PATIENT FOCUSED
MEDICINES DEVELOPMENT

Highlighting Recent Trends in the Fast-Evolving Patient Engagement & Patient Experience Data Landscape

Last updated: Autumn 2021

Highlights from this paper

- In recent years, patient engagement has become more prevalent in medicines development
- The development and use of patient experience data is one way to further engage patients
- Regulators and HTA bodies are increasingly embracing patient experience data to help with decision-making
- Current regulatory and HTA guidance and approaches are helping to set expectations and drive evidence generation
- The requirements critical in providing patient experience data (for example, the tools, users, purpose, timing, and impact) still need to be defined
- This clarity and definition will help to broaden the development and use of patient experience data and increases the impact that PXD will have on healthcare decision-making
- All stakeholders need to adapt their processes to maximize the utility of patient experience data and share the insights generated by patient engagement

Overview

Patient engagement / patient involvement (referred to as PE in this document) has become a central feature of medicines development over the last decade. Industry, authorities, regulators and health technology assessment (HTA) bodies are increasingly embedding patient and care partner perspectives in their work.

As many organizations and stakeholder groups progress to address the gaps that still exist with engaging patients, it is important that the healthcare community as a whole is also aware of the evolving regulatory and HTA landscape. Regulatory and HTA stakeholders are clearly signalling that a deeper understanding of patients' needs and perspectives will help their decision-making.

The evidence needs of regulatory and HTA bodies have driven the evolution of medical studies and particularly the package of evidence generated by pivotal clinical studies. An increased focus on patient perspectives and experience will inevitably lead to a greater understanding of the factors that will identify future assets that should be prioritized for further development. Although the regulators and HTA bodies are not the only stakeholders that are embracing patient engagement and patient experience data (referred to as PED or PXD in this document), their focus on this area will drive a more patient-centric approach to health technology developments.

This paper provides a snapshot of current efforts and approaches that are helping to clarify regulatory and HTA expectations of patient engagement and patient experience data across authorities in North America, Europe and Asia.

While not exhaustive, this overview highlights the clear trend towards more systematic and comprehensive use of patient engagement and patient experience data by authorities in these regions. Taken together, **they illustrate an important shift in the development and assessment of new medical products**. This paper aims to inform and empower all stakeholders involved with patient engagement and patient experience data to better understand its value and increasing consideration across the healthcare system.

Part of this dialogue includes understanding and clarifying the definition of patient engagement and patient experience data. In addition to understanding the patient perspective, patient engagement can also include qualitative and quantitative studies used to develop, describe and communicate these perspectives. A clear example of a helpful definition of PXD is that featured in the US Food & Drug Administration (FDA) guidance on the 21st Century Cures Act of 2016[1] (see table). The FDA is required by legislation to make public the PED used as part of their decision making. This table is included in approved packages to fulfil this requirement.

It describes PXD as "data that is collected by any person with the intention to provide information about patients' experiences with a disease or condition, including the impact of the disease or condition or related therapy or clinical investigation, and patient preferences with respect to treatment of the disease or condition."[2]

Patient Experience Data Relevant to this Application (check all that apply)

1	☐	The patient experience data that were submitted as part of the application include:		Section of review where discussed, if applicable
2		☐	Clinical outcome assessment (COA) data, such as	
3			☐ Patient reported outcome (PRO)	
4			☐ Observer reported outcome (ObsRO)	
5			☐ Clinician reported outcome (ClinRO)	
6			☐ Performance outcome (PerfO)	
7		☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	
8		☐	Patient-focused drug development or other stakeholder meeting summary reports	
9		☐	Observational survey studies designed to capture patient experience data	
10		☐	Natural history studies	
11		☐	Patient preference studies (e.g., submitted studies or scientific publications)	
12		☐	Other: (Please specify):	
13	☐	Patient experience data that were not submitted in the application, but were considered in this review:		
14		☐	Input informed from participation in meetings with patient stakeholders	
15		☐	Patient-focused drug development or other stakeholder meeting summary reports	
16		☐	Observational survey studies designed to capture patient experience data	
17		☐	Other: (Please specify):	
18	☐	Patient experience data was not submitted as part of this application.		

