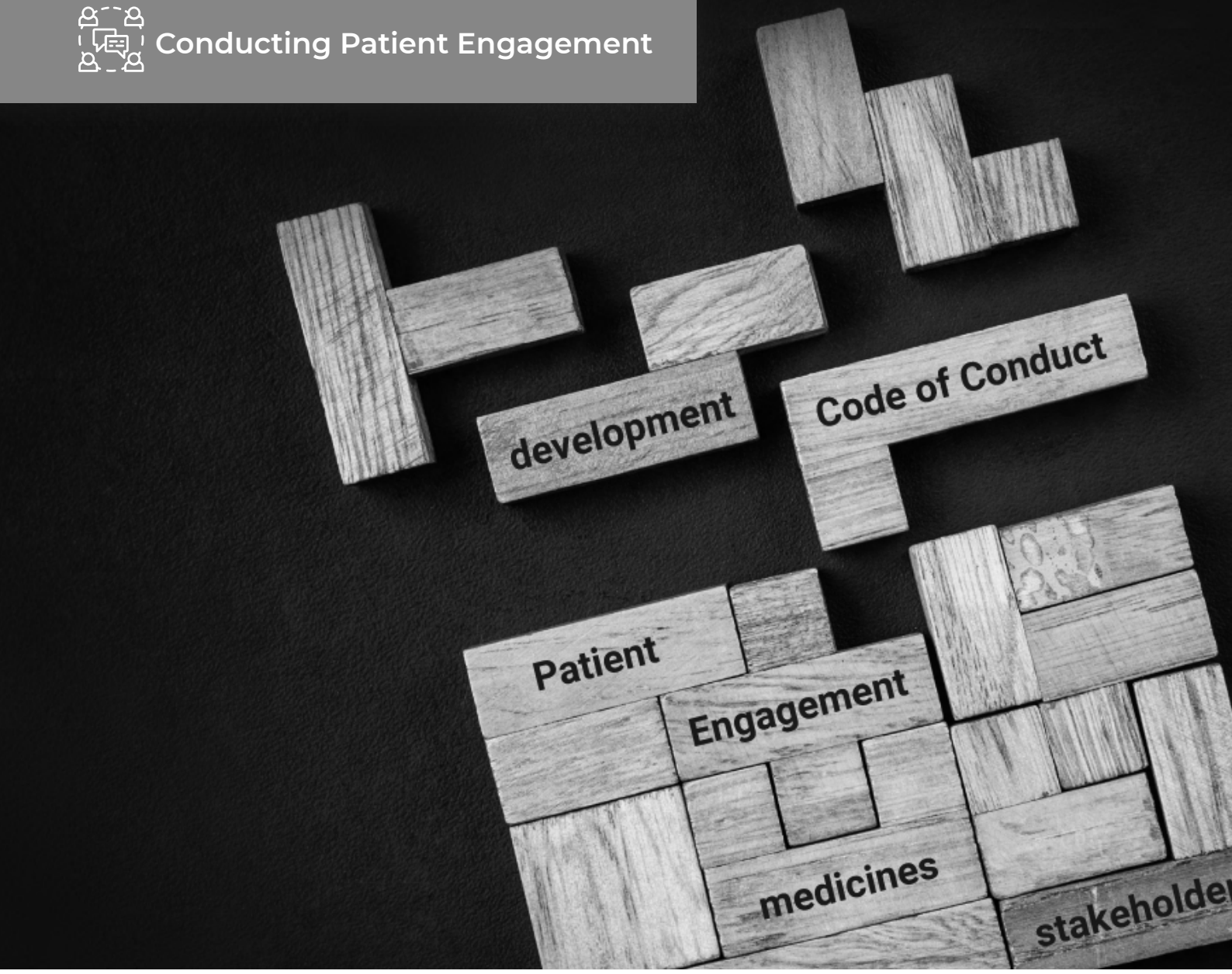
PARADIGM
Patients Active in Research and Dialogues for an Improved Generation of Medicines

innovative medicines initiative

Conducting Patient Engagement



Code of Conduct for all stakeholders involved in patient engagement activities within medicines development

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Executive Summary

Involvement of patients in the research and development process (R&D) of new medicines is a widely accepted approach to ensure relevance and suitability of the treatment under development, to improve the development process and to optimally protect patients participating in clinical trials. Collaboration is beneficial for all parties as pharmaceutical companies, academic institutions, competent authorities, ethics committees and HTA bodies can benefit from patients' insights in disease conditions and treatment needs, and patients get an opportunity to impact the development of treatments for their disease.

Due to the different backgrounds, underlying interests, expectations and contributions a successful collaboration of the different stakeholders requires mutual trust, competencies and a respectful, ethical, and non-discriminational behaviour based on mutually agreed rules. This Code of Conduct, jointly developed by a large team of experts from the patient community, pharmaceutical industry, regulatory authorities, HTA bodies, academia and not-for-profit organisations, aims at reducing the risks for conflicts and hurdles in patient engagement activities by defining the conditions for fruitful collaboration. It emphasizes that ethical values and mutually agreed contractual conditions including declaration of interest, intellectual property rights and fair compensation are essential. Transparency, confidentiality and data protection need to be reliably ensured by all partners. Fair access to patient engagement opportunities but also availability of suitable, clearly defined resources and competencies form the basis for collaboration that can achieve the jointly defined objectives.

All stakeholders of the patient engagement community should voluntarily integrate the rules of this Code of Conduct into their collaborations and insist on adherence by all partners.

Purpose of the document

This "Code of Conduct for all stakeholders involved in patient engagement activities within medicines development" is intended to be a stand-alone document that highlights, summarises and refers to the key patient engagement principles, rules and recommendations for collaboration presented in the different PARADIGM documents in the Toolbox in a comprehensive, understandable format.

