RISING TIDE Foundation

Patvocates

Recommendations for patient organisations and patient advocates on their involvement in collaborative research projects

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Why should research projects engage with patient advocates and patient organisations?

The importance and merits of the involvement of patients, caregivers, patient advocates, patient experts and patient organizations in research and development are commonly acknowledged and offer benefits for all involved parties. Patient involvement also makes sure that clinical and medical research work more effectively together and deliver what most matters to patients. The discovery, development, and evaluation of new treatments is also improved if patients provide input throughout the design, conduct, and evaluation of studies and projects.

These improvements are based on the collaborative identification and understanding of patients' unmet needs, their research priorities, patient-centric clinical study design, and meaningful outcome measures and study endpoints. Patient involvement may prevent potential challenges that patients may face during the conduct of a study. Patient involvement also strengthens the public credibility of the evidence generated, enables more effective dissemination of research results outside of scientific target groups, and strengthens uptake and use of research outcomes in clinical practice.

How can patient organisations or advocates engage in research projects effectively?

There are different methods and models how patient advocates and patient organisations can engage in the different phases of collaborative research projects – while research projects are being designed, when collaborative groups apply for funding, when applications are being reviewed, and when research projects are being implemented. Patient engagement can be established in the funding framework, partnering concept, project design, grant application, application review, project implementation, and dissemination of project outcomes. It may also require training for patient advocates to contribute to research projects effectively, and training for researchers on how to involve patients in the most effective manner.

This guidance document was developed for patients and patient organizations in national and international disease-specific or cross-disease settings to prepare for and implement patient involvement during the grant application phase and implementation phase of research projects. It is structured into five sections:

- **Organizational models and coordinating, contributing and advisory roles in research projects with examples for potential contributions** of the patient community to a research project.

- Patient engagement in the **definition of research questions and topics of Calls for Proposals**, and in the promotion of Calls for Proposals that Patient Engagement will happen.

- **Identifying researchers, collaborative projects and patient partners for collaborative projects**, and how they may find each other during the application phase.

- **Involvement of the patient community during the application phase** before a project has been funded, including models of funding patient contributions during that phase (e.g. with grants for time or tasks).

- **Involvement as patient reviewers:** Potential assessment questions to help score applications for the level and quality of their proposed patient engagement. These questions should be listed in the application guide to help applicants in developing their patient engagement plan for their grant application.

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1. Glossary

Term	Definition
Patient engagement	Patient and public engagement covers the various ways in which the activity and benefits of higher education and research can be shared with the public in a two-way process. Engagement encourages researchers to listen and interact with the general public. Engagement also helps discussion with the public at a general level and to be able to talk about topics like research ethics. Public engagement can include opportunities for researchers to discuss their preliminary ideas for future studies. Researchers might also get people involved as contributors and in conducting part of a research project as "citizen scientists".[1]
Patient involvement	Patient and public involvement means that research is carried out "with" or "by" members of the public, rather than "to", "about" or "for" the public. The word "public" can refer to patients, potential patients, caregivers and people who use health and social care services. It can also refer to somebody from an organization who represents people that use services, and members of the public. Patient and public involvement focuses on a specific research project, program or process.[1]
"Involvement" as used in this document	Involvement in clinical trials/clinical research, and basic and translational research.
Patient	The term "patient" is often used generally. It does not reflect the input and experience that patients, patient advocates and patient organizations use when working (collaborating) with other groups. In this document, "patient" includes individual patients, caregivers, patient advocates, patient organization representatives and expert patients (discussed in section 2.1). When an individual patient is engaged, it is suggested that the relevant patient organization, if one exists, is informed and/or consulted to provide support and/or advice. The type of input and mandate or scope for the involved person should be agreed in any collaborative process prior to engagement.[2]
Patient community	Formal and informal networks of patient organizations and patients, patient advocates, experts etc.
Call For Proposals	A Call for Proposals (CFP), sometimes also called Request for Proposals (RFP), is a formal, structured procedure by a funding institution that invites research teams to submit proposals for carrying out a specific research project, based on specified goals, requirements, deliverables, budgets and other terms. The goal of a Call for Proposal is to ensure that the funding institution can chose the best project amongst competitive bids.

