.	Revise line 115–116 to: "...undertaken by a cross-functional study team with relevant patient preference methodological, statistical, and clinical expertise." This addition highlights the need for a qualified statistician on the team, ensuring methodological rigor in design and analysis.
PSI	117	117	2.4 De Novo Work may not always be justified	Consider adaption of header, because "post-marketing evaluation" are not mentioned anymore in the following text.	
Avicenna Alliance Public and Patient Involvement Task Force	120	132	2.4 De Novo Work may not always be justified	We suggest including the possibility of patient involvement, whereby patients play an integral role in co-designing the study. The current narrative tends to portray patients as 'data sources', which may introduce inherent bias into the study design. Instead, we advocate for patient representatives to be recognised as integral study partners, contributing to the co-design of PPS as part of the interdisciplinary team referenced in line 115.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Chiesi Farmaceutici	120	132	2.4 De Novo Work may not always be justified	Section 3.1 should more clearly distinguish between qualitative and quantitative Patient Preference Studies (PPS) as methodologically distinct but equally valid scientific approaches	Revise Section 3.1 to explicitly state that qualitative and quantitative PPS have distinct but equally valid scientific roles, and that standalone qualitative PPS may constitute decision-grade evidence when appropriate to the research objective.
Chiesi Farmaceutici	120	132	2.4 De Novo Work may not always be justified	The guideline would benefit from information on when qualitative PPS alone may be sufficient to inform regulatory use	Provide information on circumstances where qualitative PPS alone is sufficient, such as attribute identification, interpretation of patient-reported outcomes, or contextualisation of benefit–risk considerations where quantification is not required.
Chiesi Farmaceutici	120	132	2.4 De Novo Work may not always be justified	Harmonisation with existing regional frameworks is a stated objective of ICH E22. The treatment of qualitative PPS should therefore be consistent with EMA and FDA positions, which recognise the regulatory value of qualitative patient input when methodologically rigorous and fit for purpose.	Ensure alignment of E22 language with EMA and FDA practice by explicitly recognising qualitative PPS as potentially sufficient and decision-relevant when appropriately justified.
Chiesi Farmaceutici	120	132	2.4 De Novo Work may not always be justified	Some language in the guideline appears to frame qualitative research as preparatory or secondary. This framing is inconsistent with contemporary regulatory practice and may discourage appropriate use of qualitative PPS where it is the most robust method.	Revise language across the guideline to avoid characterising qualitative PPS as inherently exploratory or secondary, unless explicitly linked to a specific use case.
European Hematology Association (EHA)	120	120	2.4 De Novo Work may not always be justified	While the definition is technically correct, it is purely conceptual and risks being interpreted in a vacuum. In hematology, where treatment decisions are often urgent and involve high-risk trade-offs (e.g., transplant vs. novel agent), the distinction between a stated preference in a study and the final decision made with a clinician is critical. The current text does not prevent the potential misuse of PPS results to imply that a preference equates to an informed treatment choice.	It must be explicitly recognized that a preference measured in a study is not equivalent to an individual's final informed consent for a treatment. This is particularly important in hematology for decisions with irreversible consequences (e.g., allogeneic stem cell transplant) or novel therapies with unknown long-term risks. Study reports should state that preferences inform, but do not replace, shared decision-making.
Patient Engagement Professional Society (PEPS)	121	132	2.4 De Novo Work may not always be justified	Section 3.1 frames qualitative PPS as research that 'typically informs the design of quantitative studies.' In the context of a harmonised international guideline, this implies a methodological hierarchy in which qualitative work is preparatory and quantitative work is definitive. This position is explicitly inconsistent with the stances taken by both EMA and FDA, which recognise qualitative, quantitative, and mixed-methods research as carrying equivalent scientific validity in generating patient experience data. The EMA Draft Reflection Paper on Patient Experience Data (EMA/CHMP/PRAC/148869/2025) and FDA PFDD Guidance 2 (Methods to Identify What Is Important to Patients, February 2022) both affirm the independent scientific standing of qualitative methods.	Revise Section 3.1 to state explicitly that qualitative and quantitative PPS carry distinct but equally valid scientific roles, and that standalone qualitative PPS constitutes decision-grade evidence in contexts where it is the most fit-for-purpose method for the research objective. Remove or qualify language that frames qualitative research as typically preparatory to quantitative research.
Patient Engagement Professional Society (PEPS)	121	132	2.4 De Novo Work may not always be justified	The guideline provides no guidance on the circumstances in which qualitative PPS alone is sufficient to inform a regulatory use without subsequent quantitative confirmation. This creates ambiguity that may lead sponsors to treat quantitative confirmation as a de facto requirement even where it is not needed or justified.	Provide guidance on the circumstances in which qualitative PPS is sufficient to inform a regulatory or HTA use without subsequent quantitative confirmation, and remove any language elsewhere in the guideline that frames qualitative research as preparatory or secondary.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Patient Engagement Professional Society (PEPS)	121	132	2.4 De Novo Work may not always be justified	The treatment of qualitative methods in E22 diverges from the positions of both EMA and FDA, working against the stated harmonisation objective of the ICH process. Harmonisation requires consistency with existing regional frameworks, not divergence from them.	Ensure the treatment of qualitative methods in the guideline is consistent with the positions of EMA (EMA/CHMP/PRAC/148869/2025) and FDA (PFDD Guidance 2, February 2022) on qualitative, quantitative, and mixed-methods research as detailed in Section 1 of the PEPS consultation response.
EFPIA	123	128	2.4 De Novo Work may not always be justified	The current description of qualitative and quantitative patient preference studies (PPS) could be clarified to better reflect their distinct purposes and methodologies. As written, the text primarily contrasts "non-numerical" and "numerical" approaches, which may not fully convey the depth and role of each type of study. Revising this section to emphasize these conceptual differences will improve clarity and ensure alignment with established guidance and best practices in benefit–risk assessment.	Replace current text with the following: Qualitative patient preference studies use nonnumerical, exploratory methods to elicit patient views and experiences, helping to identify and define attributes, outcomes, and decision-making factors that are important to patients. Quantitative patient preference studies build on this understanding by applying structured, numerical methods to measure preferences,
EUCOPE	125	125	2.4 De Novo Work may not always be justified	"...for example, in the form of interviews…". We would add focus groups.	"...for example, in the form of interviews **or focus groups**…".
EUCOPE	126	127	2.4 De Novo Work may not always be justified	It would be helpful to list parenthetical examples of the types of preference research that is conducted and considered (qualitative and quantitative).	
Thermo Fisher Scientific	126	128	2.4 De Novo Work may not always be justified	Add the word "relative" as PPS can only provide insights on the relative importance of the attributes included in the study.	Suggest revising sentence to: "Quantitative PPS can be used for example, to produce numerical estimates of the relative importance patients assign to attributes or the degree to which patients state they are willing to make trade-offs among different attributes".
EFPIA	130	131	2.4 De Novo Work may not always be justified	The sentence "Quantitative PPS are designed based on insights gained from previous qualitative research" should be earlier in the paragraph (when quantitative PPS is mentioned for the 1st time) at line 125	
Syneos Health CRO	130	131	2.4 De Novo Work may not always be justified	The sentence "Quantitative PPS are designed based on insights gained from previous qualitative research" implies the expectation that qualitative PPS always precede quantitative PPS, which may not be the case in each and every case.	Suggest rewording to "Quantitative PPS are typically designed based on insights gained from previous qualitative research."

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Thermo Fisher Scientific	130	131	2.4 De Novo Work may not always be justified	Suggest revising the following sentence to include other types of preliminary research (as mentioned in section 2.3) that may inform quantitative PPS. While insights from previous qualitative research can be an important input to the design of a quantitative PPS, qualitative research is not always required and there are contexts where other forms of research are also important. For example, in a regulatory study, a more top down approach considering the clinical trial endpoints and how these may be included as attributes may be relevant.	Suggest adding: "Quantitative PPS are designed based on insights gained from preliminary research, including literature reviews, reviews of relevant clinical trial data and endpoints and qualitative research (see section 2.3)."
Acute Leukemia Advocates Network	133	165		Missing QoL	
Breakthrough T1D	133	174	3.2	We believe this section is particularly useful in describing example situations where PPS can inform regulatory decision-making throughout the development process. To further expand the utility of this section, we believe it would be useful to cite or include real-world examples where PPS have been used in actual regulatory decisions.	
Eurordis - François Houÿez	133	147	3.2	Another possible atrribute to be tested in PP studies could be the environment impact of the medicine, provided objective and complete information would be made available. Without making the choice of a medicine too complex, it could be important to factor in this impact and see if patients could inform on which benefit would compensate for this impact. This could be particularly relevant for products with high environmental impact (antibacterials, hormones...) , as a variable to be captured during a PP study and/or shared-decision making.	
Patient Engagement Professional Society (PEPS)	133	151	3.2	The guideline's primary orientation is toward the regulatory submission use case, with other applications—trial design, endpoint selection, risk management, and post-marketing evaluation—treated as secondary. For many organisations, particularly those in early development, a PPS that informs clinical study design may have a greater near-term impact than one intended for a benefit-risk dossier. Section 3.2 provides useful examples but does not give equal weight to non-submission contexts.	Revise Section 3.2 to give equal prominence to non-submission applications of PPS—including trial design, endpoint selection, risk management, and post-marketing evaluation—and provide practical examples for each use case.
Patient Engagement Professional Society (PEPS)	133	151	3.2	The guideline does not reference the potential role of PPS in Health Technology Assessment (HTA) submissions. Consistency of patient preference evidence across regulatory and HTA contexts is an increasingly live issue for sponsors, and clarity on the cross-submission usability of PPS data would be of direct practical value.	Reference the potential role of PPS in HTA submissions, and provide clarity on the cross-submission usability of PPS data, given that consistency of patient preference evidence across regulatory and HTA contexts is an increasingly live issue for sponsors.
PSI	133	194	3.2 / 4.1	While ICH E22 outlines principles for clarity, comprehension checks, and cognitive burden (Section 4.6.2), it does not explicitly require a structured patient-education process before eliciting preferences. For safety-critical benefit–risk questions—especially those involving rare but severe adverse events—patients' baseline risk literacy, prior knowledge, and misconceptions can substantially distort preference data. Without a standardized patient-education component, stated preferences may reflect misunderstanding of safety attributes rather than true risk tolerance, thereby endangering the validity of benefit–risk modelling and any subsequent quantitative benefit–risk analyses.	This is especially relevant because E22 repeatedly expects PPS to potentially contribute to benefit–risk assessment (e.g., Section 3.2, Section 4.1) yet leaves the burden of patient comprehension to ad-hoc instrument desig and recommendation is to adapt for it. Introduce an explicit requirement for a standardised patient-education component prior to preference elicitation. This enhances the reliability of stated risk tolerance, reduces cognitive bias, and ensures that PPS inputs used in benefit–risk assessments reflect informed patient understanding rather than misunderstanding.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Thermo Fisher Scientific	133	147	3.2	This section describes a range of potential uses of PPS across drug development, but the document provides limited clarity on how PPS evidence is expected to inform specific regulatory decision contexts - for example what are in-scope regulatory decision points (regulatory approval, label restrictions etc.), and how evidence needs differ in early development versus regulatory evaluation. Benefit-risk is mentioned, but the document does not provide decision-relevant examples, for example stating that preference evidence may support approval in a population subgroup where benefit-risk is preference sensitive, or e.g. a PPS could be used to inform which dose receives regulatory approval.	Consider clarifying how the described uses of preference evidence may translate into regulatory decision contexts. For example, the guideline could distinguish between PPS uses that primarily support drug development activities (e.g. endpoint selection, trial design) and those that may inform regulatory evaluation (e.g. interpretation of benefit–risk trade-offs, consideration of subgroup-specific benefit–risk trade-offs, risk management strategies, supporting orphan drug designation). Clarification may aid consistency in PPS design and interpretation. Please also clarify or provide an example of risk management or mitigation strategies e.g. monitoring, dietary restrictions, or anything else intended to be covered.