1. Introduction

Patient engagement is the meaningful and active contribution of patient-specific expertise with regard to the collaboration of patients, patient advocates, patient representatives and/or carers in decisions, activities and information dissemination within the medicines' lifecycle. It supports the contributed expertise of other relevant stakeholders. However, the collaborating stakeholders have different roles and thus different interests and motivation for collaboration within the medicines' life cycle. These different positions can create conflicts and hurdles to successful collaboration and impact. In recent years it has been increasingly suggested that the traditional opposite positions of those who are in need of new medicines and those who work on developing them should be overcome. Involving patients in specific medicines' lifecycle activities can be hampered by a lack of knowledge and expertise of contributing patients about the science and methodology of medicines development and thus can be a limiting factor to the input patients can provide. Also a lack of knowledge and experience of the engaging stakeholders in how to successfully integrate the patients' contributions can limit the success of the collaboration. Initiatives to systematically increase the knowledge of patients but also that of the other stakeholders about fruitful patient engagement have been successfully implemented (e.g., by EUPATI (European Academy on Therapeutic Innovation, the EURORDIS (European Organisation for Rare Diseases), EPF (European Patients Forum) and PFMD (Patient Focused Medicines Development)). These initiatives led not only to an increase in the capacity of the patient community to actively contribute to medicines research and development but to also to an increasing awareness of the benefits of patient involvement in patient-centred medicines development. To further facilitate patient engagement in practical terms, common values, ethical principles and rules for the collaborating partners have to be agreed and systematically and consistently implemented.

There is no European or international legislation defining the rules for patient engagement in medicines' lifecycle activities. However, there are more and more guidelines and recommendations that cover different aspects and conditions of the collaboration between patients, sponsors, ethics committees, competent authorities or HTA bodies.

PARADIGM (Patients active in research and dialogues for an improved generation of medicines) was an IMI funded multi-stakeholder consortium to provide a framework for structured, effective, meaningful and ethical patient engagement along the lifecycle of medicines. The project focused on three decision-making points: research priority setting; clinical trial design; and early dialogues with regulators and health technology assessment (HTA) bodies. The result of the consortium / the output of the consortium is a comprehensive set of tools and practices

to support the integration of the patient perspectives into medicines development beyond the focal areas of the project. Patient engagement should be a standard practice to improve medicines development and deliver results that are focused on patients' needs.

This Code of Conduct is based on - and refers to - the principles, rules and recommendations presented in different documents of the PARADIGM Toolbox. Fact Sheets summarising the different documents are in the Annex of this Code of Conduct. This Code of Conduct was commented in consortium and public consultations by patients, academia, pharma companies, not-for-profit organisations, ethics committees, competent authorities and HTA bodies.

2. Purpose and Scope

This Code of Conduct describes mutually acceptable ethical and professional standards to enable successful and meaningful collaboration between patients, carers, patient advocates, representatives of patient organisations, academic or commercial sponsors and their service providers, healthcare professionals, ethics committees, competent authorities, and HTA bodies. It addresses the values, ethical principles, and rules for all stakeholders involved in these collaborative activities. By protecting all involved stakeholders' interests and rights and by ensuring reliable transparency in such collaboration, this Code of Conduct intends to facilitate systemic, comprehensive and consistent patient involvement in all aspects of medicines' research, development and access to treatment activities.

3. Ethical Values and Principles for Patient Engagement in the Life Cycle of a Medicine

The following values form the basis for patient engagement activities[1,2,3,4]:

- **Relevance:** Like all other experts engaged in the life cycle activities of a medicinal product, patients and carers have unique knowledge, perspectives and experiences that can contribute to patient-relevant, efficient research and development, and access to treatment.
- **Fairness:** All patient engagement partners have the same rights to be given the opportunity for contribution to the research, development and access to medicines process and to have access to knowledge and experiences that enable effective engagement.

- **Equity:** Patient involvement in medicines life cycle activities contributes to equity by enabling the integration of the diverse needs of patients with particular health issues into the outcomes of benefit-risk balancing processes of the diverse stakeholders.
- **Capacity-building:** Patient engagement rules address and overcome barriers to involving patients in medicines' life cycle activities and help build capacity for holistic stakeholder contributions in all respective processes.

The following ethical principles should guide patient engagement activities amongst all stakeholders:

- **Respect:** All patient engagement partners communicate with and treat all involved with the same respect, consideration and courtesy, with special attention to non-discrimination as defined by WHO's gender, equity and human rights roadmap. In particular, no patient can be discriminated against for reasons of health literacy nor lack of training nor by the fact that processes need to be adapted to their needs and capacities to ensure their meaningful involvement.
- **Integrity:** All patient engagement stakeholders commit to the integrity of their behaviour in all steps of each process.
- **Trust:** All patient engagement partners assume positive intent, suspend judgement and build trust with each other concerning their motives as well as their confidence to contribute to the common goal of ultimately providing benefit to patients.
- **Clarity of purpose:** Each party should be clear about the reason for and the planned outcome of the collaboration – and the ultimate benefit for patients.
- **Beneficence:** All activities and outcomes are performed with the common goal of benefit to patients.
- **Non-maleficence:** All patient engagement partners intend to do no physical, social or psychological harm to any involved stakeholder.
- **Equality:** All patient engagement partners treat all involved stakeholders as equals.
- **Transparency:** All patient engagement partners commit to full transparency about all aspects of the collaboration.
- **Independence:** All patient engagement partners commit to independence of their contributions from decisions and strategies arising out of the interests of their organisation.

4. Contractual Framework

Collaboration between patients and pharmaceutical companies, academic institutions, competent authorities, ethics committees or HTA bodies should be based on **written agreements**, signed by both parties before the start of the patient engagement activity.

The agreement should define in clear and easy to understand wording

- the purpose
- roles and responsibilities
- terms and conditions of the collaboration

The agreement should cover legally relevant aspects, such as

- confidentiality
- intellectual property rights
- copyright
- data protection
- independence
- declaration and conflict of interest
- anti-bribery compliance
- liability
- compensation
- dispute resolution
- a statement to the effect that outcomes of and experiences with the patient engagement activity will be jointly reported.

In the appendices the details of the agreed tasks and timelines as well as of the financial and data use conditions should be described.

Supporting documents for developing a contractual agreement

Broadly agreed **templates** with detailed explanations about the meaning of the legal terms as provided in the **"PARADIGM Patient Engagment Agreements Explained"**[5] should be used when possible. This can be supported by **existing guidance**[6] to enable complete comprehension of all conditions, responsibilities, rights and obligations by all engaging partners.

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Compensation

Clear and transparent **compensation rules** should be ensured for all contributing partners, applying recognised fair market values. The compensation rules should ensure that **no undue inducement** or other aspects limit the autonomy of all contributing partners in their decision to engage with other patient engagement stakeholders.

Project elements

The written agreement should foresee timely mutual **information on changes** of tasks, timelines, resources and contractual conditions.