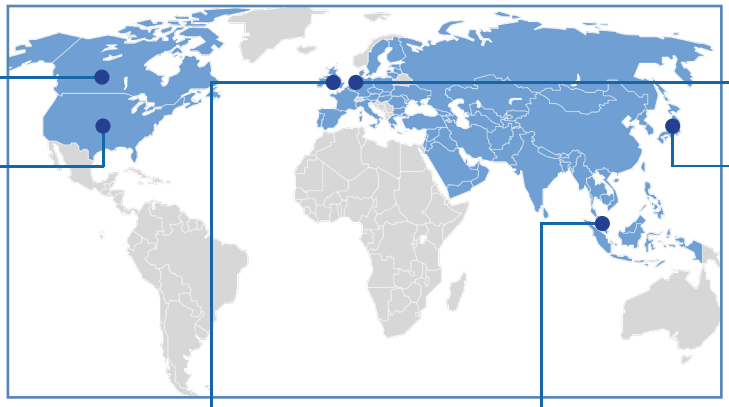
On a global level, authorities are also conducting consultation exercises to understand the needs of stakeholders (see map). Along with providing guidance to industry, academia, healthcare providers and others on how to generate high-quality data, the growing number of statements and guidance documents has highlighted variations in how key terms are defined and thus the need for greater alignment and harmonization.

Global alignment for consideration of PE & PED

"When people participate in the reviews, it adds to the **transparency, accountability, and credibility** of the recommendations made" - **CADTH** (2020)

"A **globally harmonized approach** to inclusion of the patient's perspective in a way that is methodologically sound and sustainable for both regulated industry and regulatory authorities" - **ICH** (2020)

"Revise PE methodology … to reflect EMA's evolving approach to **patient data** and enhanced patient involvement." - **EMA** (2020)



"Advancing use of systematic approaches to collecting and utilizing robust and meaningful patient and caregiver input to **more consistently inform** regulatory decision-making" - **FDA** (2018)

"We want to see more **patient participation** in our drug review and pharmacovigilance activities" - **PDMA** (2020)

"When new applications for selected medicines are received, the applicant company will be asked for **evidence on the patient involvement activities** they undertook when developing their product." - **MHRA** (2021)

"Accelerating **systematic and meaningful** patient **involvement** in health systems is one of 6 strategic areas of focus in the Asia-Pacific" - **CoRE** (2014)

The **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)** responded to this need by publishing a reflection paper on Patient-Focused Drug Development (PFDD) and "identified key areas where incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making". The paper was open for consultation from November 2020 until March 2021.

The substantial feedback received during this consultation period highlights the momentum behind patient engagement. This prompted the ICH to step up its efforts in this area and to engage appropriately with non-ICH stakeholders throughout the process. The updated, and final, version of the reflection paper (endorsed by the ICH Assembly in June 2021) reflects the comments accepted by ICH. The feedback included tangible proposals for the development of guidance and was considered to fall within the scope of ICH activities. This will be considered when guideline work commences, as will be the numerous references to existing tools and guidance.[3]

The Future: Collaboration and Harmonization

While the use of patient engagement practices has been growing for the past two decades, there remains many different engagement models with various levels of involvement. The use of patient experience data is relatively new in comparison, with many stakeholders still experimenting with different approaches. The increased focus on this area by regulators and HTA bodies reflects a wider trend towards a growing demand for high-quality insights from patients and patient advocates.

By hearing directly from patients and collecting appropriate evidence on the patient experience (i.e. PXD), all stakeholders can identify areas of future health care, management and treatment that would be truly transformative. A collaborative, empowering, inclusive approach to PE will help to streamline, harmonize and broaden the development and use of PXD which will ultimately benefit the patient and their family.