Thermo Fisher Scientific	133	175	3.2	The document describes potential applications of preference data but does not include illustrative examples demonstrating how preference evidence has informed regulatory assessments. Examples of how patient preference evidence has influenced benefit–risk evaluation, subgroup considerations, or approval decisions would be beneficial.	Consider including existing publicly-available case studies showing how preference evidence has been used in regulatory assessments. These could be in an appendix and referred to from this section.
EFPIA	134	135	3.2	To reinforce the importance of considering preference studies as part of overall drug development planning, an edit is suggested here to mention preference studies as part of drug development planning (with a cross-reference to section 2.6 in which this topic is discussed more extensively).	Examples of the use of PPS in the difference phases of development are described below. These examples are meant to illustrate potential uses of PPS. As discussed in section 2.6, specific plans for PPS can usefully be considered as part of overall drug development planning
Avicenna Alliance Public and Patient Involvement Task Force	136	147	3.2	We consider this to be an excellent outline of PPS uses. It will also serve as an important reference for study leaders and sponsors when assessing the value of PPS, as well as public and patient involvement more broadly.	
Cancer Patients Europe	136	147	3.2	The examples focus on clinical and regulatory aspects but underrepresent quality of life, daily functioning, and long-term survivorship burden	Add examples such as impact on daily living and autonomy and long term survivorship considerations
EUCOPE	136	136	3.2	Re the list of common uses of PPS, consider adding preference for a specific device or pharmaceutical form, and in general studies informing pharmaceutical development choices.	
Lymphoma Coalition	136	137	3.2	The examples provided are useful; however, several highly relevant applications remain insufficiently addressed. In diseases such as lymphoma, patients do not evaluate treatments based solely on benefit–risk considerations, but also on factors such as uncertainty, durability of response, treatment sequencing, and the preservation of future therapeutic options. The draft does not explicitly account for clinical contexts in which treatment is sequential and where prior and future options significantly influence decision-making. This is particularly important in lymphoma, where the value attributed to a given therapy may vary depending on whether it enables bridging to subsequent interventions (e.g., transplant or CAR-T), preserves future lines of treatment, or is administered in later-line settings.	Mention that, in diseases involving sequential treatment decisions, PPS should consider prior therapies, expected future options, and line of therapy as part of context, sampling, and interpretation. Also, add bullets such as: informing tolerance for uncertainty, including uncertain long-term outcomes; informing preferences regarding treatment sequencing and preservation of future treatment options; identifying patient priorities when balancing short-term burden against long-term outcomes.
EFPIA	137	137	3.2	It's not clear to whom the 'treatment priorities' are priorities - arguably it should specify patients for clarity (given historically, lack of clarity has lead to some PPS being critiqued for serving the sponsor's priorities/agenda).	Modify : Identifying **patient** treatment priorities
Eurordis - François Houÿez	137	137	3.2	And informing on the extent patients need the medicine in question	Identifying treatment priorities and the need for a new medicine
PSI	137	168	3.2	L137-147 and L148-L168: A list of common uses of PPS is shown followed by a textual description that explains some of the items in the list. A more structured display, e.g. using a table format might be useful and would avoid repetition. The list of potential uses could be sorted according to categories like design (especially endpoints), interpretation, risk thresholds.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	138	141		The examples: endpoint/outcome selection, relative importance of endpoint components, meaningful change of an outcome connect with typical Clinical Outcome Assessment (COA) work. It is not clear how COA and Preference work connect, could be combined, should be kept separately.	A reference to COA-related guidances would be helpful and especially a description how COA and Preference work connect, could be combined, should be kept separately for the given examples. Adding clarity will help bringing COA and Preference researchers together and making best use out of their skill set and experience driving for better patient-related outcomes.
Eurordis - François Houÿez	138	138	3.2	For a subsequent trial, PP studies can also inform on the preferred dose, when PK/PD studies reveal a dose-effect and before the dose for confirmatory trials is selected	Informing outcome/endpoint selection **or dose** for a subsequent clinical trial
Eurordis - François Houÿez	138	138	3.2	And also for evidence generation as part of real-world studies	Informing outcome/endpoint selection for a subsequent clinical trial and/or other clinical studies, eg real-world data collection
EFPIA	139	139	3.2	The relative importance of components of a composite endpoint can be valuable, but knowing the relative importance of attributes overall is more common use of PSS	Add a bullet for assessing the relative importance of attributes
EFPIA	141	141	3.2	For the point regarding "informing meaningful change" it would be great to have a bit more detail or information here to explore how this compares to existing regulatory guidance (PFDD guidance 3 and 4) and best practices. My current reading is that this is another potential option to support meaningful change exploration, depending on the available evidence and the COA measure being used. My reading is that this should be seen as a potential option that can be used depending on the situation. Therefore I would be great to have a little bit more detail and information here to ensure agreement	
EFPIA	143	144	3.2	In the section that describes common uses of PPS, mode of administration is called out in terms of what could be identified as something that matters to patients. There are many non-clinical endpoints that may matter to patients beyond mode of administration	Identifying non-clinical treatment characteristics that matter to patients such as mode of administration;
Eurordis - François Houÿez	143	143	3.2	And other treatment modalities, eg based on the treatment characteristics, would patients prefer the medicine be prescribed by specialised doctors only, dispensed in hospital pharmacies only etc.	
Thermo Fisher Scientific	146	150	3.2	One of the items listed under common uses of PPS is 'Informing recruitment and retention strategies'. While a PPS study could be used for this purpose the earlier sections of the guideline do not seem to address this topic. For example in Section 1.3. the stated preference methods are explained as being about specific outcomes or treatment alternatives, but this use case seems more about trial design where the alternatives would be hypothetical clinical trials with different trial design characteristics and understanding how changes in design might impact recruitment and retention.	Suggest this point is removed from the list and is instead combined with the text below the list: PPS conducted at an early stage of development could also provide information about unmet needs, priorities for disease management, patients' willingness to participate in clinical studies, inform clinical study recruitment and retention strategies, among others.
TEDDY	147	148	3.2	Add some speciifc examples of how PPS could be tailored and relevant for children, for example in improving treatment adherence by identifying features (e.g., formulation palatabilty, dosing frequency, route of administration) that are more acceptable to children.	
Avicenna Alliance Public and Patient Involvement Task Force	148	151	3.2	You raise an important point regarding patients' willingness to participate in clinical studies. We would add that it is crucial to understand patients' motivations and expectations for participation, and how these compare with potential barriers to participation.	
EFPIA	150	151	3.2	"This type of early information is often, but not always, qualitative and may be used to inform the development of subsequent PPS". Not clear if the qualitative investigation mentionned is part of the PPS or not.	"This type of early information is often, but not always, qualitative and may be used to inform the development of subsequent **quantitative** PPS".
Thermo Fisher Scientific	150	151	3.2	It has been stated earlier that formative qualitative work can inform quantitative PPS. Therefore, we suggest removing this sentence since items such as willingness to participate in clinical trials may be elicited through a quantitative PPS: "This type of early information is often, but not always, qualitative and may be used to inform the development of subsequent PPS"	Remove this sentence: "This type of early information is often, but not always, qualitative and may be used to inform the development of subsequent PPS"

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Avicenna Alliance Public and Patient Involvement Task Force	152	160	3.2	We consider this section to be an important discussion of the perceived importance of endpoints. In particular, we suggest adding consideration of how clinical study endpoints align with quality-of-life outcomes, as endpoints such as biomarkers may have limited or no direct relevance to tangible changes in a patient's quality of life.	
EFPIA	161	162	3.2	Would be good to have an example on how PPS can be used to help inform interpretation of the trial results.	
EUCOPE	161	162	3.2	"At a later stage in drug development, PPS can be used to help inform interpretation of the trial results": how? It would be useful if some examples were listed.	
Thermo Fisher Scientific	166	167	3.2	To be more precise, would suggest reframing "PPS can provide measures of risk thresholds that can inform benefit-risk assessment" to "PPS can provide measures of acceptable risk thresholds from the patient perspective that can inform benefit-risk assessment"	Adjust "PPS can provide measures of risk thresholds that can inform benefit-risk assessment" to "PPS can provide measures of acceptable risk thresholds from the patient perspective that can inform benefit-risk assessment"
Avicenna Alliance Public and Patient Involvement Task Force	169	174	3.2	You raise an important point regarding the opportunity to assess preference heterogeneity. An additional consideration is the challenge of ensuring population representativeness, for example by confirming that PPS participants reflect the population to be treated, minimising potential biases, and ensuring that language or cultural barriers during assessment are not lost in translation.	
EFPIA	169	172	3.2	Suggest revising to be more concise.	with characteristics potentially associated with <u>different</u> ~~differences in~~ preferences.
EFPIA	169	174	3.2	A PPS can also aim to identify sub-groups of sub-categories of patients according to there preference, which can help to inform health intervention. Sub-groups do not necessarily have to be pre-specified.	Add a sentence stating more clearly that PPS can aim to identify sub-groups (clusterize or stratify a population) according to their preference
EORTC	169	172	3.2	The guidance does not clearly explain how preference heterogeneity should be taken into account when applying PPS results. If such heterogeneity is observed, it is unclear whether the preferred approach is to identify relatively homogeneous subgroups in which straightforward conclusions can be drawn (for example, subgroup-specific preferred endpoints), or whether preferences should be summarised across the entire target population (for example, through a composite or weighted approach based on patient characteristics). Clarification on the recommended strategy would help ensure consistent interpretation and use of PPS findings.	
European Hematology Association (EHA)	169	174	3.2	Possible heterogeneity in preferences between patients and potential subgroups is described here. Here, it would also be useful to mention the distinction between "at risk" patients, whose preferences are likely to be representative of future patients, and actual patients. The latter group has real experience with the condition and/or possible treatment, which can be valuable, but their preferences may also be influenced by cognitive biases (e.g., post-decision justification). Furthermore, EHA's patient community note that a patient's preferences are dynamic and change with disease stage, relapse, treatment experience, toxicity, family situation, and prognosis. This should be acknowledged within the guideline.	Consider adding after line 174 the following two statements: "Preferences from both "at risk" patients—whose views are likely to be representative of future patients—and from actual patients can provide valuable and complementary insights. While actual patients have direct experience with the condition and/or potential treatment, making their perspectives particularly valuable, their preferences may also be influenced by cognitive biases (e.g., post-decision justification)." "Preferences may also change over time within individuals as disease status, prior treatment experience, prognosis, and life circumstances evolve."
Lymphoma Coalition	169	174	3.2	Preference heterogeneity is described across subgroups, but not longitudinally within the same patient over time. Preferences are dynamic and change with disease stage, relapse, treatment experience, toxicity, family situation, and prognosis.	After line 174, add: Preferences may also change over time within individuals as disease status, prior treatment experience, prognosis, and life circumstances evolve.
EUCOPE	171	171	3.2	Editorial	Line appears to require formatting.
European Hematology Association (EHA)	174	175	3.2	EHA proposes adding a section between 3.2 and 3.3 with suggestions on typical personnel (e.g., clinical research nurses) who can conduct PPS and how to involve patients outside of the routine medical visits.	Consider adding this additional discussion point.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Avicenna Alliance Public and Patient Involvement Task Force	176	180	4	We would find it helpful to reference or name defined standards and practices. The statement 'internationally recognised scientific standards and recommended practices' is somewhat vague and open to interpretation. In conjunction with the statement that 'it is up to the applicant to explain how the results are intended to support their regulatory submission, and to justify that the data submitted meet the regulatory requirements', there is a risk of gravitating towards a lowest common denominator that may not be in the best interest of patients.	
