

GLOBAL

Personal Experience, Expectations and Knowledge (PEEK): Clinical Outcome Assessment Strategy Framework





CCDR+

centre for community-driven response

Purpose

To provide pharmaceutical teams with guidance and a consistent method for translating PEEK patient experience evidence into COA and outcome-measurement strategy globally, while adapting the resulting evidence plan to the regulatory, clinical-trial and HTA expectations.

This Framework is relevant to markets in the United States, United Kingdom, Australia, Canada, European Union, Germany, France, Switzerland and Japan.

Centre for Community-Driven Response (CCDR) | Personal Experience, Expectations and Knowledge (PEEK)

1. Executive proposition

The central scientific question is global: what treatment effects matter to patients, how should those concepts be measured, and does the proposed clinical development programme generate evidence that is meaningful to patients? The regulatory and reimbursement consequences of that evidence differ by market. The Global PEEK COA Framework therefore separates a common scientific core from jurisdiction-specific modules.

Global proposition

PEEK provides a systematic patient-evidence foundation from which pharmaceutical PCO/COA, Clinical Development and cross-functional teams can identify patient-important outcomes, define and prioritise concepts of interest, challenge proposed COAs, identify evidence gaps, and plan a globally coherent outcome-measurement strategy with market-specific regulatory and HTA extensions.

Framework architecture

Layer	Purpose	Output
A. Common scientific core	Consistent PEEK method used across markets	Global Patient Evidence & COA Strategy
B. Global evidence architecture	Distinguish evidence that should be common from evidence that requires local adaptation	Global core + local evidence plan
C. Regulatory modules	Translate the core strategy into market-specific development expectations	Regulatory evidence considerations
D. HTA/value modules	Ensure trial outcomes can support downstream value assessment	HTA/reimbursement evidence considerations
E. Country evidence map	Document gaps, decisions, owners and next actions	Market-specific COA Evidence Map

Priority modules

Market	Regulatory interface	HTA/value interface	Primary reason for module
United States	FDA	US payer/value evidence as relevant	Most explicit PFDD/COA methodological framework
United Kingdom	MHRA / ICH	NICE	Links trial outcomes, patient involvement and HTA
Australia	TGA / ICH	PBAC	Strong patient-relevant outcome and HRQoL/economic link (In theory)
Canada	Health Canada / ICH	CDA-AMC; INESSS in Quebec	Patient input is embedded in reimbursement review
European Union	EMA / ICH	EU HTA Joint Clinical Assessment + national HTA	Increasing convergence of regulatory and EU-level clinical assessment
Germany	EMA/BfArM/PEI as applicable	G-BA / IQWiG	Patient-relevant outcomes and PRO duration/interpretation are highly consequential
France	EMA/ANSM as applicable	HAS	Growing explicit use of PROs in HTA
Switzerland	Swissmedic / ICH-aligned development	FOPH/BAG	Independent reimbursement system focused on effectiveness, appropriateness and economic efficiency
Japan	PMDA / MHLW / ICH	MHLW/C2H cost-effectiveness pathway as applicable	Important strategic market requiring local regulatory and linguistic/cultural adaptation

2. Common scientific core: PEEK COA

The scientific core is deliberately jurisdiction-neutral. It should be completed once for a development programme and then stress-tested against each market module.

Stage	Core question	PEEK contribution	COA output
1. Define context	Who is the target population and what benefit is expected?	Disease/treatment journey, subgroups, unmet need	Draft context of use / treatment-benefit hypothesis
2. Understand experience	What symptoms, impacts and burdens define the patient experience?	Mixed-method qualitative + quantitative evidence	Patient experience conceptual model
3. Identify what matters	Which aspects of feeling, function and daily life matter most?	Importance, frequency, severity, priorities	Meaningful aspects of health
4. Define treatment success	What would patients regard as a successful treatment?	Goals, expectations, meaningful improvement	Candidate treatment-benefit concepts
5. Prioritise concepts	Which concepts are important, treatment-relevant and measurable?	Patient importance + burden + subgroup evidence	Prioritised concepts of interest
6. Select COA type	Who is best placed to report/assess the concept?	Self-report feasibility, observer context, function	PRO / ClinRO / ObsRO / PerFO decision
7. Map measures	Do existing measures cover the patient-important concepts?	Concept-to-item/domain comparison	Coverage map and gap analysis
8. Plan evidence	What remains to establish fit-for-purpose measurement?	Identify patient evidence gaps	Qualitative, cognitive, psychometric, interpretation work
9. Integrate endpoints	How will COAs contribute to trial objectives/endpoints?	Patient rationale for relevance	Sponsor-led endpoint and analysis strategy
10. Localise	What changes across regulatory/HTA markets?	Local PEEK evidence where needed	Country modules and evidence plan

PEEK evidence domains

Domain	Key question for COA strategy
Symptoms	Which symptoms are most important, burdensome and treatment-relevant?
Function	What physical, cognitive, social or role functions do patients want to preserve or regain?
Quality of life	Which broader consequences of disease and treatment matter?
Treatment goals	What are patients trying to achieve?
Successful treatment	How do patients define benefit in their own terms?
Meaningful improvement	What degree/type of change would be noticeable and worthwhile?
Treatment burden	Which administration, monitoring and practical burdens matter?
Tolerability	Which adverse effects matter and when does burden outweigh benefit?
Trade-offs	What benefits justify which risks/burdens?
Unmet need	What important outcomes remain inadequately addressed?
Heterogeneity	How do priorities differ across stage, prior treatment, age, geography or other relevant groups?