Emerging Trends in the Fast-Evolving Patient Engagement & Patient Experience Data Landscape

Interest in Patient Engagement & Patient Experience Data Requires Clarity & Guidance

Over the last decade, patient engagement (PE) in medicines development has become increasingly normalized. In particular, one aspect of PE that is playing a greater role in healthcare decision-making is the inclusion of patient experience data (PED, also referred to as PXD throughout this document[4]) **in the regulatory process.** According to guidance published by the US regulator, the Food & Drug Administration (FDA), on the 21st Century Cures Act of 2016, patient experience data is defined as "data that is collected by any person with the intention to provide information about patients' experiences with a disease or condition, including the impact of the disease or condition or related therapy or clinical investigation, and patient preferences with respect to treatment of the disease or condition."[5]

Regulatory agencies (such as the FDA, or the European Medicines Agency (EMA)) and Health Technology Assessment (HTA) bodies[6] are progressing to incorporate the voice of the patient and patients' lived experience through the use of PXD more systematically in their review and approval processes for new product submissions and value assessments. In 2018[7], 70.8% of drug application dossiers approved by the FDA Centre for Drug Evaluation & Research (CDER) reported using PED in the drug review. In 2019, PED was reported as relevant for 81.3% of drugs approved in 2019.[8]

In the recent June 2021 ERG Report, *Assessment of the Use of PED in Regulatory Decision-Making*[9], many FDA interviewees expressed an interest in receiving, reviewing, and using more patient experience data (as long as the patient experience data are scientifically sound)".[10] However, many stakeholders have stated that "they do not know how FDA uses patient experience data in regulatory decision-making" [4,11] and have expressed a need for clarity and alignment in the collection and use of PXD [4,12]. As part of the broader discussion of including patient perspectives in key healthcare decisions, healthcare stakeholders are requesting additional information and guidance on patient engagement activities (sometimes referred to as patient and public involvement (PPI)) that are increasingly more relevant for regulatory and HTA submissions.

Global Regulatory Agencies Respond with Increased Consideration for PE & PXD

With the recognized need for increased clarity and structure to the PE & PXD landscape, **the last 12-24 months have been crucial.** There has been a strong global movement amongst major stakeholders announcing new PE & PXD guidances, open consultations and documentation highlighting their priority focus on PE & PXD.

The ERG report[5], also assessed the use of PED by the FDA and found that PED usually takes the form of considering PROs and COAs for primary endpoints in the risk-benefit analysis, and other patient experience data is used for background and context for the review. Many FDA staff, applicants and other stakeholders said they look forward to the development of more fit-for-purpose tools to better utilize PED. This increasing desire to further explore patient engagement and consider PED is echoed by other regulatory agencies, including in the United Kingdom and the United States of America as illustrated below.

June 2020

Regulators in North America have also provided more direction recently. **The FDA (USA) Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER)** offered detailed guidance for industry, staff and other stakeholders on collecting comprehensive and representative input (June 2020) from patients. This builds on the implementation of the Cures Act Section 3001 requirement through the inclusion of a table ("PED table") that indexes the types of PED considered by the FDA.[14]

January 2021

Similarly, the **European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP)**, which provides recommendations on the approval and use of medicines in Europe, suggests reaching out to patient organizations when medicines are in active development to fully appreciate patients' experience and concerns about their conditions and understand aspects that are important for patients. The pilot phase for CHMP's early contact with patient / consumer organisations was initiated in January 2021 and includes a template for contacting patient organizations.

March 2021

The MHRA announcement followed the conclusion of the open consultation of the **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)** Reflection Paper published in March 2021. This publication sets out key areas where the incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development, and inform regulatory decision-making. The new ICH guidelines are proposed, "to provide a globally harmonized approach to inclusion of the patient's perspective in a way that is methodologically sound and sustainable for both the regulated industry and regulatory authorities"[13].

May 2021

In May 2021, the **Medicines and Healthcare Products Regulatory Agency (MHRA, UK)** announced the launch of a one-month consultation on a draft "Patient Involvement Strategy". The MHRA wants to adopt "a more systematic approach to listening to and meaningfully involving patients and the public". Specifically, "when new applications for selected medicines are received, the applicant company will be asked for evidence on the patient involvement activities they undertook when developing their product."

A recent example involving the pharmaceutical company Pfizer and the submission of an osteoarthritis patient preference study (PPS) (risk/benefit) with the Biologics License Application (BLA) of Tanezumab (a monoclonal antibody against nerve growth factor as a treatment for pain) illustrates the increasing communication and growing transparency of CDER.[15]

The FDA was critical of the PPS study in its presentation to the advisory committee: "[The] study…followed good research practices in design and conduct", but the FDA identified "methodological issues with the patient preference information submitted that render it uninformative for regulatory decision making"[16]. Tanezumab was not approved by the FDA, however, FDA and expert presentations [17, 18] delivered at the advisory committee represent a major step in clarifying the Agency's expectations for PPS. The **feedback received from the FDA** has been summarized in the following checklist to help inform PPS for regulatory decision-making.