EFPIA	176	180	4	The FAQ document mentions that it's acceptable to run preference studies within a clinical trial. It would be helpful to have an explicit statement to that effect in the body of the guidance.	New paragraph prior to sectoin 4.1: "Preference studies can be conducted within a clinical trial or as a stand-alone study".
EFPIA	178	180	4	The draft states, "… and to justify that the data submitted meet the regulatory requirements" Because of the definite article "the", it is unclear what specific "regulatory requirements" are being referred to. Recommend removing "the" so the sentence refers to regulatory requirements in general.	… data submitted meet ~~the~~ regulatory requirements.
EU EYE	181	194	4.1	The examples focus on utility, yet it is important for examples to include treatment characteristics that matter to patients such as mode of administration as this is linked directly to patient burden. For example it is particularly important to understand the emotional and physical qualities of pain for eye patients. https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/patient-experience-of-injections-in-age-related-macular-degeneration/	Consider adding a patient-centric example in addition to efficacy which is a regulatory term.
European Hematology Association (EHA)	181	181	4.1	EHA considers that the scoping process is critical, yet the guidance is generic. Hematologic diseases have unique, non-negotiable attributes that, if omitted, invalidate a study's relevance. For example, a PPS in chronic lymphocytic leukemia (CLL) that fails to include 'risk of specific infections' or 'need for immunoglobulin replacement' ignores core determinants of patient choice. The current text does not mandate the depth of clinical and patient engagement required to identify these disease-specific attributes.	Add the following text: "For chronic, progressive, or life-threatening conditions, the scoping report must document a structured process involving: (1) a review of clinical guidelines and published patient-reported outcome studies specific to the disease, (2) consultation with a minimum of three independent clinical hematologists, and (3) iterative feedback from a patient advisory panel representing varied disease stages and treatment experiences. The final attribute list should include a rationale for exclusion of any clinically salient factor raised in this process."
Lymphoma Coalition	181	194	4.1	The examples are strongly framed around regulatory utility. That is reasonable, but the section would benefit from recognising patient-centred objectives too. A PPS may be valuable even if its contribution is to clarify what matters most to patients in a given decisional context.	Consider to add: …Research objectives may also include clarifying which outcomes and trade-offs matter most to patients to support patient-centred development and communication.
EFPIA	184	185	4.1	The text states "The research question(s) refine the research objective into answerable question(s)." However, it is not simply that the question(s) are answerable, but that they can be answered by the planned preference study.	"The research question(s) refine the research objective into question(s) to be answered <u>in the planned preference study</u>."
EFPIA	188	189	4.1	In "assessing the relative importance of attributes that align with the proposed efficacy endpoints", it is unclear that the relative importance refers to the relative importance over the defined ranges of the attributes. This is particularly important given the next statement referring to relative importance er unit change in attribute.	Change "assessing the relative importance of attributes that align with the proposed efficacy endpoints" to: "assessing the relative importance of attributes over their ranges in the preference study" (or similar)
TEDDY	190	190	4.1	While designing research objectives and question, it would be relevant to consider that age could be mention specifically age variable among key subgroups, as some specific consideration on endpoints, for example, could be different in different age subgroups, particularly in paediatrics	determining whether the relative importance varies by disease stage and key subgroups, **including age**

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Patient Engagement Professional Society (PEPS)	196	208	4.2	The guideline does not address a question that is operationally central to its uptake: under what circumstances is a PPS the appropriate or preferred method, as distinct from a standard quantitative patient experience survey? The absence of this distinction contributes to both under-use (sponsors defaulting to simpler instruments without considering stated-preference methods) and over-design (PPS methodology applied where a simpler approach would suffice). PPS using stated-preference methods is specifically designed to elicit trade-offs—how patients weigh competing attributes under conditions of constraint—which standard surveys cannot reliably reveal.	Articulate clearly the types of regulatory questions for which stated-preference methods generate evidence that a standard survey instrument cannot, particularly those involving benefit-risk trade-offs, threshold acceptability, or attribute prioritisation under constraint.
Patient Engagement Professional Society (PEPS)	196	208	4.2	Without clear criteria distinguishing when PPS is necessary versus when a standard instrument suffices, sponsors face uncertainty about method selection and risk disproportionate application of PPS requirements.	Define the circumstances in which a standard quantitative patient experience instrument may be sufficient, so that PPS requirements are not applied disproportionately in contexts where they would not materially improve the quality of the evidence.
Patient Engagement Professional Society (PEPS)	196	208	4.2	The guideline states there should be 'a clear rationale for the choice of methods used' but does not provide guidance on how sponsors should document and justify their choice between a PPS and a standard survey instrument.	Provide guidance on how sponsors should document and justify their choice of method, ensuring that a well-reasoned decision to use a standard survey over a PPS does not create an unexplained evidential gap in the submission.
Patient Engagement Professional Society (PEPS)	196	208	4.2	The discrete choice experiment (DCE) has become the dominant stated-preference method to a degree that creates a practical risk: sponsors and reviewers increasingly treat DCE as the de facto regulatory standard, even where other methods would be more appropriate, more feasible, or better matched to the research question and patient population. The guideline acknowledges methodological diversity ('many methods are available,' 'newer or alternative methods may also be appropriate') but does not address the conditions under which alternatives to DCE are explicitly acceptable for regulatory submissions. For sponsors who lack DCE expertise or are working with populations for whom DCE is cognitively burdensome, the absence of explicit regulatory affirmation of alternatives creates uncertainty that suppresses methodological innovation.	Explicitly affirm that non-DCE stated-preference methods are acceptable for regulatory submissions where they are fit-for-purpose for the research question, patient population, and decision context, naming the principal alternatives alongside DCE: best-worst scaling, swing weighting, the threshold technique, and ranking-based approaches.
Patient Engagement Professional Society (PEPS)	196	208	4.2	The guideline directs researchers to published literature for information on available methods but does not itself provide guidance on conditions favouring different method classes, leaving sponsors dependent on case-by-case scientific advice on method acceptability.	Provide guidance on the conditions under which each major class of stated-preference method is most appropriate, to support sponsors in selecting and justifying methods without requiring case-by-case scientific advice.
Patient Engagement Professional Society (PEPS)	196	208	4.2	The evidential standards for non-DCE methods in regulatory submissions are unclear, making it difficult for sponsors to assess feasibility and design studies with confidence.	Clarify the evidential standards for non-DCE methods used in regulatory submissions, so sponsors can assess feasibility and design studies with confidence.
Patient Engagement Professional Society (PEPS)	196	208	4.2	The current evidence base is heavily skewed toward DCE, reflecting historical practice and resource constraints rather than a hierarchy of methodological validity. Without an explicit acknowledgement of this, the evidence base may be misread as endorsing DCE primacy.	Acknowledge in the text that the current evidence base is heavily skewed toward DCE, and that this reflects historical practice and resource constraints rather than a hierarchy of methodological validity.
Thermo Fisher Scientific	196	167	4.2	Suggest adding after patient population 'including feasible sample size' as this is also relevant and critical in harder to reach populations or rare disease.	The choice of method can depend on several factors, including the research question(s), the patient population (including feasible sample size), and the number of attributes or scenarios to be assessed.
European Hematology Association (EHA)	200	202	4.2	While details on available methods for quantitative PPS fall outside the scope of this guideline, as mentioned in line 203-205, it might be good to (briefly) mention that discrete choice experiments are usually the model of choice, and most commonly used.	Consider adding: “Discrete choice experiments are generally the model of choice for quantitative PPS.”
Breakthrough T1D	201	202	4.2	The Analytic Hierarchy Process (AHP) is another well-established method for multi-criteria decision analysis (MCDA) that has been used in patient preference studies. Regulatory authorities, such as the EMA, have used this method in other areas of benefit-risk assessment. This method should also be cited in this section. In addition, MCDA, including AHP, is part of the methodological toolbox used by health technology assessment bodies to formally integrate patient preference information into their decision-making.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
TEDDY	202	202	4.2	While designing PPS, it would be relevant to consider specifically the need for age-adapted methods for PPS involving children and adolescents (e.g. visual and interactive tools, discrete choice experiments, storytelling, or play-based techniques, etc.)	
PSI	203	0	4.2	The guideline advocates for good study design, but I think it lacks specific technical criteria for methodological rigor, such as validation of preference elicitation methods, handling of biases, and statistical power calculations. It could potentially Incorporate detailed methodological standards, including validation procedures, bias mitigation strategies, and criteria for sample size determination.	standards to include validation procedures, bias mitigation strategies and criteria for sample size determination
PSI	205	208	4.2	This is an important recognition, as recruiting large samples for quantitative preference studies (like DCEs) in rare diseases is challenging. However, the guideline does not currently offer direction on how to handle this scenario. Without guidance, sponsors might be unsure how to proceed when patient numbers are low.	After line 207, add a clarifying sentence such as: "In cases of very small patient populations (e.g. ultra-rare diseases) where standard quantitative methods are not feasible, sponsors should consider alternative approaches. For example, they might use simpler elicitation techniques, collect richer qualitative preference data, or collaborate across regions (see Section 2.5) to pool patient input, in order to obtain meaningful insights without overburdening patients."
Avicenna Alliance Public and Patient Involvement Task Force	207	208	4.2	Highlighting the potential challenges associated with very rare disease research, particularly regarding the practicability of certain methodologies, is highly pertinent. An illustrative example may be helpful, including clarification of why some methodologies may not be feasible in this context.	
EFPIA	207	208	4.2	As written, the statement "In small populations such as in very rare diseases, some methodologies may not be feasible" gives the impression that this is the most important or only consideration in method selection, though the text before indicates otherwise. The text should introduce this point about very rare diseases as an example of a rational for method selection.	"For example, in small populations such as in very rare diseases, some methodologies may not be feasible."
European Hematology Association (EHA)	207	208	4.2	EHA notes that the guideline briefly mentions that some methodologies may not be feasible in very rare diseases. However, given the importance of patient preference research in rare conditions, it may be helpful to expand this point and acknowledge the practical challenges of conducting such studies in small patient populations.	Consider revising the sentence on rare diseases to: "In rare diseases, with very small patient populations, traditional methodologies may not always be feasible. Flexible approaches, including qualitative or mixed-methods studies, may be needed to capture meaningful patient preferences."
Patient Engagement Professional Society (PEPS)	207	208	4.2 / 4.4	E22 Section 4.2 notes that 'in small populations such as in very rare diseases, some methodologies may not be feasible,' and Section 4.4 acknowledges that sample size for qualitative PPS tends to be smaller. However, no alternative approaches or methodological adaptations are proposed. For conditions where patient numbers make conventional sample size assumptions and quantitative preference elicitation structurally inapplicable, the guideline provides no pathway.	Include dedicated guidance on methodological adaptations for rare diseases and small populations, including the evidential role of qualitative PPS, sequential study designs, and adaptive approaches.
Patient Engagement Professional Society (PEPS)	207	208	4.2 / 4.4	It is unclear whether the methodological flexibilities established in other ICH guidelines for small population contexts—including ICH E17 on multi-regional clinical trials (EMA/CHMP/ICH/453276/2016, adopted June 2018)—apply in principle to PPS, or whether separate guidance is needed.	Clarify whether the methodological flexibilities already established in other ICH guidelines for small population contexts—including ICH E17 on general principles for planning and design of multi-regional clinical trials—apply in principle to PPS, or whether separate guidance is needed.
Dr Yewande Okuleye	209	238	4.3	The list of key characteristics is helpful but incomplete. Preferences may differ not only by demographics, disease stage, or treatment experience, but also by prior interactions with healthcare, trust or mistrust, and barriers to care access. These factors may materially shape treatment trade-offs and preference heterogeneity, but are not explicitly recognised in the current list.	The guideline should explicitly acknowledge prior care experiences, trust in healthcare, and care access barriers as potentially relevant characteristics for sampling plans and interpretation of PPS findings.