Confidentiality

The article on confidentiality should also define the extent to which the patient is **allowed to share confidential information** with relevant members of his/her patient organisation or other persons or interested parties, in order to create the required input to the contracted activities.

Duration

The written agreements should be formulated in such a way that trust is built and that development towards **long-term relationships** between the partners is enabled where relevant and desirable.

5. Competing Interests, Conflict of Interest, and Conflict Management

All stakeholdes in patient engagement activities provide their contributions based on an individual societal and professional context. Patients may collaborate with different stakeholders in parallel. This can create **competition between the interests** of their partners and may affect an individual's impartiality but does not necessarily constitute a conflict.

In contrast, a **conflict of interest** describes a situation in which the individual's judgement may be affected by a secondary interest, as defined by the other partner(s).

The conflict might lead to

- a lack of objectivity,
- potentially biased decision-making
- serious damage of the reputation of individuals or organisations.

This might ultimately cause suboptimal decisons during medicines development.

The **early identification of potential competing interests** is key to effectively manage them upfront in order to avoid or limit the extent of the conflict and the subsequent impact to the partener's ability for further interaction.

Therefore, all patient engagement activities should be based on a **Declaration of Interest**, provided by all partners, **to identify potentially competing areas** that could lead to a conflict of interest in their collaboration[7].

Declaring an interest does not necessarily imply the existence of any conflict, nor should it automatically disqualify a person from participating in the activities of the engaging stakeholder.

Mitigation strategies should be mutually agreed between the parties and documented. They may vary according to the stakeholder type:

- one option is diversifying the workforce capabilities of a patient organisation to allow for simultaneous engagement with regulators/HTA bodies/payers and (several) medicines developers.
- another option, especially applied by regulatory authority partners, may be the establishment of some restrictions or special status[8] to enable the right patient expertise in some of their activities under exceptional circumstances, i.e. where the required patient expertise is very limited (e.g. orphan diseases with small numbers of patients or certain vulnerable populations).

As a matter of principle, every stakeholder organisation involved in patient engagement should **develop and enforce a policy to manage competing interests**. Policies should in particular clarify how a previous engagement with a medicines developer (or any other stakeholder) could undermine the integrity of the patients' contribution and therefore its impact. The policies should follow these principles[7]:

- **Proportionality:** Is the policy most efficiently directed at the most relevant potential conflicts?
- **Transparency:** Is the policy comprehensible and accessible to the individuals and institutions that may be affected by the policy?
- **Accountability:** Does the policy indicate who is responsible for enforcing and revising it?
- **Fairness:** Does the policy apply equally to all relevant groups within an institution and in different institutions?

If agreements and/or policies are not followed by any of the involved parties, then a **breach**

of trust can occur and **mediation and dispute resolution** must be put in place to ensure the integrity of the process. Alternatively, engaging agreements may include provisions considering the **immediate termination of an agreement** if either party breaches trust or breaches a contract or a contract clause.

Multi-stakeholder created and agreed recommendations should be consulted when policies and templates for declaration of interest and conflict of interest management are developed[7].

6. Intellectual Property, Confidentiality and Data Protection

6. 1. Intellectual Property

Intellectual property (IP) protection is critical to fostering innovation.

In collaborative projects between stakeholders, e.g., pharmaceutical companies and patients or patient organisations, IP provisions/rules are essential and should apply equally to all partners in the projects. The IP provisions should support the objectives of the project while respecting the interests of all project partners and should be mutually agreed in a project agreement.

The following **IP principles** should equally apply to and be accepted by all partners:

- When data, know-how or tools are brought to a project by one of the partners before the project starts, they are called **"Background"**. The respective partner exclusively keeps the IP rights for this "Background".

  The acceptance as "Background" applies if all of the following conditions are met:

  - is **held** by a partner before the partner joined the project,
  - is **needed to implement** the project **or exploit the results**, and
  - is **identified and agreed upfront** by the partners.
- Results which are generated under the project and which lie within the scope of the project objectives are defined as **"Foreground"**. A general rule is that "Foreground" belongs to the participant that generates it. Results owners are free to decide on the best protection modalities. Where two or more participants have jointly generated specific "Foreground" they should agree on **"Joint ownership"**.
- **"Sideground"** means results or other output generated by a partner under the project but outside of the project objectives. The IP rights for "Sideground" also remain with the inventing/creating partner.

- **"Access rights"** to results generated within the project should be granted on an equal basis to all partners. "Access rights" for exploitation purposes should be negotiated on a case-by-case basis. **"Open access"** dissemination of project results should be aimed for, but this is subject to legitimate interests and therefore results that may generate value can also be protected by the project partners.
- **Dissemination of the Foreground** as well as timelines and modalities for dissemination (e.g. through websites, publications in scientific journals, etc.) should be agreed between the partners and enacted as soon as reasonably practicable[9].

Intellectual Property provisions in project agreements should be flexible, allowing to be adapted to the needs of an individual project and its participants. To fulfill transparency, patient engagement projects require reporting and dissemination of their results[9] since this type of information is not considered commercially confidential. Exceptions may apply if mutually agreed upfront.

6. 2. Confidentiality

The same **confidentiality obligations** should apply to all partners in a project, including subcontractors and any third parties involved through being a participant in the project. It is recommended that each participant treats confidential information of other partners with the same degree of care as their own confidential information. The Partners should ensure that their subcontractors and involved third parties are bound to a strict need-to-know basis only and that their compliance with equal confidentiality obligations are part of the project agreement.

Exceptions to the general confidentiality obligations may be agreed between the participants in the project agreement. Participants may precisely identify the information exchanged between themselves that is subject to confidentiality restrictions, or information for which confidentiality is not considered as an issue.

Principally, patients should have the **right to consult with members of their patient organisation** to maximise their contributions. This should include the possibility to share confidential information as far as required for the consultation. In such a case a patient's organisation should be considered as a third party as covered by the project agreement.

6. 3. Data Protection

In Europe the **General Data Protection Regulation** (GDPR)[10] is a set of rules about how organisations/companies should process the personal data of data subjects. GDPR lays out responsibilities for organisations to ensure the privacy and protection of personal data, provides data subjects with certain rights, and assigns powers to regulators to ask for demonstrations of

accountability or even impose fines in cases where an organisation is not complying with GDPR requirements.

For all Patient Engagement projects all parties should respect the GDPR rules and applicable national legislation[11]. The applicability of the GDPR for the respective intended Patient Engagement activity should be evaluated and followed where appropriate.

