

# Patient engagement with the European Medicines Agency

## Position Paper

September 2020

**Aim:** This position paper aims to emphasize the importance of obtaining patient input in the development of medicines and of reflecting this input in the regulatory and HTA decision making process. EuropaBio recognises the huge benefits that patient engagement in drug development can bring to patients' care and quality of life, as well as to the entire healthcare system. Among other aspects, patient involvement helps to improve protocol research questions, understand appropriate comparators, and identify patient relevant endpoints. The efforts made by Regulators and HTA bodies in Europe to consult with patients when discussing medicinal products are much appreciated and fully supported. EuropaBio would like to advocate that patient engagement and the patient's voice is also more consistently and transparently reflected in regulatory/HTA assessment and decision-making processes which should be supported by appropriate guidance. EuropaBio is sharing this position paper with the European Medicines Agency (EMA) to advocate a European guidance framework on patient engagement that allows sufficient flexibility but enables alignment on cornerstone requirements with key stakeholders and draft FDA guidance, as well as considering the outcome of initiatives, such as the IMI PREFER project.

---

## Background

There is a clear desire from different stakeholders for more guidance on expectations of Agencies regarding patient engagement during drug development. It is critical to achieve alignment on this topic and dialogue with different Health Authorities is needed. Moreover, EuropaBio notes that while patient engagement activities are ongoing at FDA and EMA, the extent and nature of these initiatives are currently not well aligned. Inclusion of Patient Focused Drug Development (PFDD) in the 21<sup>st</sup> Century Cures Act as well as PDUFA VI legislation in the US means that significant activity is now being driven by the FDA and work on four PFDD draft guidance documents is ongoing.<sup>1</sup> These outline systematic approaches on how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision making. All four guidance documents are expected to be available by 2021 and will cover:

- 1) **Guidance 1: Collecting Comprehensive and Representative Input**  
**Public Workshop:** [Patient-Focused Drug Development: Guidance 1 – Collecting Comprehensive and Representative Input](#)

---

<sup>1</sup> <<https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development>>



**Draft Guideline:** [Patient-Focused Drug Development: Collecting Comprehensive and Representative Input. Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders.](#)

- 2) **Guidance 2: Methods to Identify What is Important to Patients Public Workshop:** [Patient-Focused Drug Development Guidance: Methods to Identify What is Important to Patients and Select, Develop or Modify Fit-for-Purpose Clinical Outcome Assessments](#)

**Draft Guideline:** [Patient-Focused Drug Development: Methods to Identify What Is Important to Patients Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders](#)

- 3) **Guidance 3: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Public Workshop:** [Patient-Focused Drug Development Guidance: Methods to Identify What is Important to Patients and Select, Develop or Modify Fit-for-Purpose Clinical Outcome Assessments](#)

- 4) **Guidance 4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making Public Workshop:** [Patient-Focused Drug Development: Guidance 4 – Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making](#)

In Europe, the current regulations guarantee patient representation in several EMA scientific committees (Pharmacovigilance Risk Assessment Committee, Paediatric Committee, Committee for Orphan Medicinal Products and Committee for Advanced Therapies). In addition, patients are members of the Patients' and Consumers' Working Party and are represented on the EMA management board. EMA has also published some guidance documents related to the collection of patient-reported input during medicines development:

- [Reflection Paper on the Regulatory Guidance for the Use of Health-Related Quality of Life \(HRQL\) Measures in the Evaluation of Medicinal Products.](#)
- Appendix 2 to the EMA guideline on the [Evaluation of Anticancer Medicinal Products in Man - Use of Patient-Reported Outcome \(PRO\) Measures in Oncology Studies](#)
- [Revised framework on the interaction of the Agency with patients and consumers and their organisations](#)

The recently published '[Regulatory Science to 2025](#)' strategy and corresponding stakeholder [workshop](#) in November 2019 resulted in further recognition by EMA on the importance of ensuring the patient voice is systematically incorporated throughout drug development, associated evidence generation and decision-making and the need to develop new EMA guidance on patient data collection. EMA plans to revise the existing engagement methodology and review and update EMA's existing '*Revised framework for interaction with patients and patient organisations*' to reflect EMA's evolving approach to patient data and enhanced patient involvement in EMA scientific committees. Additionally, EMA intends to coordinate the approach to patient reported outcomes (PROs) and promote use of core health-related quality-of-life PROs. Additional methodologies to collect and use patient data for benefit-risk assessment will be explored.