European Hematology Association (EHA)	209	238	4.3	EHA's patient community notes that although the guideline mentions "diversity" and "representative samples," it does not go far enough in requiring proactive, explicit inclusion of underserved and hard-to-reach groups or in addressing real barriers to participation (e.g., low health literacy, language barriers, limited digital access, under-resourced settings). Inclusion and exclusion criteria need to be carefully considered to promote diversity so as to include as many different groups of patients that may benefit from the intervention as possible. Our patient community warns that without stronger direction, patient preference studies will tend to recruit the most accessible—often more educated, digitally engaged, highly activated patients—while excluding marginalized individuals whose characteristics may differ from the majority, raising both equity and ethical concerns and limiting the validity and usefulness of findings.	Consider adding more explicit discussion of considerations to promote diversity.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Patients' Forum	209	238	4.3 Study Sample	Certain populations are often underrepresented in clinical research (see also section 4.8), including pregnant people, immunocompromised individuals, older and younger patients, etc. These populations may have distinct preferences regarding treatment benefits and risks, which may influence benefit-risk assessment and decision-making. Where relevant to the research objective, consideration should be given to including underrepresented and underserved populations and ensuring that their perspectives are adequately captured. This may require tailored recruitment strategies, adapted study materials, or subgroup analyses. New barriers to inclusion, such as lack of digital skills, also require specific strategies as many studies rely on surveys and other online tools.	'Particular attention should be paid to the inclusion of populations that are often underserved and underrepresented in clinical research. Recruitment strategies and study adaptations should be considered to facilitate their participation where appropriate.
Lymphoma Coalition	209	238	4.3	Diversity is mentioned, but too briefly. The section should be more explicit on inclusion and on barriers to participation. PPS can easily over-represent highly activated, digitally engaged, better educated patients. This is a major concern from an equity perspective.	Suggested addition: ...Researchers should proactively identify and address barriers to participation among under-represented or marginalised groups whose preferences may differ and whose exclusion may bias results. Consider also to expand the list to include factors such as: socioeconomic status education and health literacy digital access language disability minority or migrant status geography and travel burden
Marieke Heisen, Patvocates	209	209	4.3	Quality of the sample in terms of bots and frauds not discussed here. This has become a substantial issue over the past years, especially when survey participants receive a fee. It is mentioned in lines 340-341, concerning data quality. But it should be mentioned under recruitment strategy as well (too late in the process to only address as part of data quality checking).	
Avicenna Alliance Public and Patient Involvement Task Force	211	212	4.3	We suggest providing guidance or a reference on how to address the challenge of sample representativeness for PPS. Given recent advances in public and patient involvement, some patient associations or individuals may be more active than others, which may lead to certain contributors being overlooked and introduce bias.	
European Heart Network (EHN)	214	216	4	Linking representativeness directly to equity.	Proposed addition: “Representativeness should include consideration of groups whose experiences or preferences may differ because of social, economic, demographic, or geographic factors, including groups that may be less likely to participate in research.”
PSI	214	216	4.3	Can the guidance include recommendations for how to adress differences in population? They recommend diverse popularuons but it may be important to include strategies for cross-culture adaptation	include strategies for cross cultural adaptation, subgroup analysis
LEO Pharma	215	225	4.3	Preferences often evolve over the course of a chronic disease. Patients who are "treatment-experienced" or refractory to multiple therapies often have significantly different risk-tolerance profiles compared to treatment-naïve patients. Accounting for this heterogeneity in the PPS study design and reporting is critical for interpreting PPS results correctly. Additionally, in chronic dermatologic diseases characterised by episodic flare–remission patterns, patient preferences may vary substantially depending on current symptom severity (e.g., itch intensity, lesion extent, sleep disturbance). Sponsors may need to document or control for disease state variation at the time of PPS participation, as this can materially affect stated preferences and interpretation.	Recommend that sponsors consider and document the "treatment journey" stage of the study sample, as prior experience with biologics or systemic therapies in chronic conditions can be a major source of preference heterogeneity.
European Hematology Association (EHA)	217	225	4.3	It would be good to mention that the key characteristics to consider are generally defined by literature review and the qualitative part of the research (i.e. patient interviews)	Revise lines 217-218 to say: "Key characteristics to consider when developing a sampling plan emerge from literature review and patient interviews, and include those potentially associated with differences in preferences, such as…"
European Patients' Forum	217	223	4.3 Study Sample	Include socio-economic characteristics as relevant variables influencing preferences. Socio-economic factors such as income, education and employment status can influence health behaviours, treatment access, preferences and outcomes. Considering socio-economic characteristics can improve representativeness of PPS samples and identification of preference heterogeneity.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Patient Focused Medicines Development (PFMD)	217	234	4.3	Section 4.3 addresses representativeness as a methodological quality standard but does not adequately address the structural barriers that systematically limit the representativeness of PPS samples. Stated-preference methods impose inherent demands on health literacy, numeracy, and cognitive capacity that are unevenly distributed across patient populations. Patients with lower health literacy, those whose first language differs from the study language, those from lower socioeconomic backgrounds, and those from historically underserved racial and ethnic communities are all at structural risk of underrepresentation. The demographic characteristics listed in Section 4.3 (participant characteristics, disease characteristics, treatment experience, and 'other relevant characteristics such as risk attitudes and health literacy') treat diversity as a sub-category of sampling design rather than as an equity consideration warranting dedicated attention.	Expand Section 4.3 to address equity as a distinct dimension of sample design, identifying the structural barriers (health literacy, language, socioeconomic status, cultural context, geographic access) that systematically limit the representativeness of PPS samples, and provide guidance on mitigation strategies proportionate to the study population and context. Include explicit guidance on measuring and reporting participants' health literacy and numeracy as a means of accounting for preference heterogeneity, consistent with the approach recommended in IMI-PREFER guidance. Expand the list of key sampling characteristics to include ethnicity, cultural background, socioeconomic status, and disability status.
Syneos Health CRO	217	223	4.3 Study Sample	While the emphasis on diversity and inclusion is appropriate and several important metrics are identified, the framework would benefit from a more comprehensive consideration of social determinants of health.	Factors such as environment, access to healthcare, and socioeconomic status should be explicitly included to ensure a more representative population. Additionally, age may be an important variable depending on the disease area. These factors can significantly influence patients' perceptions of quality of life and their willingness to make treatment trade-offs and therefore should be incorporated into the overall approach.
European Heart Network (EHN)	219	219	4	"Demographic diversity" is too vague on its own.	Revision: • Participant characteristics, including demographic diversity and other characteristics relevant to inequity and access, such as sex, gender, gender identity, socioeconomic status, education, geographic location, disability, and health literacy;"
Thermo Fisher Scientific	222	223	4.3	Suggest revising text in this line to clarify that risk attitudes and health literacy will not impact recruitment within the sampling strategy	While not impacting recruitment, other relevant characteristics (e.g., risk attitudes, health literacy) may be collected to describe the sample and to support prespecified subgroup analyses.
European Heart Network (EHN)	224	225	4	Making sentence more actionable	Revision: "Particular attention should be paid to any subgroups with potentially different preferences who may be less likely to participate in the PPS, including socially disadvantaged populations, people with lower health literacy, those with limited digital access, and rural populations where relevant."
EU EYE	226	229	4.3	The text acknowledges culture and healthcare similarity, but it needs to acknowledge that preferences are also shaped by other factors such as access limitations, reimbursement/affordability, health literacy, logistics, etc. More importantly the text must acknowledge that legislation differences among regions or Member States in EU have a profound impact on patient preferences and choices in therapies by defining the scope of autonomy, enabling shared decision making, regulating access to treatments and determining the limits of consent. Example: A Discrete-Choice Experiment to Assess Patient Preferences for Long-Acting Injectable Treatments in Opioid Use Disorder in Australia, Finland, Germany, and Italy https://link.springer.com/article/10.1007/s11469-025-01605-z#Tab3	Consider adding rephrasing to read: the similarity of culture, health care delivery and legislative system including differences in access to and reimbursement for treatments/diagnostics ….
European Hematology Association (EHA)	226	229	4.3	Out-of-pocket payment for prescription medication costs is an important characteristic that might influence differences in preferences between regions and should be mentioned here. Likewise, for rare diseases, access to diagnosis, specialized care and treatment can vary significantly across countries. These differences may influence patient preferences and should be mentioned.	Consider adding points on these considerations.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	230	234	4.3	EHA notes that a range of recruitment strategies may need to be employed. Indeed, while recruitment through advocacy groups may affect participant characteristics, it also enables access to informed and under-represented communities. Patient organizations play an essential role in ethical recruitment, fostering trust, and ensuring relevance.	Consider revising the text to: "There are different types of recruitment strategies, and the choice of strategy can depend on the objective of the study. It is important to consider how recruitment strategies can impact the representativeness of the target population, and consider whether using a range of recruitment strategies is appropriate. For example, people who are part of panels, advocacy groups, clinical trials, recruited online, or receive care at speciality clinical sites, may have different characteristics compared to the target population. Nevertheless, patient advocacy organizations can also play a significant role in supporting ethically sound recruitment practices, fostering trust, and facilitating access to patient communities, including those that may otherwise be neglected."
Lymphoma Coalition	230	237	4.3	The text notes that recruitment via advocacy groups may yield different characteristics, which is true, but it risks sounding like a limitation without acknowledging the benefits of patient organisations in reaching informed and otherwise under-represented communities. Patient organisations are often crucial partners in ethical recruitment, trust-building, and ensuring relevance.	Revise line 233–234 to say: …may have different characteristics compared to the target population; however, patient advocacy groups may also facilitate ethically appropriate recruitment, trust, and access to patient communities, including groups that might otherwise be overlooked.
Patient Focused Medicines Development (PFMD)	230	234	4.3	Section 4.3 lists patient advocacy organisations alongside clinical trial sites and online panels as equivalent sources of potential selection bias, without acknowledging their distinctive role as partners in reaching patient populations that may be inaccessible through other channels. For rare diseases, chronic conditions with low clinical capture, and therapeutic areas where patient organisations serve as primary community touchpoints, this framing risks discouraging researchers from pursuing advocacy organisation partnerships precisely when they are methodologically most valuable.	Revise the reference to advocacy group recruitment in Section 4.3 to reflect a balanced treatment of selection characteristics across all recruitment channels, with explicit acknowledgement of patient organisations' particular value as recruitment partners in populations that may not be reachable through clinical or online channels.
TEDDY	230	235	4.3	Young Persons Advisory Groups (YPGs) have an increasing role in scientific research design, planning and conduct, including supporting recruitment. PPS is an area in which their contribution must be sought. For example, the YPAGs within the TEDDY KIDS Network can be considered active partners in the PPS, ensuring that the voices of children and young people are effectively integrated into decision-making processes.	There are different types of recruitment strategies, and the choice of strategy can depend on the objective of the study. It is important to consider how recruitment strategies can impact the representativeness of the target population. For example, people who are part of panels, advocacy groups, clinical trials, recruited online, or receive care at speciality clinical sites, may have different characteristics compared to the target population. For paediatric studies, Young Persons Advisory Groups (YPAGs) could support recruitment.
European Heart Network (EHN)	235	236	4	This is important for relevance to the average patient, not just the most visible patient groups.	Addition: "Recruitment strategies should, where feasible, include approaches that reach beyond specialist centres, advocacy-engaged populations, or online panels alone, in order to better capture the experiences of patients who are less connected to healthcare systems or research networks."
ACRO	239	250	4.4	ACRO welcomes the recognition, in lines 207-208, that some methodologies may not be feasible in very rare diseases. ACRO recommends including reference to these situations within section 4.4, Sample Size.	Add new text "The feasibility of the sample size should be considered, for example, in studies regarding rare diseases. While most quantitative PPS research has been conducted using discrete choice experiments, methods such as thresholding may be more appropriate where there are smaller numbers of potential participants.