7. Access to Information and Transparency

Access to comprehensive, reliable information is a fundamental right that is particularly relevant in topics where there is rapidly growing knowledge, numerous sources of information prone to fake news, and value to scientific, societal and commercial interests.

All partners in patient engagement activities should strive to make their information rapidly and comprehensively accessible in formats suitable for all partners involved and the public at large. A recent best practice example is the legally required "Lay Summary" of clinical trial results within one year[11]. The highest possible degree of transparency will increase all involved stakeholders' knowledge and mutual trust. Additionally, it will help to make medicines' life cycle activities more efficient by establishing a level playing field that allows all stakeholders involved to learn from past successes and failures.

The right of access to information includes all areas of interest in medicines' lifecycle activities, e.g., from a

- scientific
- methodological
- technological
- collaboration
- communication

point of view. However, the information should not only be disseminated but efforts should be made to **reach all stakeholders** that might be interested in this information. The information should be understandable without potentially appearing to be promotional.

Efficient and reliable dissemination of **patient-relevant information requires input from** the end user, in particular **patients and carers**, to ensure that the often complicated content can be understood, also in its relevance for decision-making and actions.

Unrestricted access to information should not only include research, development, and HTA-related results but also timely information on **opportunities for education and collaboration**.

8. Accessibility of Patient Engagement Opportunities

The need for patient involvement is rapidly growing but **finding partners is a major difficulty**, especially because

- diverse patient perspectives should be taken into consideration and
- successful collaboration depends on the involved patients' competency level and capacity required in the respective activity.

Finding suitable representatives of small patient populations as in rare diseases and vulnerable populations can be particularly challenging[12].

To facilitate matching the needs and opportunities, all partners **planning patient engagement activities** should strive to prepare and disseminate clearly defined, comprehensive and easy to understand information on upcoming and completed collaboration[15] activities through at least one of the following formats:

- publicly accessible information platforms
- organisations' own website
- directed calls for collaboration

The information should contain the patient engagement **activity's objectives and timelines** as well as the **needed competencies** and **capacities** for engagement in a manner that is understandable for the respective patients.

Definition of the expected patient profile should be based on a structured mapping of the required patient competency level per task.

In case of patient engagement **activities in vulnerable populations** the engagement seeking partner should consider the involvement of the caregiver in addition or instead of the patient, taking into consideration the type of input required and the envisaged potential burden for the patient.

Patients or patient organisations with interest, capabilities and capacity for patient involvement activities should provide their respective information proactively on neutral communication platforms for patient engagement and/or respond to professionally presented calls for collaboration.

Rules of engagement with the other partners should be decided and established within all partners' own organisations before collaboration with other partners is negotiated and agreed.

Patients or patient organisations should provide the collaboration-seeking partners with

detailed and comprehensive **information on the recommended patient's knowledge, skills and capacities** available for collaboration. From the provided information the collaboration seeking partner should be able to compare the patient's competencies with the task and competencies matrix prepared for the engagement activity.

Before the start of the collaboration, all patient engagement partners should enable clarity about the expected and provided level of diversity and representativeness of input.

There should be mutual agreement that engaged patients provide their input as an equal member of the expert team, including accountability for their input, with the aim to achieve a joint outcome. In that capacity, the patient or patient representative should ensure objectivity in assessments, decision-making and advice as well as independence from his/her organisation's interests and strategies.

9. Representativeness

All stakeholders in the medicines' life cycle activities contribute scientific, methodological, technical, regulatory, ethical or financial knowledge to the project, acquired by education and professional experience. In contrast, patients (and their carers) contribute their personal (or patient organisation members') health experiences and treatment needs which can be very different from that of other patients with the same disease. This raises the question to what extent are **patients' contributions to a project representative for all other patients with this condition**. Scientific methods like registries are a recognised way to systematically collect information on disease experience and could serve as evidence for contributing patients' perspectives in those projects.

Engaging stakeholders should therefore **define for each task which input and level of representativeness is desirable**[13]. According to these needs the engaging stakeholders should seek ways to engage a range of patients, e.g.,

- from different disease stages,
- from different regions and healthcare systems,
- with different levels of experience in medicines development processes.

The required need might be user testing or anecdotal input, scientific or methodological competency, or participation in an advisory board or political representation. Experience with the disease can be based on personal suffering from the disease or from gathering inside knowledge when working for a patient organisation.

Before collaboration is confirmed the **partners should ensure that they have a common understanding of the patient's level of representativeness**[13].

Before and during patient engagement activities, patient organisations should strive to improve the representativeness of their delegate. The patient representative should provide regular and systematic feedback to his/her patient organisation concerning missing desirable or required information identified during the patient engagement activity.

10. Competencies and Capacity-Building

The tasks in medicines' lifecycle require from all involved a wide variety of competencies. "Competency" is defined as the combination of knowledge, skills and attitudes[13].

The required level of competencies differs: for example,

- testing of patient information sheets, lay summaries or package inserts concerning readability and suitability for lay persons benefit from review by patients that do not know about the development methodologies of those patient-aimed documents.
- On the other hand, contributions to research target and molecule selection require highly developed scientific, methodological and Health-technology Assessment competencies.

When patients want to get involved in such activities, they should first critically assess their level of competencies in the areas in which they wish to contribute. Efforts should be made to fill knowledge gaps by learning from trustworthy sources[14]. Patients have experience in living with their disease but when they also understand the scientific and methodological complexities in the joint project they better understand the other partners' position and constraints. Contributions provided on such basis will increase value and acceptance of the input by the other partners.

Scientific, methodological, regulatory or ethical experts provide advice on a certain topic in medicines development without a personal interest. But patients in an advisory capacity are also concerned parties. This changes the processes of how a team acquires knowledge on the topic and how decisions are reached in a project. All involved parties should systematically elaborate the new process and make all possible efforts to increase their competency in optimised patient engagement, also taking into consideration the specific physical and organisational needs of patients[14].

Quality and reliability of the input from all involved partners as well as efficient communication and collaboration are essential for the efficiency in achieving the common goal of better

treatment options for patients. Therefore, **all partners should constantly strive to increase their knowledge in the areas of their contributions as well as their communication and collaboration skills.**

To ensure equity, patient involvement is relevant in all areas of indications and all stages of the medicines' life cycle. Therefore, constant increase of capacity, the availability of competent resources, partners experienced in patient engagement and maximising the efficiency of patient involvement should be a common goals for all partners in medicines' lifycycle activities.