EMA welcomed the multi-stakeholder request to foster global alignment on the scientific methodology to gather patient contribution to drug development. This is a welcome inclusion and gives stakeholders an opportunity to work with the EMA to develop a carefully considered roadmap for the future.

Recently, a Reflection Paper was released by the FDA and the European Commission with a **proposal for an ICH Guideline to Advance Patient Focused Drug Development**. The reflection paper identifies a series of drug development and regulatory decision-relevant questions at different stages of the drug life cycle and proposes potential guideline work for ICH to outline methods and standards to be applied when addressing these questions concerning patient involvement during drug development. It suggests the development of two new ICH guidelines. EuropaBio advocates that all the work done to-date in this area by EMA and FDA should be considered in these ICH guidelines:

1. **New ICH guideline** addressing what to measure in a clinical trial, including refining the set (list) of important impacts and concepts from patients, to select or develop fit for purpose clinical outcome assessments (COAs) that can demonstrate change, defining endpoints, and meaningful change. The scope of this guideline would include:
  - Qualitative methods to identify disease/treatment impacts important to patients that would be candidate concepts for measurement with patient reported outcome (PRO) measures or other types of COAs;
  - Main document could focus on considerations for PROs;
  - Annexes could be included for other COA types such as observer-reported (ObsRO), clinician-reported (ClinRO), performance-based measures (PerfO), etc.
2. **New ICH guideline** addressing methods for elicitation or collection of assessments of the relative desirability or acceptability to patients of specified alternative outcomes or other specified alternative attributes.

EuropaBio welcomes the suggestion by the European Commission and FDA to develop international guidance on PFDD. It would be helpful for EMA to engage with FDA and discuss the alignment of activities in this area sooner than the proposed starting point for an ICH guideline in September 2021.

## Ongoing Patient Engagement Initiatives

- **IMI PREFER project on Patient Preferences in Benefit-Risk Assessments during the Drug Life Cycle**

Aims to strengthen patient-centric decision making throughout the life cycle of medicinal products by developing evidence-based recommendations to guide industry, Regulatory Authorities, HTA bodies, reimbursement agencies, academia, and health care professionals on how and when patient-preference studies should be performed and the results used to support and inform decision making. The IMI PREFER consortium is supported by a Regulatory Advisory Group consisting of regulators from FDA, EMA and national Agencies who provide feedback on



expectations from an Agency perspective. In addition, there is a joint EMA/EUnetHTA qualification procedure currently ongoing to qualify a framework and Discrete Choice Experiment as one method for performing patient preference studies to inform regulatory and HTA-body medical product decision-making. The outcome of the qualification procedure will hopefully contribute to EMA guidance on patient preference studies.

- **IMI PARADIGM<sup>2</sup>**: aims to provide a framework that enables structured, effective, meaningful, ethical, innovative, and sustainable patient engagement. It will develop processes and tools for three key decision-making points: research and priority setting, design of clinical trials, and early dialogue with regulators and HTA bodies.
- **EUPATI<sup>3</sup>**: provides training of patient experts on medicine development, clinical trials, medicine regulation and HTA review, offers and maintains a Toolbox on Medicine Development, and coordinates a network of national platforms for patient advocates.
- **CIOMS XI<sup>4</sup> on patient involvement in the development and safe use of medicines**: a global forum which is formulating a Points to Consider on patient involvement throughout the medicine life cycle. The guidance will provide a comprehensive overview of present knowledge and existing initiatives and will address a wide range of the remaining challenges and practice gaps.
- **TransCelerate** has provided Patient Experience Initiative tools that are intended to provide more effective ways to engage with patients in the design and execution of clinical studies. The Patient Protocol Engagement Toolkit (P-PET), a comprehensive set of materials that sponsors and other stakeholders can use to engage patients during protocol development. The goal of this engagement is to improve patient experience and reduce patient burden as a study participant.
- **Patient Focused Medicine Development (PFMD)**: a multi-stakeholder initiative of patient representatives, academics, pharma companies and patient advocates, aimed at co-creation and implementation of a globally standardised meta-framework for patient engagement to make patient engagement more consistent, effective and meaningful. The final Patient Engagement Framework will be a comprehensive package that includes guidance, templates, toolkits, learnings and experiences from existing patient engagement projects through case studies and practical, real-world examples.