Acute Leukemia Advocates Network	239	250		The section on sample size discusses methodological considerations but does not explicitly acknowledge situations where patient populations are very small.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	239	250	4.4	While this section covers methodological aspects, it does not directly address cases where patient numbers are very low. In the context of rare blood diseases, the patient population can be extremely small. This limitation may impact how traditional PPS methods are applied, and the guidance should take this challenge into account.	Consider adding: "In the context of rare diseases with limited patient populations, obtaining large sample sizes is often impractical. Under these circumstances, studies utilizing smaller samples supplemented by qualitative data can yield meaningful insights into patient preferences."
Lymphoma Coalition	239	250	4.4	The section is broadly correct, but could be more precise. Sample size section should mention saturation for qualitative work and justification for subgroup analyses	Suggested addition: ...For qualitative PPS, mention that adequacy may be informed by thematic saturation or similar conceptually appropriate criteria. For quantitative PPS, recommend justification where subgroup analyses are intended but may be underpowered.
EFPIA	240	250	4.4	While it is important that this section is included, it fails to provide any strong recommendation that improves the quality of a PPS.	Enhance the value of this section by adding a sentence at the end of it to state something along the lines of "The applicant should always justify the pre-specified target sample size in the PPS."
PSI	240	248	4.4	This guidance is sound. To implement it, sponsors will need to determine an appropriate sample size often by using statistical calculations or simulations (especially for DCEs where no simple formula exists). The guideline currently doesn't mention any technique for sample size planning, but adding such a recommendation would strengthen its practicality for statisticians.	
Thermo Fisher Scientific	240	250	4.4	Sample size for a preference study generally cannot be estimated a priori, since insufficient data points are known on which to base such as estimate. Therefore, sample size is often based on rules of thumb given the objectives of the preference study, consideration of sample sizes used in similar studies, and feasibility within the resources and time available to complete the PPS. Suggest acknowledge this in the guidelines.	
EFPIA	241	243	4.4	The text states: "While the sample size for qualitative PPS tends to be smaller than quantitative PPS, it should include diverse perspectives to capture variability in preferences within the target population." While diverse perspectives are the goal, the smaller size of qualitative PPS inherently limits diversity.	The guidance should change the implicit requirement for diverse perspectives to be a desirable goal that may not always be obtainable in qualitative research. In cases where it cannot be obtained, the researcher should defend the relevance of the PPS results.
EFPIA	242	242	4.4	It is not clear how to ensure qualitative sample size captures diverse enough preferences. Depending on the objective of the qualitative study, the sample size may be evaluated based on conceptual compleness and saturation.	It would be helpful to have explicit criteria for defining sufficient diversity of preferences and stopping rules.
European Heart Network (EHN)	246	246	4	*[…] sample should include a* ***sufficient*** *number of participants […]* Is there an official threshold in percentage? "Sufficient" is a very flexible term.	
Dr Yewande Okuleye	251	285	4.5	This section could better clarify that relevant attributes may extend beyond classic efficacy and safety outcomes. Depending on the research objective and treatment context, patients' choices may also be strongly shaped by treatment-process and care-burden features such as monitoring burden, frequency of hospital attendance, disruption to work or school, need for urgent care, or uncertainty about durability of benefit. If such attributes are omitted, PPS may produce a narrow account of what patients value and reduce the usefulness of findings for assessing real-world acceptability and applicability.	After the existing examples of attributes, add wording such as: Depending on the research objective, attributes may also include treatment-process and care-burden characteristics that materially influence treatment choice or acceptability.'
EFPIA	251	273	4.5	the attribute selection should be further detailed with practical information and highlight the variety of outcomes that can be used including patient reported outcomes measures and measures not limited to endpoints (e.g. drug characteristics)	
EFPIA	251	251	4.5	Consider adding clearer lay language definition of "attributes and levels" with examples	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
LEO Pharma	251	267	4.5	The guideline focuses heavily on efficacy and safety outcomes as "attributes." In dermatology, however, the mode of administration (e.g. cream vs. ointment vs. injection) and cosmetic properties (e.g. greasiness, staining, smell) can be important drivers of patient preference, adherence, and longterm use. In addition, delivery device characteristics (e.g. autoinjector pen vs. syringe, needle size and usability, or availability of different topical dispensing formats such as foam vs. cream) can substantially influence treatment burden and ease of administration. These elements meaningfully contribute to real world patient acceptance and effectiveness. Explicit acknowledgement would help ensure such characteristics are recognised as scientifically relevant determinants of patient preference rather than being misinterpreted as marketing considerations. For chronic dermatologic diseases, treatment burden attributes — including frequency of application, time required for application, quantity needed to cover large body surface areas, residue on clothing, and impact on daily routines — often represent major determinants of patient acceptability. We suggest explicitly recognising treatment burden elements as legitimate PPS attributes to ensure they are not mistakenly deprioritised relative to clinical attributes.	Suggest that the guideline explicitly include administration and delivery characteristics (e.g., skin-feel, application frequency, route of administration, delivery-device characteristics) as well as treatment-burden attributes such as application time, quantity required, residue, and impact on daily routines, as example attributes relevant for PPS
Lymphoma Coalition	251	285	4.5	Attribute development should include non-clinical and relational burdens. The section still reads as if attributes are mainly treatment characteristics in a technical sense. Patients weigh non-clinical burdens heavily, including disruption to normal life, dependence on carers, visibility of treatment, fertility, cognitive effects, work ability, and emotional burden.	After line 255, add examples such as: …impact on daily functioning, need for caregiver support, time away from work or education, frequency of hospital attendance, uncertainty, and emotional burden.
EFPIA	252	253	4.5	The section refers to attributes before defining the term. Recommend moving the definition to the start of the section.	Attributes are specific characteristics of a drug or treatment that patients consider when making treatment decisions (e.g., efficacy outcomes, side effects, frequency of dosing, and route of administration). For PPS whose methods use attributes and levels of a drug or treatment, general considerations should include: followed by the bulleted list
Thermo Fisher Scientific	252	253	4.5	Suggest change to: "Particular attention should be paid to the development of the attributes and levels", since particular attention should always be paid to development of attributes and levels. Or specify more explicitly that if the PPS is to support regulatory decision-making the attributes and levels selected must align with those used in clinical trials and for which clinical data will be available.	Suggest change to: "Particular attention should be paid to the development of the attributes and levels."
European Heart Network (EHN)	253	255	4	Revising to include issues that often matter greatly in real life and may differ across socioeconomic groups.	Revision: "Attributes are specific characteristics of a drug or treatment that patients consider when making treatment decisions (e.g., efficacy outcomes, side effects, frequency of dosing, route of administration, treatment burden, affordability, need for monitoring, and access-related considerations)."
Eurordis - François Houÿez	256	257	4.5	The description of the attributes in any survey/questionnaire should be based on eg narratives of spontaneous reports of suspected adverse drug reactions, or if collected during a clinical trial, by asking patients to describe them with their own words. MedDra preferred terms are not self-explanatory enough (eg lipodystrophy: abnormal central fat accumulation (lipohypertrophy) and localized loss of fat tissue (lipoatrophy)). Same for atrributes describing efficacy / endpoint, it is essential the terms used are user-tested with a variety of users	Attributes included should be relevant for the patients, research objective and question(s). It is essential to seek input from patients and testers to ensure questions are self-explanatory. (cf lines 264-267)
EFPIA	262	263	4.5	Poor phrasing in "... these assumptions if not met may limit the interpretability of the PPS results." Suggest edit for clarity.	Change to: …these assumptions, if not met, may limit the …"

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	264	267		More emphasis on qualitative research principles to a) identify meaniningful health concepts, b) selection of attributes and levels from qualitative research, c) matching to clinical trial endpoints, should be given. Important to build upon existing FDA PFDD guidance (and relevant ICH guidances, if any) to ensure representative input (Guidance 1), and appropriateness of methods (Guidance 2).	
Marieke Heisen, Patvocates	264	267	4.5	When selecting the attributes to include in a quantitative PPS, researchers are encouraged to engage patients in the selection process. Semi-structured interviews or focus groups could be conducted among a sample of patients where a list of attributes and their respective descriptions are presented to the participants to solicit feedback.' Interview or focus group participation are not examples of engagement. These lines are harmful for building understanding about patient engagement. An interviewee is a study participant and has no say on the study design. A patient (expert) who is engaged has a role in e.g. designing and learning from the interviews, and is part of the construct of the study design. Linked to comment lines 68-74.	
Thermo Fisher Scientific	264	267	4.5	Patients and/or patient advisors can also be engaged in selecting attributes within project steering/advisory committees. Interviews or focus groups sounds less like having patients as partners and more as research subjects within attribute development. Both are useful to have for selecting attributes.	Suggest add a sentence: "Patients and/or patient advisors can also be engaged in selecting attributes, for example via a project advisory committee."
EFPIA	272	273	4.5	This section mentions the concept of generic attributes. Further guidance would be welcome about when the use of generic attributes may or may not be acceptable to regulators, in particular whether the use of generic attributes (e.g. a risk attribute) to inform a benefit-risk decision would typically be acceptable.	
EFPIA	281	282	4.5	To add an example to illustrate this sentence: "extrapolation of PPS data beyond the levels included in the study is generally not recommended"	
EFPIA	282	282	4.5	Another very important element of selecting levels is to ensure the patient can distinguish between them. For example, the small difference between levels of 4% and 5% is unlikely to yield good preference results.	Add a bullet that the levels should be clearly distinguishable from one another (e.g. pretesting should confirm that patients reliably distinguish between the levels).
Dr Yewande Okuleye	286	377	4.6	The requirement to define context is important, but a single generic scenario may create artificial stability where preferences differ materially by clinical state or decision moment. For example, preferences expressed during an acute pain episode may differ from those expressed during a stable period. The guideline should encourage researchers to consider whether more than one scenario, or a clearly time-specific framing, is necessary when context is likely to influence preference expression.	After the existing examples of attributes, add wording such as: "Depending on the research objective, attributes may also include treatment-process and care-burden characteristics that materially influence treatment choice or acceptability."
European Hematology Association (EHA)	286	320	4.6	EHA's patient community considers that the guideline should more strongly require that instruments are developed and tested in plain, accessible language, because comprehension is a core validity issue when patients are asked to weigh complex benefit–risk trade-offs. This includes clear presentation of probabilities and uncertainty, and plain-language validation of instruments. Accessibility should also account for differing literacy levels and digital access. Studies should minimize respondent burden—particularly for people living with chronic conditions who may experience treatment fatigue or cognitive burden.	Add a statement on this point to section 4.6
Lymphoma Coalition	286	320	4.6	The section focuses on technical aspects of design but does not acknowledge that preferences are influenced by emotional, experiential, and contextual factors.	Include a statement recognising that patient preferences may be shaped by prior experiences, emotional context, and disease trajectory, and that study design should consider these factors where feasible.
Lymphoma Coalition	286	320	4.6	Instrument design should explicitly require plain language and accessibility (accesibility considerations including literacy level and digital access). Readability is mentioned, but the guideline should go further on plain language and accessibility needs. In PPS, comprehension is not a technical detail; it is a validity issue. Instruments should be accessible to people with limited health literacy, sensory impairments, fatigue, cognitive burden, or lower numeracy. In addition, reducing respondent burden is especially important for patients with chronic conditions who may already experience treatment fatigue.	Add: ...Instruments should use plain, non-technical language wherever possible and should be designed with accessibility in mind, including for participants with visual, cognitive, or fatigue-related limitations

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Avicenna Alliance Public and Patient Involvement Task Force	287	288	4.6	We recommend co-designing instruments with participants from the target group. Based on our experience, participants are often clear in expressing which instruments they prefer from a given selection and which aspects are important to ensure that the instruments are appropriate for the target audience.	
EFPIA	287	289	4.6	Please add some content about general considerations relevant to opt-out choices, and when the use of opt-out choices in an instrument would (or would not) be expected.	