11. Adherence to the Code of Conduct

Adherence to this Code of Conduct ensures an open and fruitful interaction of engaging partners with patients and their representatives to optimise the development of medicines suitable for use by the patients to be treated.

The patient engagement community should voluntarily integrate the rules of this Code of Conduct into their collaborations and insist on adherence to it in case a partner shows deviation.

12. Concluding Remarks

For the development of medicines optimally suited for the patients to be treated and with the least possible harmful impact of their daily life, communication and collaboration between well informed partners is essential. This Code of Conduct describes the essentials to make this possible.

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http://imi-paradigm.eu/PEtoolbox/identification-of-patient-representatives

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14. EUPATI Toolbox
https://toolbox.eupati.eu/

14. Annex 1: **PARADIGM Glossary**

Disclaimer: The terms used here have been defined or agreed upon within the context of this project.They should not be considered as exhaustive, finite or purposely exclusive of other considerations, but are representative of the specific focus of this project and its actions.

Code of conduct:

Collection of rules and regulations that include what is and is not acceptable or expected behaviour (PARADIGM)

Community Advisory Board:

Community Advisory Board (CAB) refers to a group of patients who offer their expertise to sponsors of clinical research and who advise several sponsors in their field. CABs are autonomous bodies, not related to the sponsor or chosen by them.

Confidentiality Agreement (CA)/Non-disclosure agreement (NDA):

Legal contract between at least two parties that outlines confidential material, knowledge, or information that the parties wish to share with one another for certain purposes but wish to restrict access to.(Wikipedia)

Consultancy:

Advice provided on company- or academia sponsored clinical trial protocols including related documents, regulatory documents or information about the products under discussion (e.g. medicinal products, biomarkers), strategic initiatives and other projects of commercial or academic relevance (PARADIGM)

Design of clinical trials:

Designing protocols, discussing patient burden, discussing patient related outcomes (PARADIGM)

Early dialogues with regulators and Health Technology Assessment bodies:

Early (multi-stakeholder) discussions between industry, HTA agencies and/or regulators (and in some contexts with payers) to discuss developmental plans for a medicinal product and to ensure they meet the requirements.

* *Early dialogue is not a decision-making time for any party. In practice it more closely resembles consultation with the chance for feedback and input (two-way communication).* (PARADIGM)

Health Technology Assessment (HTA):

Systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies. HTA is conducted by interdisciplinary groups that use explicit analytical frameworks drawing on a variety of methods. (http://htaglossary.net/health+technology+assessment)

Health technology assessment (HTA) body:

A body that undertakes or commissions health technology assessment to form recommendations or advice for healthcare funders and decision-makers on the use of health technologies (PARADIGM)

Healthcare professional (HCP):

This category of stakeholders is broad and heterogeneous as it encompasses general practitioners, nurses, clinical investigators/academics, pharmacologists, etc. (PARADIGM)

Medicine developer:

Includes any organisation involved in the research, development, manufacture, marketing and/or distribution of medicinal products and/or any other health products such as medical devices or digital solutions. Clinical/contract research organisations (CROs) or consultancy companies providing advice or services relating to the above activities, fall under the definition of medicines developers. Research organisations including universities and learned societies (i.e. an organisation that exists to promote an academic discipline, profession) are also included in the definition of medicines developers (PARADIGM)

Medicines development/medicines research and development (R&D)/ medicines lifecycle (in PARADIGM these terms are used interchangeably):

A medicines lifecycle comprises research and discovery, development (preclinical and clinical), marketing authorisation, post-approval, HTA, pricing and reimbursement, commercialization, lifecycle management and Pharmacovigilance until deregistration. (PARADIGM, adapted from: EUPATI; European Commission; EFPIA; Frontiers 'The Life Cycle of Health Technologies. Challenges and Ways Forward, Iñaki Gutiérrez-Ibarluzea et. al. 2017')

Memorandum of Understanding (MoU):

Type of agreement between two (bilateral) or more (multilateral) parties. It is not legally binding, but it expresses willingness between the parties to take forward a common line of action. (https://www.investopedia.com/terms/m/mou.asp)

Participating organisation/engaging partner:

An organisation which is organising and/or participating in a PE activity (PARADIGM)

Patient covers the following definitions:

- **"Individual Patients"** are persons with personal experience of living with a disease. They may or may not have technical knowledge in R&D or regulatory processes, but their main role is to contribute with their subjective disease and treatment experience.
- **"Carers"** are persons supporting individual patients such as family members as well as paid or volunteer helpers.
- **"Patient Advocates"** are persons who have the insight and experience in supporting a larger population of patients living with a specific disease. They may or may not be affiliated with an organization.
- **"Patient Organization Representatives"** are persons who are mandated to represent and express the collective views of a patient organization on a specific issue or disease area.
- **"Patient Experts"**, in addition to disease-specific expertise, have the technical knowledge in R&D and/or regulatory affairs through training or experience, for example EUPATI Fellows who have been trained by EUPATI on the full spectrum of medicines R&D.

(The European Patients' Academy on Therapeutic Innovation (EUPATI)

Patient community:

Patients, patient representatives including their family and carers, patient advocates and patient organisations (PARADIGM)

Patient engagement:

The effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicines lifecycle, along with all other relevant stakeholders when appropriate (PARADIGM)

Patient organisations:

Patient organisations are defined as not-for profit organisations which are [patient-]focused, and whereby patients and/or carers (the latter when patients are unable to represent themselves) represent a majority of members in governing bodies (EMA 2018a)

Payer:

Institution, organisation or individual paying for healthcare or health services (PARADIGM)

Pharmaceutical industry:

The pharmaceutical industry is comprised of many public and private organizations that discover, develop, manufacture and market medicines for human and animal health. In short, the term "industry" is used to refer to the pharmaceutical industry (PARADIGM)

Policy-maker(s) (or policymaker(s)):

A member of a government department, legislature, or other organization who is responsible for making new rules, laws, etc. (https://dictionary.cambridge.org/dictionary/english/policymaker)

Regulatory authority (or regulatory agency or in short 'regulators'):

A body that carries out regulatory activities relating to medicines, including the processing of marketing authorisations, the monitoring of side effects, inspections, quality testing and monitoring the use of medicines. (EMA)

Representative for pharmaceutical industry:

An employee of the pharmaceutical industry designated to represent the company position in project/consortium/body (PARADIGM)

Research priority setting:

Providing opinion, providing evidence and/or being part of a group that decides what is important to research. Design of clinical trials (PARADIGM)

Three main decision-making points:

The term, 'decision-making points' is defined as the key points in the development lifecycle of medicinal products. The three decision-making points relevant to PARADIGM are: research priority setting, design of clinical trials and early dialogues with regulators and Health Technology Assessment bodies (PARADIGM)

Vulnerable / underrepresented groups:

Children and young patients, people living with dementia and their carers. This definition can also include underrepresented groups (e.g. migrant and non-settled populations, substance users, incarcerated people and people with mental health disorders other than dementia). (PARADIGM)

15. Annex 2: **Fact Sheets of PARADIGM Documents**

PLANNING PATIENT ENGAGEMENT

Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Background/Rationale for the document:

Managing competing interests and conflicts of interest is of utmost importance when planning, considering and conducting patient engagement activities in medicines development.

For this reason, we developed a set of tools:

- Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders
- Short guidance on managing competing interests and conflicts of interests
- Log of patient engagement activities
- Educational scenarios on competing interests and conflicts of interest

Objective of the tool:

These tools aim at:

- Raising awareness among patients (in their role of experts by experience) and the engaging stakeholder organisations of the consequences that the act of engagement might have on patients during multi-stakeholder interactions
- Highlighting how each stakeholder could better prospectively manage competing interests, and
- Avoiding/minimising conflict of interest by suggesting risk mitigation strategies.

Summary of the content:

The main guidance is a comprehensive document outlining the definitions and types of interest, recommendations and mitigation measures as well as the considerations when engaging vulnerable populations. Examples of engagement activities and their levels of restriction are also included.

The short guidance helps clarify basic concepts and includes stakeholder-specific considerations and recommendations on conflict of interest.

The log of patient engagement activities facilitates tracking patient's involvement in a systematic manner in order to declare their interests when engaging with one or more stakeholders.

The educational scenarios provide illustrative examples to identify common situations where conflicts of interest might occur and what measures could be taken for their management.

Key message:

Together, these tools will support patients in order to take informed decisions before the engagement and help engaging stakeholders to understand the consequences that the act of engagement might have on patients during multi-stakeholder interactions in medicines development.

Enhancement of the EUPATI industry guidance

Background/Rationale for the documents:

During the PARADIGM project further expansion of specific sections of the EUPATI Guidance for Patient Involvement in Medicines Research and Development (R&D); Guidance for Pharmaceutical Industry-Led Medicines R&D guidance were required.

The working practices section required further emphasis to provide more detail on how an engagement could be defined with specific actions and to describe what should happen during pre-engagement planning and discussions to ensure mutually beneficial interactions with adequate preparation.

The considerations for events and hospitality required further emphasis to provide more detail on the level of attention needed when arranging patient engagement activities to ensure patients have the best experience.

Objective of the tool:

The suggested working practices document provides recommendations with a checklist designed to help organisers planning patient engagement activities and addresses the PARADIGM defined recommendations on the required capabilities for patient engagement.

The events and hospitality checklist is designed to help individuals responsible for coordinating and planning patient engagement activities consider specific patient needs for travel, meeting venues, accommodation and associated elements. It is written for general application across all different scenarios and aims to be simple to follow by all stakeholders involved.

Summary of the content:

The two checklists have been designed as practical tools which may be used during pre- engagement planning of patient engagement activities.

The suggested working practices checklist defines specific actions that may be appropriate to the activity and can aid discussions to ensure mutually beneficial interactions with adequate preparation. Organisers can use the rightmost column to include comments addressing considerations such as: “What is the activity?”, “who/what will it affect?”, “what impact will it have?”, “What is the benefit to the patient/community in participating?” and self-assess the quality of their preparedness and identify areas for improvement.

The events and hospitality checklist defines high level considerations for events and hospitality and is not intended to be an exhaustive list.

Key message:

The tools presented here as an enhancement of the EUPATI guidance for patient engagement in industry led R&D, give the detailed steps to follow which were purposely not addressed in the original guidance document. However, the guidance document should be read in conjunction with these recommendations. Advice given in the suggested working practices tool is not intended to be exhaustive or applicable at all times. Judgement is needed to decide whether or not a recommendation can, should or must be followed.

Recommendations on required capabilities for patient engagement

Background/Rationale for the document:

This tool provides recommendations on the competencies (understood as knowledge, skills and behaviours) and resources that each stakeholder organisation should aspire to have in place in order to plan, implement and evaluate meaningful and sustainable patient engagement (PE) activities across the medicines lifecycle.

Objective of the tool:

The objective of the recommendations is to increase preparedness of stakeholder organisations by identifying the capabilities required by those individuals involved in implementing PE activities and the resources (processes, tools and systems, organisational structure) needed within the organisation. This tool does not address the specific competencies of the patient participants involved in PE activities.

Summary of the content:

This tool shows the key themes identified for effective PE and describes the identified capabilities required under each theme including:

- Shared purpose and roles and responsibilities of all stakeholders
- Respect and accessibility
- Representativeness of all stakeholders
- Transparency in communication and documentation:
  - legal agreements and confidentiality
  - management of competing interests
  - codes of conduct and rules of engagement and
  - reach-out to and interact with patients and patient organisations
- Continuity and sustainability
  - financial compensation and
  - measuring PE impact
- What to consider when engaging with potentially vulnerable populations

Key message:

Each stakeholder can use these recommendations to analyse their own organisation's capabilities at a given moment and consider the elements described in this tool to further develop or adapt the capability model existing in their own organisations.

Patient engagement agreements explained

Background/Rationale for the document:

Patient Engagement Agreements Explained- is a tool to enable the suitability and usability of the co-created Guiding Principles and the four reference agreements – a project led by the pan-European cancer patients' network through WECAN/MPE and partnered with PFMD – for all stakeholders.