3. Global decision tools

3.1 Concept prioritisation matrix

Concept	Importance	Burden / frequency	Expected treatment relevance	Potential to change	Existing measurement	Global priority
[concept]	H/M/L	H/M/L	Y/N/?	Y/N/?	Full/Partial/None	H/M/L

3.2 COA type decision

Question	Likely COA	Examples
Can the patient directly report the experience without external interpretation?	PRO	Pain, fatigue, nausea, perceived function, overall side-effect impact
Is it an observable behaviour/sign reported by a caregiver or other observer?	ObsRO	Observable events/behaviours where self-report is not feasible
Does assessment require trained clinical judgement?	ClinRO	Clinical signs or severity ratings
Can functional performance be directly tested?	PerFO	Walking, motor, sensory or cognitive performance

3.3 Existing measure coverage screen

Patient-important concept	Priority	Candidate COA	Coverage	Content validity	Measurement properties	Population/language fit	Action
[concept]	H	[instrument]	Full/Partial/None	Adequate/?/Gap	Adequate/?/Gap	Yes/?/No	Retain/Review/Replace

Global rule

A globally common instrument is desirable only when it remains conceptually relevant, linguistically/culturally appropriate, psychometrically defensible and operationally feasible in each target population. Harmonisation should not override content validity.

4. Global evidence architecture

The framework distinguishes evidence that should normally be generated once from evidence that may need market-specific confirmation.

Evidence component	Global core?	Local adaptation / confirmation may be needed when...
Disease and treatment experience conceptual model	Usually	Care pathways, treatment availability or cultural context materially alter experience
Patient-important symptoms and impacts	Usually, with cross-market testing	Importance/ranking differs by market or subgroup
Concepts of interest	Prefer global consistency	Local clinical practice or claims require different emphasis
COA type	Usually	Self-report feasibility, caregiver role or clinical practice differs
Instrument selection	Prefer global consistency	Translation, content relevance, validation or licensing differs
Linguistic validation	No - language specific	Any translated version is used
Cultural adaptation	Market/language specific as needed	Concepts/items do not transfer cleanly
Meaningful change / interpretation	May require pooled + subgroup evidence	Baseline severity, culture or response patterns differ
Trial schedule and burden	Partly	Local trial operations or standard of care differ
HTA outcome requirements	No	National value frameworks differ
Patient involvement / patient input	Often local	HTA/ethics processes require local stakeholder input

Global-to-local workflow

- Create one global PEEK Patient Evidence Review and conceptual model.
- Agree global patient-important outcomes and candidate concepts of interest.
- Select a preferred global COA battery and document the rationale.
- Run the battery through each market module before protocol lock.
- Identify local gaps: patient relevance, translation/cultural validity, HTA outcomes, patient-input requirements and evidence duration.
- Resolve avoidable divergence early; document unavoidable country-specific additions.
- Maintain one Global COA Evidence Map plus concise country annexes.

5. Country module - United States

Strategic role

The US module is the methodological anchor because FDA has the most explicit stepwise PFDD framework connecting patient experience data to fit-for-purpose COAs and COA-based endpoints.

Interface	PEEK contribution	Key sponsor action
FDA PFDD Guidance 1-2	Representative patient input; systematic qualitative/quantitative evidence on what matters	Document sampling, methods and robustness of patient experience evidence
FDA PFDD Guidance 3	Meaningful aspects of health, concepts of interest, content coverage and gaps	Select/develop/modify fit-for-purpose COA and establish measurement properties
FDA PFDD Guidance 4 (draft)	Patient rationale and evidence relevant to meaningful change	Define COA-based endpoint, analysis, meaningful change and submission strategy
FDA COA Compendium	PEEK concepts can be compared with previously used/qualified COAs	Use compendium as a starting point, not proof of fit-for-purpose use

US evidence questions

- Does the PEEK sample adequately represent the intended trial population?
- What meaningful aspects of health and concepts of interest are supported by patient evidence?
- Does the selected COA have content validity for the concept and context of use?
- What evidence supports reliability, validity, ability to detect change and interpretation?
- How will the COA be incorporated into a trial endpoint and regulatory submission?

US PEEK value

PEEK is strongest in the transition from understanding disease/patient experience to defining treatment benefit and prioritising concepts; downstream COA validation and endpoint strategy remain sponsor-led.

6. Country module - United Kingdom

Interface	PEEK contribution	Key sponsor action
MHRA / ICH E6(R3)	Patient rationale for critical outcomes and acceptable collection burden	Integrate COAs into proportionate, quality-by-design trial planning
HRA / public involvement	Existing systematic patient evidence can identify issues for study-specific involvement	Conduct appropriate direct public involvement for the specific study
NICE	Patient-important outcomes, function, symptoms, HRQoL, treatment burden	Plan comparative outcomes, HRQoL/utility and evidence suitable for HTA

UK emphasis

Use PEEK to connect clinical-development outcome strategy with study-specific public involvement and downstream NICE evidence needs.

7. Country module – Australia

Interface	PEEK contribution	Key sponsor action
TGA / ICH E6(R3)	Patient rationale for critical outcomes and trial burden	Integrate COAs into quality-by-design trial strategy
NHMRC / HREC / consumer involvement	Patient priorities, burden and acceptability evidence	Undertake appropriate study-specific consumer involvement and ethics/governance work
PBAC	Patient-relevant outcomes, meaningful change, symptoms, function, HRQoL	Plan comparative clinical, HRQoL/utility and economic evidence prospectively

Australia emphasis

PEEK can bridge COA strategy and PBAC evidence planning by identifying patient-relevant outcomes early enough to collect them robustly in pivotal trials.

8. Country module – Canada

Canada combines Health Canada regulation with a reimbursement environment in which patient input is explicitly incorporated into drug review. Health Canada fully adopted ICH E6(R3) on 1 April 2026, reinforcing fit-for-purpose, critical-to-quality trial design.