Eurordis - François Houÿez	287	289	4.6	PP studies are hypothetical/intellectual exercices presenting different attributes and different levels that do not necessarily correspond to reality, and at a time where clinical trial results are not yet available. Before participants start responding to questions, it is important to ensure they understand the study and the hypothetical nature of the information presented. This can best be done by an explanation by a researcher, a human being, more than by reading a text or interacting with a chatbot (although chatbots are improving)	
EFPIA	288	289	4.6	Can the sentence "researchers should take action to minimise potential bias" be clarified?	
European Heart Network (EHN)	289	289	4		Addition: "Instruments should also be designed to be accessible to participants with varying levels of literacy, numeracy, health literacy, digital familiarity, disability, and language proficiency."
European Hematology Association (EHA)	290	294	4.6.1	To ensure the context is clearly communicated to patients, it may be helpful to explain that some questions pertain to potential health interventions or future treatments that are not yet available, so as to avoid creating false expectations about treatment options. It is also important to emphasize that there are no right or wrong answers, as the questions are intended to capture individual preferences.	Consider adding: "To ensure the context is clearly communicated to patients, it may be helpful to explain that some questions pertain to potential health interventions or future treatments that are not yet available, so as to avoid creating false expectations about treatment options. It is also important to emphasize that there are no right or wrong answers, as the questions are intended to capture individual preferences."
Lymphoma Coalition	291	320	4.6.1 + 4.6.2	The guideline should caution against overloading respondents with hypothetical trade-offs detached from lived reality. The guideline discusses realism and bias, but does not explicitly address the risk of presenting hypothetical choices that are too abstract or emotionally detached from actual decision contexts. Patients may respond differently to hypothetical trade-offs than they would in real decisions involving fear, urgency, family context, prognosis, or lack of alternatives.	Suggested addition: ...Researchers should consider whether the hypothetical scenarios sufficiently reflect real-world decisional context, including urgency, uncertainty, prior treatment experience, and the emotional significance of the choice.
EFPIA	292	293	4.6	It would be very helpful for readers to include a short example of how different contexts/scenarios could change preferences.	Include an example of two contexts that could be used for the same survey but that would lead to different preferences.
Acute Leukemia Advocates Network	295	322		The guideline touches on numeracy and readability but doesn't adequately address how to make studies accessible to patients with cognitive impairments, low literacy, disabilities, or those who are digitally excluded. This risks skewing results toward more educated or engaged patient populations.	
Acute Leukemia Advocates Network	295	322	4,6,2	Section 4.6.2 addresses multilingual studies in terms of "conceptual equivalence," but culture shapes what patients value, not just how they understand words. The guideline doesn't go far enough in requiring culturally adapted study designs rather than just translated ones	
Lymphoma Coalition	295	320	4.6.2	The draft addresses probabilities, but not how uncertainty itself should be communicated when evidence is immature or ranges are wide. In oncology and rare disease, patients are often asked to consider options where long-term benefit or risk is uncertain. Preferences elicited without careful communication of uncertainty may misrepresent what patients actually value.	Where relevant, the presentation of information should transparently communicate uncertainty in expected outcomes, including immature evidence, ranges of plausible effect, or unknown long-term consequences.
Thermo Fisher Scientific	295	320	4.6.2	The document recognises the importance of numeracy, framing effects, and minimisation of cognitive bias but provides limited operational guidance. The guideline could provide practical recommendations on presenting absolute versus relative risks, framing uncertainty, and using multiple formats to support comprehension. Given the well-documented impact of risk communication on stated preferences, additional clarity could strengthen studies.	Consider expanding guidance on communicating benefit, risk, and uncertainty, perhaps including illustrative best-practice principles for numeric formats, framing, and assessment of participant comprehension.

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EFPIA	296	297		Consideration of accessibility issues other than health literacy (e.g., vision impairment), which may be relevant for how the materials need to be presented	expand to "other relevant characteristics (e.g., risk attitudes, health literacy, accessibility needs)"
EFPIA	296	297		Current text: Attributes and other relevant information should be described such that they are interpreted as intended, consistently, and unambiguously across all participants Rationale: It should be emphasized that all language used to describe attributes and levels should be patient friendly.	Proposed changes: Attributes and other relevant information should be described in patient-friendly language such that they are interpreted as intended, consistently, and unambiguously across all participants.
EFPIA	299	302	4.6	The current text suggests that researchers should consider numeracy and use appropriate representations, but it does not provide actionable guidance. This could leave readers uncertain about what constitutes "appropriate" approaches. To improve clarity, we recommend specifying that researchers should rely on evidence-based risk communication strategies and existing research on presenting probabilities (e.g., numeric, verbal, and graphical formats) to enhance comprehension. This will make the guidance more practical and aligned with best practices in patient preference elicitation.	When presenting this information, the researchers should consider the following: •Numeracy (i.e., ability to understand and use numbers in making health-related decisions); Appropriate numeric, verbal, and graphic representations can help participants conceptualise probabilities •Numeracy •Account for participants' numeracy, i.e., their ability to understand and use numerical information in health-related decisions. Apply evidence-based risk communication approaches to support comprehension; e.g., numeric, verbal, and graphical representations that have been shown to improve understanding of probabilities and trade-offs, consistent scales, etc.).
EFPIA	301	303		From a health literacy perspective, it's recommended to use numbers consistently; so use the same denominator and timeframe when making comparisons, e.g., when describing rates of adverse events and so on.	
EFPIA	304	308		Plain language guidelines should be followed for all materials	
European Hematology Association (EHA)	309	311	4.6.2	Section 4.6.2 focuses on "conceptual equivalence" in translation for multilingual studies, but this overlooks how culture shapes patient values. EHA considers that study designs should take into consideration cultural adaptation, as translation alone may not capture meaningful patient perspectives. The guideline should require discussion of whether translation is enough or if validation and cultural adaptation are needed for each survey to ensure patient preferences are accurately reflected across cultures.	Add a point on validation and cultural adaptation for multilingual studies.
EFPIA	313	314	4.6.2	I do not understand what a bias could be, can it be clarified with another example than "bad" or "good"?	
Thermo Fisher Scientific	313	314	4.6.2.	Additional detail could be provided here. For example, avoid solely verbal (e.g. high, low) levels, avoid relative risks and use absolute risks etc.	
Breakthrough T1D	315	321	4.6.2	We agree that minimizing cognitive bias in PPS research is crucial for generating accurate, ethical, and actionable data, and measures should be taken to avoid anchoring or ordering effects. For the benefit of newer investigators or developers who may be interested in conducting PPS research, we suggest that this guideline provide specific examples or refer to other available resources to elaborate on how some of these design flaws may contribute to bias.	
EORTC	315	321	4.6.2	The paragraph could better acknowledge that some of the techniques listed as cognitive biases, such as framing or the use of simplified heuristics, may be necessary to communicate complex health states in a clear and understandable way. In practice, avoiding these techniques entirely may conflict with the guideline's own requirement to manage complexity and ensure participant comprehension.	
Chiesi Farmaceutici	322	345	4.6.3	While AI is mentioned as a risk of fraudulent generation of data to be triggered by quality checks/mitigations, there is growing relevance of the use of AI/digital for survey administration, recruitment and data generation	Section 4.6.3 may benefit adding "Sponsors should describe measures implemented to detect and mitigate risks associated with automated or AI-generated responses".

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	322	345	4.6.3	EHA's patient community warn that researchers should interpret quality checks carefully. Section 4.6.3 should recognize that apparently "illogical" responses may represent valid, experience-based trade-offs (e.g., high risk acceptance when options are exhausted) and that rigid exclusions can bias results by disproportionately removing input from more vulnerable or burdened participants (e.g., lower literacy/numeracy, fatigue, neurocognitive burden, distress). They note that any exclusions should be pre-specified, applied cautiously, reviewed qualitatively where feasible, and accompanied by sensitivity analyses and transparent reporting.	Add a statement on this point to section 4.6.3
Lymphoma Coalition	322	345	4.6.3	Excluding responses deemed "illogical" by the interviewer may result in the loss of valuable patient insights. Patients living with significant disease burden may express preferences that reflect a willingness to accept higher risks, shaped by their personal experiences and circumstances. These perspectives are important and should not be dismissed without careful consideration.	
Lymphoma Coalition	322	345	4.6.3	Quality checks should not over-penalise vulnerable respondents. The section is good, but it should warn that some quality checks may disproportionately penalise participants with lower literacy, fatigue, neurocognitive burden, or distress. Overly rigid exclusion based on "illogical" responses may remove exactly the patients whose preferences matter and whose lived burden affects how they process information.	Researchers should interpret quality checks carefully, recognising that responses affected by fatigue, distress, literacy, numeracy, or cognitive burden are not necessarily invalid and may themselves provide important information about instrument design or accessibility.
Patient Engagement Professional Society (PEPS)	322	344	4.6.3	E22 Section 4.6.3 raises the risk of fraudulent or AI-generated responses in online PPS, but the treatment is brief relative to the scale and pace of change in this area. Survey fraud—including bot responses, coordinated panel manipulation, and AI-generated synthetic participants—represents a genuine and growing threat to the integrity of digital PPS data, and the methods available to detect and mitigate it are evolving rapidly. As preference research increasingly migrates to online platforms, quality standards that do not evolve with the threat landscape will quickly become outdated.	Expand Section 4.6.3 to provide substantive guidance on minimum quality-check requirements for digital PPS, participant verification standards, and documentation expectations for online data collection.
Patient Engagement Professional Society (PEPS)	322	344	4.6.3	The rapidly evolving nature of digital fraud threats means that static guidance will become outdated. A commitment to periodic review would signal to the field that the guideline will remain fit-for-purpose.	Commit to reviewing and updating Section 4.6.3 on a defined schedule as the digital data quality landscape develops, given the pace of change in online survey fraud and synthetic data generation.
Syneos Health CRO	322	345	4.6.3 Implementing Quality Checks	The Guidance appropriately mentions the need for adequate quality checks, such as control questions and relevant analysis approaches, however, it could benefit from additional emphasis on technical measures for the detection of fraudulent responses / behavior (e.g., CAPTCHA and other bot detection mechanisms), in particular with respect to large-scale quantitative PPS conducted via remote research tools.	For large-scale quantitative PPS conducted via remote research tools, we recommend including additional emphasis on the need to consider appropriate technical measures (rather than adjusted analysis approaches only) for the detection of fraudulent responses / behavior, which should be considered early during the design phase.
EFPIA	330	330	4.6	Consider briefly defining "dominated-choice task", as this will not be understood by many readers. The approach of including brief definitions is already used in rows 337 and 340. Additionally, lines 330 and 339 are very similar. It is unclear how they differ – additional explanation may be warranted.	Adding a dominated-choice task (in which one of the options is objectively superior to the others) to check for illogical responses;
Thermo Fisher Scientific	330	330	4.6.3	Suggest avoiding the term 'illogical responses' as this doesn't sound very patient centered for people giving up their time to complete data collection.	Suggest revising to: Adding a dominated-choice task (where one alternative has superior, or the same, performance to another alternative for every attribute) to assess engagement and understanding of the tasks
Thermo Fisher Scientific	339	339	4.6.3	Again suggest avoiding such terminology that doesn't sound patient centered 'Illogical responses (e.g., preferring an obviously inferior option)'. This also overlaps with the dominance task in row 330 so this could be removed. Beyond a dominance task, tasks should not be presenting fully dominated alternatives.	
Breakthrough T1D	340	341	4.6.3	While AI-generated synthetic data or synthetic participants can be a useful research technique in some contexts, we agree that synthetic participants generated by artificial intelligence represent a potential source of fraudulent responses in PPS. Given that this type of AI-generated data is new and emerging, the addition of relevant resources that provide further information and guidance on how to detect such responses would make this guideline more useful.	