Patient Preference Studies for Regulatory Decision Making: Proposed Checklist Based on Feedback from Regulators

Questions each patient preference study should be able to address

1. Was patient-centered background research used to identify relevant attributes and potential subgroups? Did the decision maker have direct and early input into the design of the study?
2. Can sponsor demonstrate that attributes reflect what is important to patients, can be tied to clinical study endpoints, reflect what is important to the decision, and are described in a way that is acceptable to the decision maker?
3. Can sponsor demonstrate that attribute levels are understood by patients, encompass the range of clinical study outcomes, are described in a way that is acceptable to the decision maker, and that risk levels described using multi-format approach (verbal, numerical, graphical)?
4. Can the sponsor demonstrate that attributes are complete and that all relevant attributes are addressed in a single framework?
5. Can sponsor demonstrate that the survey instrument is understandable to patients and reliably elicits PPI?
6. Did sponsor include a scope test or other internal validity test in the preference elicitation to demonstrate that patients are paying attention to the numeric values and not just relative size (e.g., high, medium, low) of risk levels?
7. Did sponsor include other validity tests such as dominated pair, monotonicity, or repeated questions?
8. Did the question format include a real-world reference condition and opt-out or did decision maker agree that a real-world reference condition is not necessary?
9. Does the sample include patients with a physician-confirmed diagnosis and include sufficient diversity to analyze preference heterogeneity and identify preference subgroups or did the decision maker agree to an alternative approach to determining eligibility? Does the sample include patients with experience with the harm of concern (if possible)?
10. Does the analysis follow good research practices, reflect the decision maker's needs, and support results that fulfill the research purpose including possible application of preference data to clinical data?

In the Asia-Pacific region, similar trends are emerging. The **Centre of Regulatory Excellence (CoRE)** established to support the strengthening of health product regulatory systems clearly stated its prioritization of this topic in announcing, "Accelerating systematic and meaningful patient involvement in health systems is one of 6 strategic areas of focus in Asia-Pacific". Further, the **Pharmaceuticals & Medical Device Agency (PMDA, Japan)** also wants to "see more patient participation in [their] drug review and pharmacovigilance activities" and initiated a Patient Centricity Working Group in 2019 to support this objective.

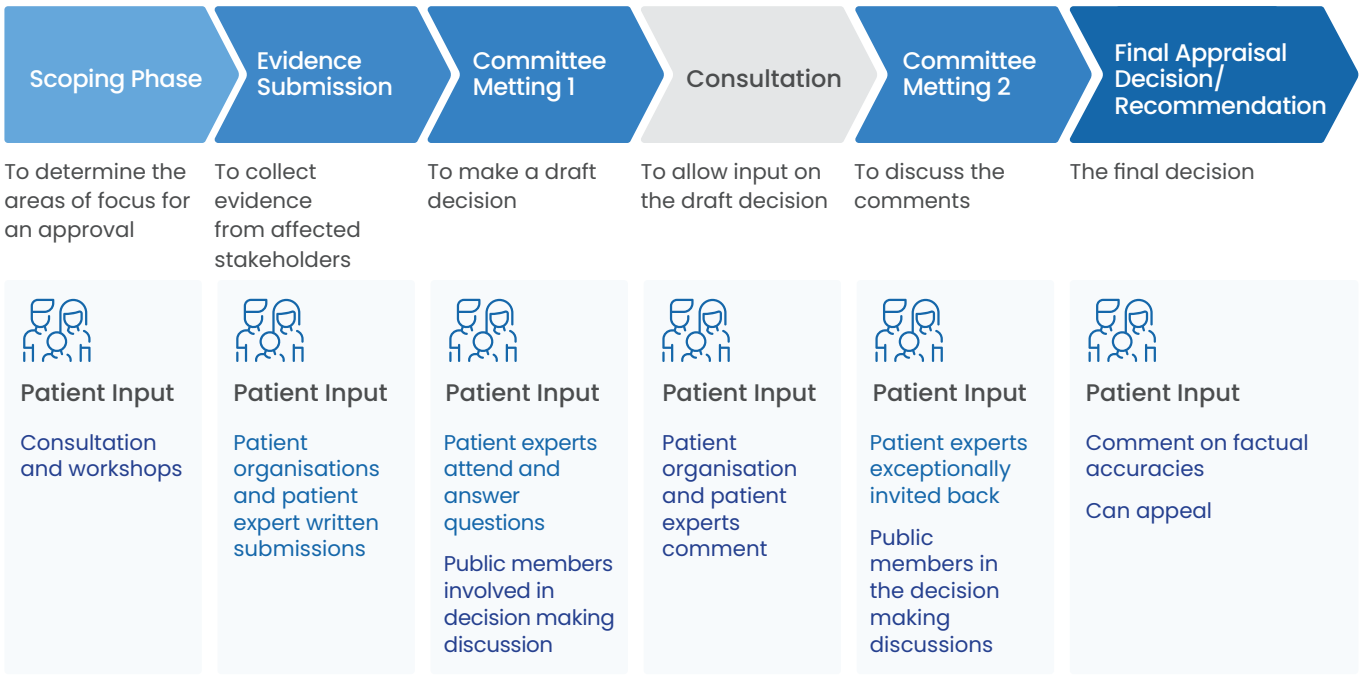
In the medical device sector, the **FDA Centre for Devices and Radiological Health (CDRH)** has issued guidance documents that emphasize the importance of including patient reported outcome measures[19] and patient preference studies[20], as early as 2009 and 2016 respectively. These are considered as one component of the scientific evidence that informs the decision in the application process. At the June 2021 Patient Engagement Open Forum[21], the following list of **lessons learned from PRO and PPI reviews by the CDRH** was shared:

✓	✓	✓	✓	✓	✓	✓	✓
Be clear about the research question (PPI) and the concept of interest (PRO)	Consult FDA early and often • Developing, modifying, or using PROs in clinical investigations • Designing PPI studies for a regulatory contex	Involve patients in the development process	Develop a thoughtful plan for recruiting patients to align with indications for use • Ensuring heterogeneity and generalizability of the study sample	Assure patient comprehension of items and response choices on the PRO and PPI surveys	Ensure PPI attributes and concepts of PROs align with outcomes of interest in clinical studies	Pre-specify analysis plan and potential subgroup analyses	Provide sufficient information for FDA to assess the quality of the study and the evidence

Relevance of PE & PXD also Recognized by HTA Bodies

In addition to regulatory agencies, while there is still some variability[22], patient engagement (PE) has also become more routine for HTA practices internationally[23]. The diagram illustrates where patients may be involved in many HTA processes.[24]

A Generalized Process for HTA and Opportunities for Patient Engagement



HTA's interest in understanding patients' experiences and preferences is also increasing.[25] For instance, there is now a dedicated Public Involvement Advisor position at the **Scottish Health Technologies Group (SHTG)** to provide further support to patient organizations and encourage increased participation in SHTG processes.[26]

In Canada, in December 2020, the **Canadian Agency for Drugs and Technologies in Health (CADTH)** published the Guidance for Providing Patient Input. This includes a Patient Input Template and explanation of how patient insights help CADTH clinical and economic teams interpret the evidence.

Given the increasing input provided by patients, it is important that they have a clear and informed understanding of the medicine that is under review in order to provide the most appropriate and beneficial input. For this reason, the **HTAi** developed a **Summary of Information for Patients (SIP)** to provide relevant plain language background information about the medicine under assessment. It is intended to help patient representatives "formulate a response to the HTA body, and comment on where the medicine could add the most value to the patient community".[14] This is currently being piloted in multiple HTA bodies globally.

In order to increase transparency, in November 2020, the **National Institute for Clinical Excellence (NICE, UK)** outlined where and which patients are involved in their HTA processes, with examples of impact. The **National Institute of Health Research (NIHR, UK)** Centre for Engagement and Dissemination is responsible for guidance (March 2020) on considering who to involve in research when seeking to capture patient experiences.

With an innovative approach, the **Health Technology Assessment International (HTAi) Interest Group for Patient and Citizen Involvement in HTA (PCIG)** has recently proposed the potential for a patient insights research platform (PIRP) for collecting and analysing patient-based communication content from social media to inform HTA bodies on patient needs and experiences.