Interface	PEEK contribution	Key sponsor action
Health Canada / ICH E6(R3)	Patient rationale for outcomes and data critical to trial objectives	Integrate COAs into scientifically sound, operationally feasible protocol and analysis plans
CDA-AMC	Evidence on living with the condition, current treatment experience, unmet need and expectations	Align clinical/PRO evidence with the value domains considered in reimbursement review
CDA-AMC patient group input	PEEK can help patient organisations systematically describe experience and priorities	Do not substitute sponsor research for independent patient-group input
Quebec / INESSS	PEEK evidence can support understanding of patient value and local context	Plan Quebec-specific reimbursement requirements separately where relevant

Canada evidence questions

- Are the outcomes important to Canadian patients and relevant to current Canadian treatment pathways?
- Does the clinical programme capture symptoms, function, HRQoL and treatment burden that may influence reimbursement deliberation?
- Can PEEK evidence help explain why a statistically significant change is meaningful to patients?
- Are local patient-group perspectives consistent with, or different from, the global PEEK evidence?

Canada emphasis

The distinctive opportunity is to connect rigorous patient experience evidence generated during development with the patient-value questions that later enter reimbursement review.

9. Regional module - European Union

The EU module should be treated as both a regulatory core and an HTA coordination layer. EMA is actively developing guidance on patient experience data, while the EU Health Technology Assessment Regulation has introduced Joint Clinical Assessments (JCAs).

Interface	PEEK contribution	Key sponsor action
EMA patient experience data	Systematic evidence on symptoms, outcomes, preferences and what matters to patients	Define how patient experience data will inform development and marketing-authorisation evidence
ICH E6(R3) in EU	Patient-relevant critical-to-quality factors and burden considerations	Build fit-for-purpose, proportionate trial design
EU HTA Joint Clinical Assessment	Patient-important outcomes can inform early thinking about relevant relative-effect evidence	Anticipate PICO/scoping and comparative evidence needs
EU patient/clinical expert involvement	PEEK can identify issues needing expert/patient validation	Engage appropriately with EU/national stakeholder processes

EU HTA timing

Joint Clinical Assessments apply from 12 January 2025 to new cancer medicines and advanced therapy medicinal products; the scope expands to orphan medicines in 2028 and all new centrally authorised medicines by 2030. For oncology programmes, this makes early alignment of patient-important outcomes, comparator strategy and evidence duration especially important.

EU emphasis

Design the global COA strategy so that the same patient-centred outcomes can serve regulatory interpretation and relative-effect assessment, while anticipating that national HTA decisions remain distinct.

10. Country extension – Germany

Germany is a high-priority HTA extension to the EU core because G-BA/IQWiG early benefit assessment places strong emphasis on patient-relevant morbidity, quality of life and adverse effects.

German issue	PEEK contribution	Implication for evidence plan
Patient-relevant outcomes	Prioritise symptoms, function and impacts patients actually value	Ensure pivotal studies collect relevant morbidity/HRQoL outcomes
PRO instrument relevance	Patient evidence can test whether instrument domains match important concepts	Avoid selecting instruments solely because they are conventional
Clinical relevance / responders	PEEK meaningful-improvement evidence can inform interpretation research	Pre-specify defensible responder/meaningful-change analyses
Duration of PRO collection	PEEK clarifies which outcomes remain important through progression/treatment	Avoid stopping patient-relevant outcome collection too early
Comparator context	PEEK describes treatment experience and burden under current care	Align with the appropriate comparator and German benefit-assessment needs

Germany emphasis

A COA strategy that is adequate for regulatory approval can still underperform in AMNOG assessment if patient-relevant outcomes are missing, collected for too short a period, or analysed in ways that do not support added-benefit assessment.

11. Country extension – France

France should sit on top of the EU regulatory core, with a specific HAS evidence lens. HAS has been developing its approach to the use of patient-reported outcomes in health technology assessment and emphasises endpoints centred on the patient.

French issue	PEEK contribution	Implication for evidence plan
Patient-centred endpoints	Identify outcomes patients consider important	Ensure efficacy evidence includes patient-centred outcomes where appropriate
PRO relevance	Map patient-important concepts to proposed questionnaires	Justify instrument choice and content relevance
Quality of life / functioning	Characterise disease and treatment impact	Collect interpretable HRQoL and functional evidence
French population fit	Identify potential differences in care pathways or priorities	Use French-language validated instruments and local confirmation where necessary
Patient contribution to HTA	PEEK can provide systematic background evidence	Maintain appropriate independent patient/association input into HAS processes

France emphasis

Use PEEK to strengthen the clinical meaning of PRO evidence: not simply whether a questionnaire score changed, but whether the measured domain reflects an outcome French patients consider important.

12. Country extension – Switzerland

Switzerland is outside the EU and therefore requires a separate market-access lens. The Federal Office of Public Health (FOPH/BAG) uses HTA to evaluate effectiveness, appropriateness and economic efficiency; Swissmedic is the regulatory authority.

Swiss issue	PEEK contribution	Implication for evidence plan
Effectiveness	Patient-important symptoms/function provide context for clinical benefit	Ensure outcomes demonstrate clinically meaningful benefit
Appropriateness	Treatment goals, burden and patient selection can inform appropriate use	Clarify which patients value and are likely to benefit from treatment
Economic efficiency	HRQoL, burden and resource impacts can contextualise value	Coordinate patient outcomes with economic evidence generation
Swiss context	PEEK can identify local care-pathway or access differences	Confirm transferability of global evidence to Swiss practice/languages

Switzerland emphasis

Keep the global COA battery where possible, but explicitly test transferability across Swiss clinical practice and language regions and connect patient-important benefit to the EAE value framework.

13. Country extension – Japan

Japan should use the global scientific core with a strong local-adaptation layer. PMDA and MHLW operate within the ICH framework, but Japanese-language measurement, cultural relevance, local clinical practice and reimbursement/economic-evaluation requirements need to be planned explicitly.