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EURORDIS	340	341	4.6.3 Implementing Quality Checks	Fraudulent responses resulting from multiple survey submissions should be mitigated through appropriate controls. As informed consent is required, mechanisms should be in place to detect duplicate responses. Due to the use of multiple recruitment channels, the same individual may register more than once for the same PPS. Synthetic participants generated by AI present a potential risk. This risk may be mitigated through direct interaction between a researcher and each participant to confirm their authenticity and ensure that the study objectives are understood.	
Eurordis - François Houÿez	340	341	4.6.3	Fraudulent responses by completing the survey multiple times: as a consent is requested, it should be possible to detect duplicate responses. As participants will be contacted via different channels depending on the recruitment strategies, it may happen that the same person registers twice for the same PP study. Duplicates should be detected early. Synthetic participants generated by AI is a risk, here again, if a human person / researcher interacts directly with each participant to ensure study objectives are understood, then this risk could be mitigated	
European Hematology Association (EHA)	342	342	4.6.3	With regards to inconsistencies in response from the same participant, EHA considers that this would be expected as responses will be subjective in many cases and may depend on how a patient is feeling that day, for example, have they recently experienced new side effects or a change in treatment response.	Consider adding clarifying language to this point
Lymphoma Coalition	346	377	4.6.4 + 4.6.5	Pretesting and piloting should encourage testing with diverse and harder-to-reach patients. The text is strong, but could be more explicit that pretesting/piloting should include patients with different literacy levels, disease burden, and backgrounds.	Pretesting and piloting should, where feasible, include participants with diverse educational, linguistic, and clinical backgrounds, including individuals likely to face higher cognitive or practical burden when completing the PPS.
EFPIA	347	348	4	Pretesting and piloting an instrument serve different purposes, and both are essential 347 steps in developing the instrument	both are essential, but elsewhere it endorses a risk-proportionate "quality by design" approach and also warns quality checks should not add unnecessary burden. The absolute wording could draw comments from stakeholders working in small populations or constrained settings.
EFPIA	351	351	4.6	Important that not that just the questions are clear, but the attributes and levels are relevant	"questions and attributes are clear, relevant, and understandable…"
EFPIA	352	366	4.6.4	I find the pre-testing very heavy, with interviews (quali) and cognitive debriefing. Alternatives could be added, such as working with few patients for developing the interview guide and the questions of the survey. Or could the pre-testing and piloting be grouped for the survey?	
EFPIA	352	372	4.6.4/4.6.5	The difference between pre-testing and piloting for qualitative PPS is not clear to me and seems very artificial. Pre-testing mentions 'ensuring that the questions are clear, relevant, and capable of eliciting detailed, meaningful responses. The pretest helps identify any issues with the flow of the interview, the comprehensibility of the questions, and the overall structure' and piloting mentions 'identify issues with question wording, interview length, and the interviewer's approach'. In reality, I wonder if a distinction is made for qualitative research.	If pretesting is meant to purely validate the instrument and piloting aims to assess validity of the whole study plan, please add more detailed objectives to piloting accordingly for clear differentiation (line 368 - 377), particularly for qualitative PPS.
Thermo Fisher Scientific	352	372	4.6.4-4.6.5	It is unclear what the difference between pretesting and piloting is in the context of qualitative PPS. It would be helpful if the differences between pretesting and piloting qualitative PPS could be clarified further (e.g question wording and interview length are listed in both sections). Or whether for qualitative PPS in fact only one set of pre-test/piloting is needed to cover all aspects mentioned in the current guideline for pretesting and piloting. For quantitative PPS we agree that qualitative/cognitive pre-testing is needed as well as a quantitative pilot.	
European Heart Network (EHN)	353	354	4	Pre-testing should also be used as an opportunity to identify questions relevant to the patients but not listed in the PPS.	
Thermo Fisher Scientific	358	359	4.6.4	Suggest moving this sentence to the paragraph above as this is applicable for both qualitative and quantitative PPS. That is, researchers should also consider the study population (e.g., if fatigue is common) and the maximum length of not only interviews, but also surveys, etc.	

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	360	362	4.6	The text states "For quantitative PPS using survey instruments, the process generally involves administering the survey to a small, representative sample of the target population via cognitive interviews." Small samples can rarely be representative. It may also not be necessary to pretest among a representative group - pretesting among respondents with lower health literacy and numeracy to make sure the survey is accessible may be the core priority.	The recommendation is to remove "representative" from this statement. "For quantitative PPS using survey instruments, the process generally involves administering the survey to a small representative sample of the target population via cognitive interviews" Consider whether to add content that is more realistic about the limitations of a small sample to be representative and that the small sample's heterogeneity should be based on the needs for the particular survey.
EFPIA	362	366	4.6	"These are usually conducted iteratively" – the concept of iteration is hard to follow without making clear that the instrument is revised between iterations.	Change to something like: "These are usually conducted iteratively, using think aloud techniques where study participants voice out thought processes as they complete the survey instrument, with revisions made between iterations."
European Heart Network (EHN)	365	366	4	A tool can seem clear in a narrow sample and still fail for the broader population.	Addition: "Pretesting should, where feasible, include participants with diverse backgrounds and experiences, including participants with lower literacy or numeracy, different socioeconomic situations, and different geographic settings, to assess whether the instrument performs well across the intended population."
EFPIA	373	377	4.6	The guideline can suggest that pilot data can be combined with the full analysis sample if piloting yields no changes to the survey.	Add: "If piloting does not demonstrate survey revisions, if appropriate, piloting results can be combined with the main analysis to yield a larger sample."
Thermo Fisher Scientific	373	376	4.6.5	The guideline states that, in quantitative PPS using electronic survey instruments, piloting may help to detect technical or display issues with electronic administration. In practice, such issues should ideally be identified and addressed prior to the pilot stage (e.g. during internal testing and validation), with piloting focusing more on participant behaviour, data quality, and potential sources of bias.	
EFPIA	375	377	4.6	It is not clear from "Pilot information may also inform revisions to statistical considerations" what statistical considerations are relevant or being referenced. As an example, pilot data often help refine assumptions used in sample size estimation or in prior distributions in Bayesian analyses. Clarifying this will make the guidance more actionable and transparent for readers.	Results from the quality checks in the pilot phase help to facilitate early identification of potential sources of bias before fielding the instrument. Pilot information may also inform revisions to statistical considerations such as refined assumptions for sample size estimation, prior distributions updates, or model specification validation.
Dr Yewande Okuleye	378	404	4.7	The draft addresses between-person heterogeneity but does not explicitly consider within-person variability over time. In some contexts, patient preferences may be state-dependent or time-varying rather than stable. Without recognising this, analysis plans may implicitly treat preferences elicited at a single point in time as generalisable, which can affect interpretation of results.	Add text to Section 4.7 (e.g. within the analysis plan or sensitivity analyses discussion) stating that, where relevant, PPS should consider whether preferences are state-dependent or time-varying, and should describe how such variability is assessed or accounted for in analysis and interpretation.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
European Hematology Association (EHA)	378	404	4.7	This section provides a strong general framework for analysis planning. However, it fails to mandate the level of detail and specific strategic focus required for PPS in conditions where patient populations are often small, heterogeneous, and face high-stakes, sequential treatment decisions, as is the case in many hematological conditions.	Add to this section: "4.7.1. Prioritising Analysis of Heterogeneity: For studies in conditions with heterogeneous clinical pathways and treatment options (e.g., most hematologic malignancies), the analysis plan must explicitly identify the investigation of preference heterogeneity as a primary or key secondary study objective. Subgroups for analysis must be defined a priori based on clinically relevant variables known to influence treatment decisions (e.g., age group, fitness status, genetic prognostic markers, prior lines of therapy). The study report must present subgroup-specific preference estimates with the same prominence as aggregate results, and the clinical implications of any observed heterogeneity must be discussed in detail." "4.7.2. Adaptation for Studies in Rare Diseases: When a study is conducted in a very rare disease where pre-specified pooling across regions is not feasible or would still result in a very small sample size, the analysis plan must justify an alternative, fit-for-purpose approach. This may include: •Re-framing the study objective from estimating stable population-level preference weights to describing the range and key drivers of preferences using qualitative or mixed-methods analysis. •Employing Bayesian analytical frameworks that can incorporate prior knowledge or data from related conditions. •A detailed plan for in-depth analysis of response consistency within the small sample (e.g., individual-level analysis) to assess data validity. The rationale for this adapted approach and its limitations must be highlighted in the protocol, analysis plan, and final study report."
Lymphoma Coalition	378	404	4.7	The guideline treats preferences as relatively static, whereas in real-world settings patient preferences evolve over time with disease progression, treatment experience, and changing life circumstances. This limits the relevance of PPS for longitudinal decision-making.	Encourage consideration of the dynamic nature of preferences and, where relevant, inclusion of longitudinal or stage-specific analyses. Include guidance on longitudinal PPS approaches, repeated measures, and updating preference evidence across the disease trajectory.
Lymphoma Coalition	378	404	4.7	The section is statistically solid, but relatively thin on interpretation. A patient-centred PPS should not stop at estimating preferences. It should also explain what those preferences mean in practical terms for decision-making. Findings should be considered alongside clinical evidence and real-world constraints. Interpretation should account for subgroup differences and contextual factors such as healthcare system variability.	Add wording such as: ...The analysis and reporting should support meaningful interpretation of results, including practical implications for patient-centred decision-making, relevant subgroup differences, and limitations in applicability.
EFPIA	379	389	4.7	The guidance should clarify if it applies to quantitative PPS only or to both qualitative and quantitative. If also applied to qualitative PPS, a few consideration need to be taken into account: analysis method (inductive, confirmatory, mixed), research paradigm	Take into account and detail the specificities of analyzing data in qualitative and quantitative PPS
PSI	379	387	4.7	We strongly support the need for an analysis plan defined a priori, mirroring the discipline of clinical trial analysis plans. One potential point of confusion is the mention of hypothesis testing: many patient preference studies are descriptive (estimating preference weights or rates of trade-off) and may not involve formal null hypothesis testing unless comparing groups or testing a specific hypothesis. Clarifying that formal statistical tests are only expected when the study design warrants them would help avoid misinterpretation.	In line 383–385, modify the text to read: "…defining subgroups, and where appropriate defining any formal hypotheses and statistical tests if inferential comparisons are planned." Additionally, consider explicitly stating (e.g., in Section 4.7) that the Statistical Analysis Plan for a PPS should be finalized before data collection ends or before analysis begins.

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
PSI	379	404	4.7	ICH E22 acknowledges that PPS may be combined with clinical data in quantitative benefit–risk analyses (Section 4.7) but does not provide standards for statistical integration, such as: modelling uncertainty in safety parameters, propagation of measurement error from PPS, integrating heterogeneous risk perceptions across subgroups, dealing with preference heterogeneity when safety events are rare, or performing sensitivity analyses specifically for safety-driven endpoint Without methodological guidance on linking PPS-derived risk thresholds with actual safety event distributions, sponsors may overstate the robustness of risk–benefit trade-off models, leading to misinterpretation of acceptable risk levels in regulatory decisions. This is especially critical in scenarios where safety data are sparse, imbalanced across subgroups, or involve severe but low-frequency harms—exactly the situations where PPS inputs might unintentionally dominate the quantitative model.	Add guidance requiring sponsors to provide a transparent statistical integration framework when PPS outcomes are used alongside safety data. This prevents overstating the precision or robustness of models combining PPS and safety data and ensures that regulatory conclusions about acceptable risk levels remain scientifically sound.