The patient-led multi-stakeholder project led by WECAN/MPE/PFMD, "Reasonable agreements between patient advocates and pharmaceutical companies (RAPP)", aimed to streamline the legal framework between the patient community and the pharmaceutical industry, providing guidance for the content of legal contracts while maintaining reasonable safeguards for both contractual parties. The RAPP project applied a collaborative and consensus-driven approach to developing the "Guiding Principles on Reasonable Agreements between Patient Advocates and Pharmaceutical Companies". The Principles aim to serve as a baseline for the development of contracts and contract templates for patient advocate engagements with industry to ensure reasonable protection for signing parties and to provide guidance to patient advocates whenever they need to review a legal agreement. The goal of the Guiding Principles is not only to simplify the language and terms of typical agreements but also to prevent the addition of unnecessary clauses for either party. These Principles were then applied in the development of Reference Agreements, which are meant to be used as a resource for legal parties and patient advocacy leaders in an industry responsible for drafting agreements with the patient community.

The Reference Agreements require tailoring depending on the situation: each country has rules and regulations, different types of engagements may have unique parameters, and the people signing the agreement may have unique needs that need to be considered. Legal agreements typically need to address similar aspects of cooperation; however, the four Reference Agreements have some key differences due to the nature of the different types of activities. This depends on whether the engagement has shared objectives (e.g. collaboration), or if the patient or patient advocate is offering a service (e.g. speaking, consultancy, participation in an advisory board).

Objective of the tool:

The final outcome of this task force is a digital tool that will assist users from any stakeholder group to understand the legal requirements of these four agreements and in doing so, hopefully enables the creation and usage of agreements that are more agreeable to both the parties that are in collaboration.

Summary of the content:

- **The annotated versions** of the reference documents listed in point. These versions will provide you with additional descriptions to the sections and terminology used in the reference agreements.
- **The Guiding principles** as well as the four reference agreements as co-created by WECAN together with patients and pharmaceutical industry representatives.
  - **The Guiding Principles** aim to provide the basic understanding for the development of contracts and contract templates for patient engagements with industry to ensure reasonable protection for signing parties and to provide guidance to patient advocates whenever they need to review a legal agreement.
  - **The four reference agreements** are meant to be used as a resource for legal parties responsible for drafting agreements with the patient community → Use them as is if they fit your purpose or use them as a basis to create your own contracts.
- **The glossary** will provide you with detailed descriptions on the terminology that was highlighted as potentially difficult to understand.

Patient engagement in medicines development: Recommendations on how to find the right match for the right patient engagement activity

Background/Rationale for the document:

During the analysis of existing practices and processes of patient engagement in the context of the PARADIGM project, a clear gap was identified under the theme 'Selection of participants and adequate representation'. This related to a description of the steps followed to identify patient representatives between the engaging partners.

Generally limited documentation exists on how patients and their representatives are selected prior to an engagement activity. This may be because co-design of selection criteria with the patient community is still evolving and is not yet standard practice, and this task is often managed internally within individual organisations, with published case studies of patient engagement not currently providing that information.

This document aims to address this gap by providing recommendations on the elements associated with identifying patients and their representatives to partner in patient engagement activities.

Objective of the tool:

This document specifically addresses what to consider when identifying the patients or their representatives' together with associated competencies to help match the right individuals for the right activity.

Summary of the content:

- Key principles for the set of recommendations
- The steps to follow when finding the right matches for the right activity
- Recommended topics to consider about the patient organisations (POs) that could guide the decision about which are the best suitable POs to contact
- Check list of the elements to consider before engaging with a patient organisation to work on a patient engagement activity
- A competency table to identify the main attributes that would be the most suitable for a given patient engagement activity
- Methods and short description on how and when to best use them to capture insights from patients and their representatives

Key message:

Detailed considerations to be taken into account for the identification of appropriate participants when planning the engagement of patients/POs in various activities related to medicines development.

CONDUCTING PATIENT ENGAGEMENT

The code of conduct

Background/Rationale:

There is no European or international legislation defining the rules for patient engagement in medicines' lifecycle activities. Guidelines and recommendations exist covering different aspects and conditions of the collaboration between patients, sponsors, ethics committees, competent authorities or HTA bodies. However, an overarching Code of Conduct, facilitating patient engagement in practical terms, common values, ethical principles and rules for the collaborating partners is missing. Substantiated by the project's own gap analysis, PARADIGM aims to close this identified gap by developing this Code of Conduct to be applied by all stakeholders involved in patient engagement activities within medicines development.

Objective:

This Code of Conduct is intended to be a stand-alone document that highlights, summarises and refers to the key patient engagement principles, rules and recommendations for collaboration presented in the different PARADIGM documents in the Toolbox in a comprehensive, understandable format.

Fact Sheets summarising the content of the different documents can be found in the Annex of this Code of Conduct. It should be read in conjunction with these.

Summary of the content:

This code of conduct contains sections on the following topics:

- Ethical Principles for Patient Engagement in the Life Cycle of a Medicine
- Contractual Framework
- Competing Interests, Conflict of Interest, and Conflict Management
- Intellectual Property, Confidentiality and Data Protection
- Access to Information and Transparency
- Accessibility of Patient Engagement Opportunities
- Representativeness
- Competencies and Capacity Building
- Adherence to the Code of Conduct
- References
- Annex 1: Fact Sheets of PARADIGM Documents

Key messages:

This Code of Conduct describes the essentials for meaningful collaboration of all stakeholders involved in patient engagement activities within medicines development.

Adherence to this Code of Conduct is essential to ensure an open and fruitful interaction of engaging partners with patients and their representatives.

All stakeholders of the patient engagement community should voluntarily integrate the rules of this Code of Conduct into their collaborations and insist on observance, especially in cases of non-compliance.

Working with Community Advisory Boards: Guidance and tools for patient communities and pharmaceutical companies

Background/Rationale for the document:

Community Advisory Boards (CABs) can improve research by providing direct and independent advice from the community of patients about different aspects of a clinical trial in ways that are more inclusive from the perspective of patients. Setting up and running a CAB requires careful planning, organisation, follow-up, monitoring and evaluation.

Objective of the tool:

The objective of this toolkit is to offer information, material and references that can support patient communities and pharmaceutical companies with different backgrounds (such as different levels of expertise, or from different disease areas) interested in setting up, running or engaging with CABs.

Summary of the content:

The toolkit on Community Advisory Boards (CABs) contains 8 different documents (1 guidance and 7 other tools):

The CAB Guidance contains three different sections. Readers can consult the entire guidance document as a general guiding tool for CABs or use the separate sections according to their needs and specific focus in engaging with patient communities.

CABs at a "glance": This tool is a brief summary providing a high-level overview of how a CAB operates.

Comparative tables for three existing CABs: This table provides information about three different approaches for setting up or running a CAB.