Japanese issue	PEEK contribution	Implication for evidence plan
ICH-aligned trial design	Patient rationale for outcomes and critical-to-quality data	Integrate COAs into PMDA/MHLW development strategy
Japanese concept relevance	Compare global patient-important concepts with Japanese patient evidence	Conduct local concept confirmation where transferability is uncertain
Translation / linguistic validation	PEEK can identify language-sensitive concepts and response patterns	Use validated Japanese versions and appropriate linguistic/cultural validation
Meaningful change	Local PEEK data can test whether interpretation is transferable	Assess pooled versus Japan-specific interpretation evidence
Value / economic evidence	Treatment burden, function and HRQoL can support value narrative	Coordinate COA/HRQoL strategy with applicable Japanese reimbursement and cost-effectiveness planning

Japan emphasis

Do not assume that a US/EU patient-evidence package transfers automatically. Preserve the global concepts where scientifically justified, but prospectively test linguistic, cultural and clinical-context equivalence.

14. Cross-market planning matrix

Evidence question	US	UK	AU	CA	EU	DE	FR	CH	JP
Explicit patient-focused regulatory framework	High	Med	Med	Med	Increasing	EU core	EU core	Med	ICH/local
HTA importance of patient-relevant outcomes	Varies	High	High	High	High/JCA	Very high	High	High	Relevant
Direct patient/patient-group input in HTA	Varies	Yes	Yes	Yes	EU/national	Yes	Yes	Contextual	Contextual
HRQoL / utility planning importance	High	Very high	Very high	High	High	High	High	High	High
Need for local language/cultural validation	English/Spanish etc.	English	English	English/French	Multi-language	German	French	DE/FR/IT	Japanese
Best PEEK role	PFDD/COA foundation	COA + NICE bridge	COA + PBAC bridge	COA + patient-value bridge	Regulatory + JCA bridge	Patient-relevant benefit	PRO/HTA relevance	Transferability + value	Local transferability

Protocol-lock questions

- Have we identified the same core patient-important outcomes across priority markets?
- Which concepts are global, and which require local confirmation?
- Does the proposed COA battery cover those concepts in every required language and population?
- Will PRO/COA collection continue for long enough to answer regulatory and HTA questions?
- Are meaningful-change and responder analyses planned early enough?
- Are HRQoL/utility measures suitable for UK, Australia, Canada, EU/national HTA, Switzerland and Japan?
- Where is direct local patient or patient-group involvement required in addition to PEEK evidence?
- Can one evidence-generation plan avoid duplicative post-launch studies?

15. Global PEEK COA Evidence Map - master template

Development programme	Indication / product / phase:
Priority markets	US ☐ UK ☐ AU ☐ CA ☐ EU ☐ DE ☐ FR ☐ CH ☐ JP ☐
Target population	
Expected treatment benefit	
Global patient experience model	
Top patient-important outcomes	1. 2. 3. 4. 5.
Meaningful aspects of health	Feeling/symptoms: Functioning: Broader impact/HRQoL:
Prioritised concepts of interest	
Proposed COA types	PRO ☐ ClinRO ☐ ObsRO ☐ PerFO ☐
Proposed global COA battery	
Adequately covered concepts	
Partially/uncovered concepts	
Global patient-evidence gaps	
Content validity / psychometric gaps	
Meaningful-change / interpretation gaps	
Language / cultural adaptation gaps	
HTA / HRQoL / utility gaps	
Local patient involvement required	
Country-specific additions	
Decision owners / next actions	

Decision principle

The objective is not identical evidence in every market. It is one coherent scientific rationale, with the minimum justified local adaptation needed to remain patient-relevant, fit-for-purpose and decision-useful.

16. Pharmaceutical implementation model

Stage	Lead contributors	Output
1. Global PEEK evidence review	PEEK + Patient Engagement + PCO	Patient experience conceptual model
2. Concept prioritisation	PCO/COA + Clinical Development + PEEK	Global patient-important outcome set
3. COA mapping	COA experts + PEEK	PRO/ClinRO/ObsRO/PerFO strategy and coverage map
4. Global measure selection	COA + Biostats + Clinical + Operations	Proposed global COA battery
5. Market-module review	Regulatory + HEOR/Market Access + local affiliates	Country gap matrix
6. Evidence-generation plan	Cross-functional team	Qualitative, psychometric, interpretation, HRQoL and local evidence plan
7. Protocol integration	Clinical Development + Biostats + Regulatory	Endpoint hierarchy, schedule, SAP considerations
8. Pre-submission / HTA readiness review	Regulatory + Market Access + PCO	Regulatory/HTA evidence readiness map
9. Learning loop	PEEK + global/local teams	Update patient evidence and future development strategy

Recommended workshop sequence

Workshop	Purpose	Typical participants
Global Patient Evidence Workshop	Agree what matters and treatment-benefit concepts	PEEK, PCO, Clinical, Patient Engagement, Medical
COA Strategy Workshop	Select COA types/measures and identify measurement gaps	PCO/COA, Clinical, Biostats, Regulatory
Global Market Evidence Workshop	Stress-test strategy against regulatory/HTA modules	Regulatory, HEOR, Market Access, affiliates, PCO
Evidence Action Workshop	Assign studies, owners, timing and decision points	Cross-functional programme team

17. Worked global oncology example

Hypothetical scenario: a global programme for a systemic therapy in advanced cancer. Survival and tumour-response endpoints are central. PEEK evidence indicates that patients also prioritise fatigue interference, maintaining independence, symptomatic treatment toxicity, overall tolerability and time able to participate in normal life.