EFPIA	381	382	4.7	The idea of combining preference and clinical data is introduced abruptly, potentially leaving readers confused why this is introduced and why it is addressed so briefly. Additionally, the paragraph on the analysis plan for quantitative PPS ("For quantitative PPS, the analysis plan …") focuses solely on quality checks. While important, this is but one element of the analysis of quantitative PPS.	Since the combination of preference and clinical data is restricted to quantitative PPS, this concept could be better introduced in the paragraph on quantitative PPS, along with a few other key concepts related to combination, such as the use of sensitivity analyses accounting for uncertainty in both the preference and clinical data. Suggest moving to lines 390-396
Thermo Fisher Scientific	381	382	4.7	Footnote 7 notes "Quantitative benefit-risk analysis (qBRA) may combine data from quantitative PPS and clinical trial data. Detailed discussion of qBRA is outside of the scope of this guideline." Since qBRA is important in a regulatory context we suggest referencing the qBRA guidance here again so that readers can find additional information on qBRA in another source if not covered within here.	Refer to qBRA guidance available outside of this guideline - the Professional Society for Health Economics and Outcomes Research (ISPOR) best practice documents on Patient Preference Methods and Quantitative Benefit-Risk Assessment
EFPIA	385	385	4.7	Grammar edit	"and where appropriate, testing of hypotheses."
European Hematology Association (EHA)	386	389	4.7	Such assessments should include a statistician or a researcher with expert competence in statistics.	Consider replacing the word "researcher" with "statistician", or including a discussion of the potential role of a medical statistician.
PSI	390	398	4.7	This focus on data quality is excellent and will improve trust in PPS results. One further enhancement would be to explicitly encourage assessing the reliability and validity of preference data (e.g., external validity by comparing stated preferences to real-world choices where possible).	After line 394, add a sentence such as: "Researchers are also encouraged to assess the reliability and validity of the preference data. For example and, if applicable data exist, a comparison of stated preferences with actual patient choices can help validate the findings externally."
Thermo Fisher Scientific	393	396	4.7	Suggest adding that if observations are removed to create the primary analysis set, not only should the results of the full analysis set be presented, but also a rationale for removing observations should be included.	Suggest revising to: If the data quality checks result in removing observations to create the primary analysis set, the results of the full analysis set (including removed observations) should be presented to demonstrate the impact of removing these observations on the study results and a rationale for removing observations should be provided."
PSI	397	401	4.7	We appreciate the emphasis on exploring preference heterogeneity in lines 169–174;, as understanding subgroup differences is crucial for applying preference data in benefit–risk assessments. However, the guidance could further advise on analytical methods to investigate heterogeneity, not just pooling strategies. Many modern PPS analyses use statistical techniques (e.g., latent class models, mixed-logit random parameters, or subgroup stratification) to identify and quantify distinct preference segments within the sample.	Augment the text to prompt analysis of heterogeneity. For example, add to line 398–400: "…facilitate the assessment of consistency in preferences across regions or other relevant subpopulations... Where notable preference heterogeneity is anticipated, researchers should consider analytical techniques (for instance, appropriate subgroup analyses or models that capture variance in individual-level preferences) to characterize and report distinct preference patterns within the population."

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
Syneos Health CRO	402	404	4.7 Analysis Plan Lines	Sensitivity analyses are appropriately addressed; however, the guideline could also encourage transparency regarding preference heterogeneity and subgroup differences, especially when these differences may have implications for regulatory decision-making.	Strengthen emphasis on reporting subgroup variation and its implications: "Where preference heterogeneity or meaningful subgroup differences are identified, these should be transparently reported and interpreted in the context of the intended population. Applicants should discuss the potential implications of subgroup differences for benefit-risk assessment, labelling considerations (as applicable), or post-marketing data needs.
Acute Leukemia Advocates Network	405	424		There's no expectation that study sponsors share results back with the patient communities who participated — a practice increasingly considered an ethical obligation in patient-centered research.	
Cancer Patients Europe	405	413	4.8	Reporting is focused on regulatory submission, not accessibility to patients.	Add recommendation to produce patient-friendly summaries of PPS results.
EFPIA	405	422	4.8	For qualitative study, recommend the well establish guidelines for reporting qualitative studies (COREQ, SRQR)	Add precision for reporting qualitative studies, especially the COREQ & SRQR guidelines
European Hematology Association (EHA)	405	423	4.8	EHA's patient community suggest that section 4.8 should go beyond CTD-focused reporting by expecting sponsors/researchers to share PPS results back with participants and patient communities in clear, accessible language as part of ethical, patient-centered practice.	Consider adding language to encourage feedback to participants and patient communities.
European Patients' Forum	405	424	4.8 Reporting and Submission to CTD Modules	Transparency regarding how PPS results influence regulatory and development decisions supports trust and realistic expectations among patients and stakeholders. When PPS results are partially used, or not used in a specific submission or in the regulatory assessment, they may still provide methodological or scientific value for future drug development. Explicit recognition supports efficient use of patient contributions and encourages continued investment in PPS. In addition, sometimes, patients may not express a clear preference, with responses evenly distributed across attributes or levels, providing limited guidance on treatment prioritization, endpoint selection, or benefit-risk trade-offs. This could reflect either a poorly designed study or genuine uncertainty. Even in such cases, sharing the findings with regulators can be valuable, though industry views may differ. Was this issue addressed by the ICH E22 guideline developers?	ADD: "Transparency regarding the role of PPS in regulatory decision-making is encouraged. Study sponsors should describe how PPS results were considered in the development programme and whether they informed decision-making fully or partially.In cases where PPS results are not used in a specific regulatory submission, consideration should be given to documenting the reasons and the potential relevance of the findings for future research or drug development. In addition, regulators should also be transparent about the use of PPS to support a regulatory decision, for example through public assessment reports.''
Eurordis - François Houÿez	405	424	4.8	In addition to where to present PP study results in the CTD and regulatory dossier, the importance of communicating the findings to patients and organisations that contibuted to the research should be highlighted (using appropriate format and content).	
Lymphoma Coalition	405	423	4.8	Reporting is framed only for CTD/regulatory purposes. There is no mention of returning findings to participants or making results understandable to patient communities. Ethical and respectful patient involvement includes communicating results back in accessible language.	Add: ...Researchers and applicants are encouraged to prepare an accessible plain-language summary of PPS objectives, methods, and key findings for participants and patient communities.
Marieke Heisen, Patvocates	406	406	4.8	The PPS should be included in CTD modules 2 and 5.' This line is assuming all readers are familiar with earlier ICH guidelines. I recommend placing this in context of ICH M4, which explains the CTD structure.	
EFPIA	407	407	4.8	The FAQ document mentions that it's acceptable to run preference studies within a clinical trial. It would be helpful to have specific advice about the approach to a preference study report for this scenario (is the preference study report expected as part of the clinical trial report or as a stand-alone preference report)?	The PPS report structure can be based on (with adaptations as appropriate) the structure of clinical study reports (CSRs) (ICH E3(R1)). When conducting a preference study within a clinical study, it is recommended that the preference results are reported in a stand-alone prefernece study report (rather than as part of the clinical study report).

Name of organisation or individual	Line from	Line to	Section number	Comment and rationale	Proposed changes / recommendation
EFPIA	408	409	4.8	"The PPS report structure can be based on (with adaptations as appropriate) the structure of clinical study reports (CSRs) (ICH E3(R1)). " The reader may interpret this statement as implying that the CSR's structure is the only valid structure to use for PPS. The text should be changed to be clear that there is flexibility to use the structure of any well-designed scientific report.	"The PPS report structure can be based on (with adaptations appropriate) the structure of other scientific reports such as clinical study reports (CSRs) …."
European Heart Network (EHN)	411	413	4	Need to assess whether the findings are truly applicable to the population affected.	Addition: "The report should describe participant characteristics relevant to the interpretation and generalisability of the findings, including characteristics associated with inequity or differential access where relevant."
EFPIA	414	415		When including patient experience data in a regulatory submission, best practice expectations are that the applicant should explain how the patient experience data is expected to inform the regulatory decision. This best practice also applies to patient preference information. Section 4.8 of the guideline does not include explicit advice that the applicant should explain, in the regulatory submission, how the patient preference information is expected to inform the regulatory decision-making.	The PPS may be referenced in multiple locations, most frequently within Module 2. **When discussing the patient preference information, the applicant should describe how this PPI is expected to inform the regulatory decision-making.**
PSI	419	423	4.8	This is very helpful, as it tells sponsors exactly where and how to incorporate patient preference evidence in a regulatory submission. The term "critical assessment of the PPS" is important; to ensure regulators trust the data, that assessment should discuss study limitations, biases, and relevance to the decision. Making expectations for that discussion more explicit would be beneficial.	In line 419–421, after "along with a critical assessment of the PPS", add a clarifier, for example: "(i.e., a discussion of the study's methodology, validity, and limitations, and how its results influence the benefit-risk conclusions)."
EU EYE	339	339	4.6.3	Illogical responses (e.g., preferring an obviously inferior option) EU EYE would recommend caution regarding the use of illogical responses given the repulsion effect when people are presented with choices https://www.sciencedirect.com/science/article/pii/S0010027722001524 In addition 'illogical' responses may be justified through behavioural economics, psychology, and context-dependent decision-making. While such responses may violate strict logical models (like expected utility theory), these decisions are often rational within the person's own subjective framework, which may prioritize factors like emotion, cognitive ease, or social status over raw utility. While irrational on paper, these choices often serve hidden, emotional, or strategic purposes that maximize values other than raw utility https://pubmed.ncbi.nlm.nih.gov/17100791/	Consider deleting illogical responses or rephrasing acknowledging that illogical responses may be indicative of personal values other than utility.
ACRO	29	48	1.3	ACRO welcomes the clarity on the scope of the guideline. This section is helpful is stating what is included (patient stated-preference studies) and what is not included (carer preferences or healthcare professional preferences, patients reported outcome measures).	
Faculty of Pharmaceutical Medicine	104	104	2.7	Information about patient education should be provided. Is it important to note if the patient preference changes depending on the information/education that the patient is provided on the use of the drug	Change "informed consent forms" to Informed consent document consisting of patient information sheet.
Faculty of Pharmaceutical Medicine	118	119	3	Suggest including some text on situations where PPS could be of particular benefit e.g.rare diseases, new disease areas, drugs designed to cause symptom relief.	
Faculty of Pharmaceutical Medicine	136	136	3.2	It is clearly stated that the common uses of PPS included in the Guidelines is not an exhaustive list but suggest that 'subgroup identification' is included as this is relevant for regulatory and HTA bodies.	
Faculty of Pharmaceutical Medicine	143	144	3.2	Suggest also to include frequency of administration as well as mode.	
Faculty of Pharmaceutical Medicine	176	177	4	Where PPS research is used to support drug development, there is a risk that the findings of the PPS are considered relevant only to the research team and, if submitted as part of CTD, to regulators. While the guideline clearly states that PPS should "follow internationally recognised scientific standards and recommended practices", it may be useful to remind researchers that the principle of sharing research findings with participants to support trust applies as much to PPS as other research types.	

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Faculty of Pharmaceutical Medicine	200	202	4.2	The approaches can be explained in more detail	
Faculty of Pharmaceutical Medicine	240	250	4.4	The Guidance clearly states that sample size is determined by the research questions and methods. Consider including text that it's also determined by which phase of the lifecycle the drug is in e.g. early vs late development	
Faculty of Pharmaceutical Medicine	271	273	4.5	It is important to acknowledge that in PPS orientation of patients is important to get the appropriate input from the patients on the attributes and endpoints being studied. In a drug trial HCPs are trained on the conduct of the trial; whereas in PPS patients need to be inducted into the research process. In the absence of any induction and processes PPS may not give the appropriate results and in this case there should not be generalization of the study results.	
Faculty of Pharmaceutical Medicine	323	324	4.6.3	An important quality check would be whether a diverse patient population reflecting the real world scenario is selected for the PPS. for example PPS results with naive patients may diff	
Acute Leukemia Advocates Network			4,2,4,3	The guideline is largely silent on how to adapt PPS methodology for children and adolescents, including assent processes and age-appropriate instrument design.	