## Status Quo

- EMA has not yet developed clear and specific guidance around the incorporation of the patient perspective in medicinal product development. Specifically:

---

<sup>2</sup> <<https://www.imi.europa.eu/projects-results/project-factsheets/paradigm>>

<sup>3</sup> <<https://www.eupati.eu/>>

<sup>4</sup> <[https://cioms.ch/working\\_groups/working-group-xi-patient-involvement/](https://cioms.ch/working_groups/working-group-xi-patient-involvement/)>



- Guidance around acceptable methodology for collecting patient perspective data, such as patient value and patient preferences;
  - The role and value of this data in the regulatory assessment process;
  - The role of the patient community, industry and other stakeholders in the collection of patient perspectives.
- For patient perspectives to be included in drug development the patient community engages with both sponsors and regulators independently. Currently, there is little opportunity for broader discussion across the groups and this hinders efficient drug development;
  - The US provides more opportunity for patients to provide their perspective, with FDA participation, through [externally-led patient focused drug development \(PFDD\) meetings](#);
  - There should be more opportunity for incorporating the patient voice during EMA/HTA parallel consultation procedures.
  - There is a lack of coordinated activity between EMA and FDA on policy and guidance initiatives on PFDD. Constructive dialogue with EMA/EC and FDA should be considered in the near future and should involve all relevant stakeholders. This dialogue should aim at reaching alignment on cornerstone requirements for PFDD with key stakeholders and reflect the results of work conducted under other initiatives such as IMI PREFER.

## EuropaBio policy position

There is an urgent need to develop specific EMA guidance around patient engagement in drug development and how this is evaluated during regulatory assessment of medicinal products. A European perspective should be designed to consider global initiatives and align whenever possible with other Agency guidance.

1. Clear guidance on PFDD which cover all stages of development and permits flexibility in how stakeholders engage with patients and collect their perspectives.
2. Guidance should provide recommendations for capturing and incorporating patient input at clearly defined stages of the regulatory review timeline and how this input will be considered during the approval and reimbursement process, as well as proposed timelines for the additional dialogue.
3. Guidance should address both patient experience and patient preferences (the latter should consider/be revised based on IMI PREFER output).
4. Europe needs to develop an approach to enable three-way discussion between patients/patient groups, regulators and industry on drug development that meets the needs of patients.
5. European stakeholders should explore the opportunities offered by externally led PFDD meetings and consider whether this can be adapted to the European setting.
6. Focused and more technical guidance is needed on COAs/PROs. The guidance should provide recommendations for development and modification/use of existing COAs, the latter being particularly important in rare diseases. Guidance should also



address how to translate COAs into endpoints in clinical trials to inform regulatory decision making. In addition, more alignment between EMA and HTAs is required with respect to tools accepted for regulatory approval and reimbursement.

7. Patient input and data should be formally acknowledged and its use by regulators and value in decision making made transparent.

## Proposed EuropaBio actions on patient engagement in the near future

- a) Engage with the patient community, EU pharmaceutical trade associations, EMA and other EU stakeholders (such as HTA and payers) to co-develop an EU roadmap for patient engagement, which will include:
  - i. EU guidelines aligned in terms of key principles with FDA guidelines as well as considering potential updates to existing guidance documents. Europe should develop a clear vision of what its needs are in this space and work with the US at minimum to design aligned guidance based on the same methodology and systematic inclusion of key principles in terms of patient engagement activities.
  - ii. Developing an approach to enable **discussion** across patient community, regulators, payers and industry to ensure development programmes meet the needs of patients and that the evidence needed by HTA and payers is incorporated early in drug development.
  - iii. Determining what the patient community needs are in terms of providing their input and experience, understanding how this informs drug development and decision making, and what is important to communicate back to the patient community.
- b) EuropaBio continues to support ongoing patients' involvement in EMA activities, Committees, working parties and the EuropaBio Patient BioForum.
- c) EuropaBio will strengthen the dialogue with EFPIA to ensure activities are aligned and mutually supportive.
- d) EuropaBio will find ways to be updated on the outcomes of IMI PREFER project on Patient Preferences in Benefit-Risk Assessments during the Drug Life Cycle and of its potential impact in order to tune with other trade associations on the final position on patient engagement.
- e) During future EMA/European Commission stakeholder meetings focused on patients, EuropaBio will support a global convergence approach concerning patient engagement in EU regulatory procedures and impact on regulatory decision-making.
- f) Proactively engage with regulators and HTA bodies to ensure the proposed new ICH guidelines on clinical outcome assessments (COAs) and patient preference methods are fit-for-purpose and allows sufficient flexibility whilst harmonising requirements for the qualification of new instruments across regions.