PEEK finding	Global COA implication	Market-specific consequence
Fatigue matters mainly because it prevents normal activity	Prioritise fatigue interference, not severity alone	US: content validity; DE: patient-relevant morbidity and adequate duration; FR/EU: patient-centred endpoint relevance
Maintaining independence defines treatment success	Measure physical/role function	UK/AU/CA/CH/JP: connect function with HRQoL/value evidence
Patients distinguish individual AEs from overall tolerability	Capture symptomatic AEs and overall side-effect impact where justified	US: oncology PRO strategy; DE: harms and QoL; HTA markets: patient burden
Patients accept different burdens for disease control	Interpret outcomes in benefit-burden context	Supports regulatory benefit-risk narrative and local patient input
Quality of life depends on disease, treatment and normal-life participation	Use disease-specific COAs plus suitable generic HRQoL/utility evidence	NICE/PBAC/CDA-AMC/EU-national HTA/CH/JP value planning

Worked-example output

One global patient-centred outcome strategy can be designed, but its evidence must be deliberately 'multi-use': fit for regulatory interpretation, robust enough for comparative HTA, collected for an adequate duration, and supported by the language/cultural evidence required in each market.

18. Key regulatory and HTA reference points

United States

FDA. Patient-Focused Drug Development Guidance Series.

<https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical>

FDA. PFDD Guidance 3: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (final, 2025).

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-selecting-developing-or-modifying-fit-purpose-clinical-outcome>

FDA. Roadmap to Patient-Focused Outcome Measurement in Clinical Trials.

<https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/roadmap-patient-focused-outcome-measurement-clinical-trials-text-version>

European Union / Germany / France

EMA. Multidisciplinary guidelines: patient experience data.

<https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-guidelines/multidisciplinary-guidelines/multidisciplinary-guidelines-patient-experience-data-ped>

EMA. ICH E6 Good Clinical Practice scientific guideline.

<https://www.ema.europa.eu/en/ich-e6-good-clinical-practice-scientific-guideline>

European Commission. Joint Clinical Assessments under the EU HTA Regulation.

https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment/joint-clinical-assessments_en

IQWiG. Handling of scales in benefit assessments: quality of life and other PROs.

<https://www.iqwig.de/en/about-us/events/iqwig-in-dialogue/2021-handling-of-scales-in-benefit-assessments.html>

HAS. Utilisation des patient-reported outcomes (PROs) dans les évaluations des technologies de santé.

https://www.has-sante.fr/jcms/p_3553361/fr/utilisation-des-patients-reported-outcomes-pros-dans-les-evaluations-des-technologies-de-sante-des-actes-professionnels-et-dans-l-elaboration-des-recommandations-vaccinales-et-de-sante-publique

Canada / Switzerland / Japan

Health Canada. Drugs for Clinical Trials Involving Human Subjects (GUI-0100); ICH E6(R3) fully adopted 1 April 2026.

<https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/guidance-documents/guidance-drugs-clinical-trials-human-subjects-gui-0100.html>

Canada's Drug Agency (CDA-AMC). Patient Input and Feedback.

<https://www.cda-amc.ca/patient-input-and-feedback>

Federal Office of Public Health (Switzerland). HTA programme.

<https://www.bag.admin.ch/en/hta-programme>

PMDA. ICH efficacy guideline / GCP renovation resources.

<https://www.pmda.go.jp/english/symposia/0247.html>

United Kingdom / Australia

UK MHRA. Clinical trials for medicines: guidance on quality and risk proportionality.

<https://www.gov.uk/guidance/clinical-trials-for-medicines-guidance-on-quality-and-risk-proportionality>

NICE. Technology appraisal and highly specialised technologies guidance: the manual.

<https://www.nice.org.uk/process/pmg36>

Australian TGA. ICH E6(R3) Guideline for Good Clinical Practice.

<https://www.tga.gov.au/resources/resources/international-scientific-guidelines-adopted-australia/ich-e6r3-guideline-good-clinical-practice>

PBAC. Guidelines - Trial characteristics / patient-reported outcome measures.

<https://pbac.pbs.gov.au/section-2/2-4-trial-characteristics.html>

Use note

This framework is a strategic evidence-planning tool, not regulatory or HTA advice. Country requirements evolve and product-specific pathways differ. Before applying a module to a live development programme, confirm current regulator/HTA guidance and obtain appropriate local regulatory, COA, statistical and market-access expertise.

ANNEX

Common HRQoL, PRO and Symptom Measurement Tools

How established instruments can be mapped to PEEK patient evidence and COA strategy

Purpose

This annex is a practical instrument landscape for the Global PEEK COA Strategy Framework. It is not an exhaustive catalogue of all available measures. It focuses on commonly used generic, preference-based, oncology, symptom and function instruments that pharmaceutical teams are likely to encounter, and shows how PEEK can be used to test whether each instrument captures what matters to the target patient population.

A1. How to use this annex

PEEK and established COAs answer different questions. The value comes from using them together.

Question	PEEK role	Established instrument role
What matters to patients?	Concept elicitation, prioritisation, treatment goals, successful treatment, meaningful improvement, burden and trade-offs	May or may not contain the relevant concept
What should we measure?	Tests patient importance and relevance to expected treatment benefit	Provides a standardised measurement approach
Does the proposed instrument cover the concept?	Maps patient language/themes to instrument domains/items	Provides content and scoring structure
Is anything important missing?	Identifies uncovered or under-represented concepts	May require complementary instrument or further development
How meaningful is change?	Provides qualitative anchors and patient descriptions of worthwhile change	Produces longitudinal scores requiring interpretation
Can the evidence support HTA?	Explains why outcomes matter and contextualises burden/value	Generic preference-based measures may provide utilities; disease-specific measures add sensitivity

Critical distinction

PEEK should not be used to 'validate' an established COA by itself. It can provide evidence about concept relevance, content coverage, patient priorities and interpretation needs. Formal content-validity, psychometric and fit-for-purpose requirements remain instrument- and context-specific.