Checklist of tools and resources: This tool includes a list of templates and documents which can be useful when working with CABs.

Reflective questions and tracking tool: This tool contains a set of "reflective questions" and a "tracking table". It aims to stimulate reflection about different aspects to consider when setting up/running or collaborating with CABs.

Value-adding factors of a CAB from a pharmaceutical company perspective: while CABs are established to encourage patient engagement, they also offer a unique way to provide input in the development process for companies. This tool gives an overview of what CABs can deliver and how from an industry perspective.

Practical briefing guidance for industry: This tool refers to what company representatives need to consider and how to get prepared for participating in a CAB meeting.

Examples of successful outcomes of CABs and industry interaction: This tool describes three case examples of how CABs have been instrumental to provide timely patient input to change the course of the studies leading to successful outcomes.

Key message:

This toolkit intends to provide a basic set of instruments for the initiation and development of CABs. Representatives of patient organisations and pharmaceutical companies (as well as other stakeholders) are invited to consult and use this toolkit as a whole or consider its individual elements according to their needs and interests.

Patient Engagement in Early Dialogues: Tools and resources for HTA bodies

Background/Rationale:

Early Dialogues with regulators and health technology assessment (HTA) bodies are a well-established processes in which medicines developers have the opportunity to discuss their research plans and gain advice and feedback on their planned approach. Patient engagement and involvement in these dialogues is needed to ensure that patient experience, perspectives and knowledge is captured as part of this dialogue.

Engagement of patients in these Early Dialogue processes is an emerging discipline among HTA bodies, with a range of methods being piloted and used. There remains a clear need to provide adaptable tools and resources to simplify patient engagement processes for HTA bodies and provide guidance on suitable methods and approaches.

Objective of the toolkit:

The tools in this toolkit are for HTA bodies to adapt and use when engaging patients in Early Dialogue processes. Each tool has been created to be succinct and is provided in Microsoft Word so that HTA bodies can amend or add to each tool based on their own specific processes and needs.

Using this tool, HTA bodies will be able to adapt the guidances, checklists and fact-sheets to their own specific process, offering them a fast route to develop the resources needed to engage patients in Early Dialogues.

Summary of the content:

This resource contains three main sections covering the rationale for engaging and involving patients in Early Dialogues, an overview of the main methods used to engage, and a set of templates and checklists related to various methods:

- Rationale for patient involvement in HTA Early Dialogues (LINK)
- Methods used to engage patients in HTA Early Dialogues (LINK)
- Resources for HTA bodies to engage patients in Early Dialogues (LINK)

Outcomes/ Key message:

There is a clear rationale for involving patients in Early Dialogues. A range of tools have been developed to support HTA bodies to overcome barriers to engaging patients in Early Dialogues. These tools should be reviewed and adapted further in response to research, evaluation and stakeholder experiences as this relatively new field develops.

REPORTING AND EVALUATION

Patient Engagement Monitoring and Evaluation Framework

Capturing the 'return on engagement' is complex, given the many factors that influence the impact of patient engagement. This Patient Engagement Monitoring and Evaluation Framework, with metrics, was created to help partnerships between patients and/or patient organisations, bio-pharmaceutical companies, regulators and health technology assessment (HTA) bodies to self-evaluate the progress and impacts of patient engagement in the medicines development lifecycle and thereby support learning to facilitate meaningful patient engagement, understand the pathway to impact of patient engagement, demonstrate better decision-making in medicines development and assess the return on engagement for all stakeholders.

The tool consists of 87 metrics organized across four key evaluation components. Each metric is accompanied by a description and possible methods for monitoring and evaluating its progress. There is no 'one size fits all' set of metrics appropriate for every initiative or organisation. Different metrics are grouped together in sample sets relevant to specific objectives of conducting patient engagement. These sets intend to guide users of the tool in creating an M&E strategy tailored to their patient engagement initiatives or programme. Users can decide to explore all 87 metrics or can use the sample sets of metrics as a starting point.

The tool enables users to select a tailored set of metrics that aligns with their specific objectives and provides meaningful information in their context. The framework can best be tailored by following the steps:

- **Step 1:** Determine the objectives of the initiative and the purpose of M&E
- **Step 2:** Develop roadmap from input to impact and select metrics with all involved in patient engagement
- **Step 3:** Identify suitable methods and create a M&E plan
- **Step 4:** Establish a feedback loop and consider context factors

Guidance for Reporting and Dissemination of Patient Engagement Activities

Background/Rationale of the document:

The complete and reliable reporting and dissemination of all patient engagement (PE) activities is essential to ensure transparency and enable continuous broad learning for all relevant stakeholders undertaking PE. Nevertheless, this is often a neglected area and there is less awareness about its relevance and value among those involved in PE. It is still often the case that information about how a PE activity was planned and carried out, its results and impact, and the lessons learned are not available or easily accessible in the public domain. When some of this information exists, it often lacks these important details.

There is a need for practical guidance and support to help organisations involved in PE to develop adequate reporting and dissemination plans so that the important outcomes and learnings from PE activities are more readily available in the public domain for the benefit of all stakeholders.

Objective of the toolkit:

The "Guidance for Reporting and Dissemination of Patient Engagement Activities" was developed to support organisations participating in PE activities in more effective and timely planning, reporting and disseminating of information about the PE activities they had been involved in.

The tool includes guidance principles, a checklist and a template that can be used in combination with an organisations' existing documentation.

Summary of the content:

This tool recognises and builds upon the work of other relevant initiatives on the topic of reporting and dissemination of PE. However, this content is specific to PE in medicines development. It consists of three elements:

- **Guiding principles** covering themes such as:
  - the dissemination strategy, process and planning,
  - accessibility, style and format of outputs, (
  - translation into other languages
  - and involvement of patient populations in reporting and dissemination of PE activities.
- An **accompanying checklist** to help users in the planning phases, summarising the key considerations and principles to follow.
- A **template** to be used to promote consistent and detailed PE reporting, which includes the core elements (or minimum criteria) to be included in the reporting materials. An example of how the template could be completed is provided.

In addition, there is also signposting information to resources from key stakeholder groups.

Key message:

The reporting and dissemination of PE activities in the public domain in a timely, consistent and accessible manner is a crucial element in the evolution of PE in medicines development, yet it is not always appropriately addressed. Patients and patient organisations should be invited to and be supported in taking part in the reporting and dissemination of the PE activities where they have been involved.