This multi-stakeholder perspective is also being reflected by the efforts of the **Centre of Regulatory Excellence (CoRE)** in Asia-Pacific as they plan an upcoming roundtable in the Fall of 2021 to discuss, among others issues, how patient experience data can link different parts of the health system beyond HTA and how to effectively utilize PXD. In addition, a series of virtual workshops targeted primarily to health product regulators, health technology assessment bodies, selected patient representatives, and any other stakeholders who routinely use patient generated data are being planned for 2022 to raise awareness on the impact of meaningful patient involvement in clinical research, regulation, reimbursement on health, economic and social outcomes.

> In March 2021, it was announced that a tool kit co-developed by **MHRA, NICE** and **Scottish Medicines Consortium (SMC)** was available "to provide opportunities throughout the [Innovative Licensing and Access Pathway] ILAP for companies to consider the patient's experience and voice in a meaningful way in how they develop their innovative products. The patient engagement tool will consider the patient's voice and experience ….give patients the opportunity to influence the development of products that will benefit them."[27] This approach exemplifies the collaborative efforts being taken by some stakeholders to ensure alignment and consistency in patient engagement.

Collaborative, Inclusive Efforts Help to Support PE in Streamlining & Harmonizing the Use and Development of PXD to Boarder Applications

These initiatives highlight the growing prioritization, and multi-stakeholder approaches amongst regulators, health technology assessment agencies, and patient organizations, to PE & PXD. Significant progress in patient engagement and in the development and use of PXD have been demonstrated and major global stakeholders are becoming increasingly engaged.

This is an exciting time as patient engagement momentum continues. Additional guidances, documents and calls for consultation help to further define the requirements critical in providing patient experience data, the instruments and methodologies that are used to capture those experiences, how the data will be used and by whom. This will also clarify the impact that PXD will have on healthcare decision-making moving beyond the sole application to regulatory and HTA decision-making.

All stakeholders need to adapt their processes to maximize the utility of patient experience data and share the insights generated by patient engagement. This includes:

1. Increasing capacity within regulators and HTA bodies for systematic patient engagement
2. Building shared learnings on the use and utility of patient experience data for both regulatory and HTA decision-making
3. Sharing insights gained from patient engagements to avoid duplication
4. Being receptive to considering patient experience data from a wide variety of sources (to avoid the danger of having each stakeholder demand specific data that is useful only to them)
5. Building capacity within the patient community to design, generate and participate in patient engagement practices and patient experience data projects

To ensure effective patient engagement and participation, appropriately resourced capacity building to support the patient community and other stakeholders will also need to be considered and integrated. Prioritizing where and when this capacity building occurs is important. Increasing awareness and understanding of PXD, with the use of feedback loops to further inform the patient community on the use and impact of the data, will help to strengthen and empower the patient community. This will enable the patient community to further contribute and participate in the design, collection, generation and analysis of PXD.

> A collaborative, empowering, inclusive approach to patient engagement will help to streamline, harmonize and broaden the development and use of PXD for other healthcare decisions, with ultimate benefit to the patient, their family and society at large.

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[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input

[3] https://admin.ich.org/sites/default/files/2021-06/ICH_ReflectionPaper_PFDD_OutcomeOfPublicConsutlation_2021_0527.pdf

[4] Patient experience data has previously been referred to as PED. With the growing acceptance that patient experience data is part of patient engagement (PE), there is often confusion between PE and PED. For this reason, patient experience data will be referred to as both PED and PXD in this document.

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[6] HTA bodies conduct "evaluations of clinical effectiveness and/or cost-effectiveness, and may include the ethical, legal, and social implications of health technologies on patient health and the health care system." https://www.cadth.ca/about-health-technology-assessment-service

[7] Ther Innov Regul Sci 2020 May;54(3):709-716. doi: 10.1007/s43441-019-00106-1. Epub 2020 Jan 6. FDA Reported Use of Patient Experience Data in 2018 Drug Approvals Cameron M Kieffer, Alexis Reisin Miller, Benjamin Chacko, Andrew S Robertson

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[27] https://www.gov.uk/guidance/the-target-development-profile-toolkit#enhanced-patient-engagement