A2. Instrument taxonomy

Instrument family	Primary purpose	Typical examples
Generic HRQoL profile	Broad health status across diseases	SF-36/SF-12, WHOQOL-BREF, PROMIS Global Health / PROMIS-29
Preference-based HRQoL / utility	Generate health-state utilities for economic evaluation	EQ-5D-5L/3L, HUI, AQoL
Cancer HRQoL	Multidimensional cancer-specific quality of life	EORTC QLQ-C30, FACT-G
Cancer symptom / toxicity	Symptoms and symptomatic treatment adverse effects	PRO-CTCAE, MDASI
Domain-specific PRO	Detailed measurement of one symptom or function	FACIT-Fatigue, PROMIS Fatigue, pain measures, sleep measures
Disease-specific PRO	Condition-specific symptoms/impacts	EORTC modules, FACT/FACIT disease modules, disease-specific scales
Function / performance	Patient-reported or directly tested functioning	PROMIS Physical Function; PerFO tests where appropriate
Global anchors	Overall severity/change	Patient Global Impression of Severity/Change (PGIS/PGIC)

A3. Master landscape: common instruments

Tool	Type	Core coverage	Typical strategic role	PEEK relationship
EQ-5D-5L / 3L	Generic preference-based HRQoL	Mobility; self-care; usual activities; pain/discomfort; anxiety/depression + VAS	Very high for HTA/utility	Map PEEK impacts to 5 domains; flag important concepts outside EQ-5D
SF-36 / SF-12	Generic health status	Physical functioning; role limitations; pain; general health; vitality; social functioning; emotional role; mental health	High general HRQoL	Use PEEK to test whether broad domains capture disease-specific burden
PROMIS Global / PROMIS-29	Generic/domain profile	Physical, mental and social health; PROMIS-29 includes function, anxiety, depression, fatigue, sleep, social roles, pain	High, flexible	PEEK can select/prioritise PROMIS domains and identify need for additional disease-specific concepts
WHOQOL-BREF	Generic QoL	Physical; psychological; social relationships; environment + overall QoL/health	Moderate; broad QoL	Useful where PEEK identifies social/environmental context beyond health status
AQoL family	Preference-based HRQoL	Multi-attribute health domains; versions differ	High in economic evaluation, especially Australia	Map PEEK impacts to utility dimensions; assess whether psychosocial impacts favour broader AQoL versions
HUI2/HUI3	Preference-based health status	Multi-attribute functional health systems	HTA/economic evaluation	PEEK tests relevance of attributes and identifies uncaptured treatment burden
EORTC QLQ-C30	Cancer HRQoL	Function, symptoms, global health/QoL + single symptoms	Very high in oncology	Map PEEK oncology concepts to C30 scales; add site/treatment modules if gaps remain
FACT-G	Cancer HRQoL	Physical, social/family, emotional, functional well-being	Very high in oncology	PEEK tests whether patient-important symptoms/impacts require disease/treatment-specific FACIT modules
PRO-CTCAE	Cancer symptomatic toxicity	Patient-reported symptomatic adverse events	Very high for oncology safety/tolerability	Use PEEK to identify which symptomatic AEs matter most; do not treat as broad HRQoL
MDASI	Cancer symptom burden	13 core symptoms + 6 interference items; disease/treatment modules	High for symptom-focused oncology	Strong match where PEEK identifies symptom severity + interference as treatment benefit
FACIT-Fatigue	Domain-specific	Fatigue and impact on daily activities/function	High where fatigue is key	PEEK distinguishes fatigue severity, interference and meaningful improvement
PROMIS Fatigue / Pain / Physical Function etc.	Domain-specific item banks/short forms	Single-domain standardised measurement	High and flexible	PEEK selects relevant domains and tests whether standard domain definition matches patient language
PGIS / PGIC	Global anchor	Overall severity / overall change	Interpretation/anchor role	PEEK can inform wording/context and whether a global anchor reflects the change patients value

A4. Generic HRQoL and utility instruments

EQ-5D

EQ-5D-5L and EQ-5D-3L are generic preference-based measures. Both cover mobility, self-care, usual activities, pain/discomfort and anxiety/depression; the 5L uses five response levels and was designed to improve sensitivity and reduce ceiling effects relative to 3L.

PEEK evidence	EQ-5D coverage	PEEK action
Mobility / independence	Direct	Quantify importance and identify which mobility limitations matter
Self-care	Direct	Clarify independence and assistance needs
Usual activities / work / family role	Broad/partial	Determine whether 'usual activities' is sufficiently specific
Pain	Direct but broad	Identify pain type, severity/interference and whether a targeted pain PRO is needed
Anxiety/depression/emotional burden	Broad	Identify condition-specific emotional impacts not captured
Fatigue, sleep, cognition, treatment burden, social burden	Not directly represented as separate dimensions	Flag potential insensitivity; consider complementary disease/domain-specific PRO
Treatment tolerability / successful treatment	Not directly represented	Use PEEK separately as treatment-benefit context

PEEK use case

A PEEK study may show that EQ-5D is essential for HTA utility estimation but insufficient as the sole patient-centred outcome because the dominant treatment benefit is fatigue interference, cognition, sleep or treatment burden.

SF-36 / SF-12

The SF family provides broad health-status profiles spanning physical, role, pain, vitality, social and mental-health domains. PEEK can be used as a content-relevance check: does the broad profile adequately reflect the specific symptoms and functional impacts patients say treatment should change?

WHOQOL-BREF

WHOQOL-BREF is broader than many health-status measures, covering physical, psychological, social and environmental domains. WHO developed the WHOQOL system cross-culturally, which may make it useful where PEEK identifies social or environmental aspects of quality of life as central to the patient experience.

A5. PROMIS and domain-based measurement

PROMIS is a flexible measurement system rather than one questionnaire. It includes self- and parent-reported measures of physical, mental and social health, with short forms and computer-adaptive testing. The domain architecture makes it particularly compatible with PEEK concept prioritisation.

Common PROMIS domain	What PEEK should establish first	Potential decision
Physical Function	Which activities are impaired and which matter most?	Use generic physical-function measure vs disease-specific/PerFO
Fatigue	Is the key issue intensity, frequency, interference or all three?	Select fatigue form and interpretation strategy
Pain Interference	How does pain affect activity, sleep, roles and enjoyment?	Use interference rather than pain intensity alone where appropriate
Sleep Disturbance / Sleep-related Impairment	Is sleep itself important or important because of daytime function?	Choose sleep domain(s) accordingly
Anxiety / Depression	Are emotional effects disease-driven, treatment-driven or contextual?	Determine relevance to treatment benefit vs supportive context
Ability to Participate in Social Roles	Which family/work/social roles define meaningful functioning?	Potentially valuable when PEEK shows role participation is central
Cognitive Function	Which cognitive problems are experienced and consequential?	Use targeted cognitive PRO where relevant
Global Health	Is a brief overall profile adequate for the programme?	Use as broad profile, not substitute for priority disease-specific concepts

PEEK-PROMIS fit

PEEK can function as the 'domain-selection layer': rather than administering a large battery because domains are available, select the smallest set of PROMIS domains that correspond to patient-important treatment effects and add disease-specific measures only where needed.

A6. Core oncology instrument families

EORTC QLQ-C30

The EORTC QLQ-C30 is a 30-item core cancer HRQoL questionnaire and forms the basis of a modular system with cancer-site and treatment-specific modules.

PEEK concept	QLQ-C30 relationship	Potential PEEK-informed action
Physical/role/social/emotional/cognitive function	Directly represented in functional scales	Test whether the specific activities/roles patients value are adequately represented
Fatigue, pain, nausea/vomiting	Core symptom scales	Compare PEEK priority and interference findings with scale coverage
Dyspnoea, insomnia, appetite loss, constipation, diarrhoea	Single symptom items	If a symptom is a primary treatment-benefit concept, assess whether single-item coverage is sufficient
Financial impact	Included	PEEK can add depth on financial burden and access consequences
Disease-site symptoms	Often outside core	Select appropriate EORTC module or another disease-specific instrument
Treatment burden / tolerability	Partially captured through symptoms	Consider PRO-CTCAE or additional tolerability assessment

FACT-G / FACIT system

FACT-G contains 27 items across physical, social/family, emotional and functional well-being. FACIT extends this core into disease-, treatment- and symptom-specific measures. The system includes a large searchable library of validated measures.

PEEK finding	FACT/FACIT implication
Broad multidimensional cancer impact	FACT-G may provide suitable general cancer HRQoL backbone
One symptom dominates treatment benefit	Consider targeted FACIT measure, e.g. FACIT-Fatigue
Condition-specific concerns dominate	Review disease-specific FACT/FACIT module
Cognitive impact is important	Consider FACT-Cog or other fit-for-purpose cognitive PRO
PEEK identifies concepts absent from chosen module	Do not assume FACT family coverage; conduct instrument gap review

A7. Symptomatic adverse events and symptom burden

PRO-CTCAE

NCI's PRO-CTCAE was developed specifically to capture symptomatic adverse events by patient self-report in cancer clinical trials. It is available in more than 60 validated languages.

PEEK contribution	How it can inform PRO-CTCAE strategy
Which side effects patients find most burdensome	Prioritise symptomatic AE items relevant to treatment and population
What makes a side effect unacceptable	Add tolerability/benefit-burden context to toxicity frequencies
How symptoms affect function and life	Recognise that PRO-CTCAE toxicity reporting does not replace HRQoL/function measurement
Treatment expectations and trade-offs	Interpret why the same toxicity may have different meaning depending on perceived benefit

MD Anderson Symptom Inventory (MDASI)

The core MDASI measures 13 cancer-related symptoms and six interference domains, with disease- and treatment-specific modules. It is especially relevant when PEEK shows that symptom burden and interference with daily living are central treatment-benefit concepts.

MDASI construct	PEEK relationship
Symptom severity	PEEK identifies which symptoms are priority and why
Activity/walking/work interference	PEEK adds detail about which activities and roles define meaningful function
Mood/relations/enjoyment interference	PEEK contextualises psychosocial impact
Disease/treatment-specific modules	PEEK can test whether module additions match the target population's current experience

A8. Common domain-specific measures

Domain	Examples	Typical construct	PEEK relationship
Fatigue	FACIT-Fatigue; PROMIS Fatigue; Brief Fatigue Inventory	Severity + interference/function	PEEK determines whether fatigue is a priority, how patients describe it, and what change matters
Pain	Brief Pain Inventory; PROMIS Pain Interference/Intensity; disease-specific pain scales	Intensity + interference	PEEK distinguishes pain type, impact and priority relative to other symptoms
Physical function	PROMIS Physical Function; disease-specific function scales; selected PerfOs	Capability / activity / participation	PEEK identifies valued activities and whether self-report or performance is more appropriate
Sleep	PROMIS Sleep Disturbance / Sleep-related Impairment; Insomnia Severity Index	Sleep quality/impairment	PEEK clarifies whether sleep is a treatment target or downstream impact
Anxiety	GAD-7; PROMIS Anxiety; HADS-A	Anxiety symptoms	PEEK tests relevance to disease/treatment and avoids overinterpreting contextual distress as direct treatment effect
Depression/emotional distress	PHQ-9; PROMIS Depression; HADS-D	Depressive symptoms / distress	PEEK provides disease context and patient language
Cognition	PROMIS Cognitive Function; FACT-Cog; disease-specific cognitive tools	Perceived cognitive function	PEEK identifies cognitive concepts and functional consequences
Social/role participation	PROMIS Ability to Participate in Social Roles; WPAI for work/productivity	Participation / productivity	PEEK identifies which roles matter and whether employment is applicable
Global severity/change	PGIS / PGIC	Overall severity or change	PEEK can help establish whether a global judgement is meaningful and what patients consider improvement
Treatment satisfaction / burden	TSQM and treatment-burden measures where appropriate	Satisfaction, convenience, burden	PEEK can identify the dimensions of treatment experience worth measuring

Selection rule

Do not select a domain-specific instrument simply because PEEK mentions the symptom. Ask whether the concept is important, relevant to the expected treatment effect, distinct from broader HRQoL, and likely to change within the trial timeframe.

A9. Disease-specific and modular instruments

There are hundreds of disease-specific PROs. The practical role of PEEK is not to reproduce that catalogue, but to provide a systematic filter for deciding when a disease-specific measure is necessary.

Situation identified by PEEK	Instrument strategy
Generic HRQoL domains capture the main patient-important effects	Generic profile/utility + limited targeted measures may be sufficient
Core cancer measure misses site-specific symptoms	Add an EORTC disease module, FACT/FACIT disease module, MDASI module or other validated disease-specific measure
A rare-disease concept has no adequate established measure	Undertake targeted instrument review; consider adaptation/new COA development with appropriate evidence
Patient-important concept is covered but wording/context differs materially	Assess content validity and cultural/linguistic relevance before assuming fit
Caregiver-observed behaviour is central and self-report is not feasible	Consider ObsRO rather than forcing a PRO
Function is best demonstrated rather than perceived	Consider PerfO alongside/instead of self-reported function

Examples of modular families

Family	Examples of extensions	PEEK role
EORTC	Cancer-site, treatment and survivorship modules appended to QLQ-C30	Determine which module concepts are actually important in target population
FACT/FACIT	Cancer-site, chronic illness, symptom and treatment-specific measures	Choose core + targeted subscale based on PEEK concept hierarchy
MDASI	Brain tumour, breast, lung, ovarian, multiple myeloma, AML/MDS, CAR-T and other modules	Check disease/treatment-specific symptom relevance and interference
PROMIS	Domain short forms/CATs across physical, mental and social health	Build a tailored domain battery from PEEK priorities

A10. PEEK instrument mapping worksheet

PEEK patient-important concept	Patient language / evidence	Importance	Expected treatment relevance	Candidate instrument/domain	Coverage	Gap / action
[e.g. fatigue prevents normal family life]	[qual + quant evidence]	High	High	FACIT-Fatigue / PROMIS Fatigue	Partial/Full	Check interference and meaningful-change evidence

Instrument selection questions

- Does the instrument measure the same concept patients describe, or merely a related concept?
- Is the concept important enough to justify patient burden and multiplicity in the trial?
- Is the recall period appropriate for the symptom/treatment pattern?
- Is there evidence of content validity in a population sufficiently similar to the intended trial population?
- Are measurement properties adequate for the intended endpoint role?
- Is a validated translation available in every required language?
- Does the instrument support meaningful within-patient change interpretation?
- Will the measure satisfy downstream HTA needs, or is a preference-based HRQoL instrument also required?
- Could one instrument cover multiple priority concepts without sacrificing sensitivity?
- Does the proposed battery omit any high-priority PEEK concept?

A11. Suggested 'minimum sufficient' measurement portfolios

These are architecture examples, not fixed recommendations. Final selection must be indication-, treatment-, population- and endpoint-specific.

Development situation	Illustrative portfolio	How PEEK determines the final battery
Global oncology pivotal trial	Cancer HRQoL backbone (EORTC QLQ-C30 or FACT-G family) + targeted symptom/functional COAs + PRO-CTCAE + generic preference-based HRQoL where HTA requires	Prioritise treatment-benefit concepts; remove low-value duplication; add disease-specific module only for uncovered high-priority concepts
Non-oncology chronic disease	Generic/domain framework (often PROMIS or disease-specific PRO) + targeted symptom/function measure + EQ-5D or other utility measure	PEEK determines which symptoms/function domains are primary and which are contextual
Rare disease	Disease-specific COA if fit-for-purpose + targeted domain measures + generic HRQoL/utility where feasible	PEEK may be especially important for concept elicitation and identifying missing measures
Treatment with substantial symptomatic toxicity	Efficacy-related PRO(s) + PRO-CTCAE or appropriate toxicity measure + HRQoL/utility	PEEK identifies tolerability thresholds and benefit-burden trade-offs
HTA-intensive programme	Sensitive disease-specific PRO(s) + generic preference-based HRQoL + relevant function/symptom measures	PEEK connects sensitive clinical benefit with patient value and explains limitations of generic utility measures

Design principle

The goal is not the largest questionnaire battery. It is the smallest battery that adequately captures the patient-important treatment effects, supports the intended endpoint strategy, and generates the regulatory and HTA evidence needed across priority markets.

A12. Key instrument sources and access considerations

Instrument use, licensing, translation and electronic implementation requirements vary. Sponsors should verify current terms with the instrument owner/distributor before use.

EuroQol Group. EQ-5D-5L.

<https://euroqol.org/information-and-support/euroqol-instruments/eq-5d-5l/>

EuroQol Group. EQ-5D-3L.

<https://euroqol.org/information-and-support/euroqol-instruments/eq-5d-3l/>

EORTC Quality of Life Group. Questionnaires and EORTC QLQ-C30.

<https://qol.eortc.org/questionnaires/>

FACIT.org. FACT-G.

<https://www.facit.org/measures/fact-g>

FACIT.org. FACIT Measures searchable library.

<https://www.facit.org/facit-measures-searchable-library>

FACIT.org. FACIT-Fatigue.

<https://www.facit.org/measures/facit-fatigue>

HealthMeasures / PROMIS.

<https://www.healthmeasures.net/>

National Cancer Institute. PRO-CTCAE.

<https://healthcaredelivery.cancer.gov/pro-ctcae/>

MD Anderson Cancer Center. MD Anderson Symptom Inventory.

<https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools/md-anderson-symptom-inventory.html>

World Health Organization. WHOQOL.

<https://www.who.int/tools/whoqol>

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