[1] Adapted from https://www.spcr.nihr.ac.uk/PPI/what-is-patient-and-public-involvement-and-engagement
[2] Adapted from https://www.frontiersin.org/articles/10.3389/fmed.2018.00270/full#:~:text=EUPATI%20focuses%20on%20education%20and,friendly%20information%20for%20the%20public.

2. Potential roles of patients to research projects

Patients, caregivers, patient advocates, patient experts and patient organisations can play a governing, partnering, advising or reactor role in a collaborative research project. Which role works best for the individual project depends on the desired contribution and engagement level.

The following list of roles and functions of patients in patient-centric initiatives is adapted from DIA recommendations:

Patient role	Examples	Engagement level
Partnership role	● Patients provide consultation before and during a study on outcomes of importance, study design, etc. ● Patients are paid investigators or consultants ● Patients have a governance role and are part of the project's decision making ● Patients are project partners and responsible for part of the project work	High
Advisor role	● Patients serve as advisory committee members or provide advice prior to a study on outcomes of importance and study design, but have no leadership role or governance authority	Moderate
Reactor role	● Patient input is collected through surveys, focus groups or interviews rather than consulting patients directly or before a study, on study design and important outcomes ● Patients are asked to react to what has been put before them rather than being the source of the idea	Low
Trial or study participant	● Patients are recruited or enrolled as study participants, but are not asked for input, consultation or reaction	None

Adapted from: http://synapse.pfmd.org/resources/considerations-guide-to-implementing-patient-centric-initiatives-in-health-care-product-development/download

Note that the patient roles listed above may also have to be adapted to current requirements and practice of patient involvement with stakeholders in collaborative research projects, or e.g. with research funders, the pharmaceutical industry, and regulators.

2.1 Defining the term "patient" in patient engagement

The term "patient" is often used generally. It does not reflect the different input and experience that patients, patient advocates and patient organizations bring in when working with other healthcare stakeholders. To clarify terminology around the different contributions, the European Patients' Academy (EUPATI) has provided the following categories for the term "patient":

- **"Individual Patients"** are persons with personal experience of living with a disease. They may or may not have knowledge in research or drug regulatory processes. Their main role is to provide experience on their disease and treatment.

- **"Caregivers"** 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 given responsibility to express the collective views of a patient organization on a specific issue or disease area.

- **"Patient Experts"** have both disease-specific expertise and knowledge in research and/or drug regulatory affairs through training or experience. For example, EUPATI provide training for patient experts in the research and development of medicines.

Adapted from: https://www.frontiersin.org/articles/10.3389/fmed.2018.00270/full

It is important to understand that "lay patients" without previous research experience can contribute important insights at any stage of a research project. This "lay engagement" can happen in various ways – public community interviews, focus groups, or qualitative (descriptive) input are useful methods.[3]

However, useful involvement in the design or conduct of a research project often requires more than just personal experience. Wider community insights and/or technical training may be additionally needed. The different types of patient engagement in research projects described in this guide requires a significant level of know-how and expertise from the patient contributors. The level of insight of each patient contributor varies in their understanding of the concerned patient community.

Therefore, expectations of individual knowledge, experience and community insight to fulfil the role of a patient contributor need to be clarified before any engagement is initiated, and patients and patient organizations should have their own procedures and methods for developing and keeping a registry of the different skills and knowledge areas where they can be involved. Eventually, it is left to the discretion of the project leader to choose the most adequate role and model for the interaction in a specific project.

In the following sections, we describe possible partnership, advisor, and reactor roles of patients in research projects. Although these roles may not apply in all situations, examples of all of them occur in various research projects within and outside the EU.

2.2 Partnership roles

Patients can provide useful input to research projects by taking leadership roles within collaborative research teams which makes them part of the overall governance and decision making of such research projects. These roles are increasingly accepted by members of a collaborative research project, and endorsed by funders, e.g., the Innovative Medicines Initiative (IMI).

2.2.1 Coordination and supervision

- **Project Coordinator, Chair, Co-Chair or Member of the Governance Board** – patients may be full members of the governing boards (e.g. Steering Committee or

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

Management Team). In some projects, they may also take the role of project coordinator, or chair or co-chair of the governing board.

- **Coordinator, Chair or Co-Chair of a Work Package or Subproject.** Many projects are structured around well-defined work packages or subprojects. These are a group of related tasks within a collaborative research project often organized as sub-projects with defined objectives, deliverables, and milestones. Patients can play a key role in research projects by coordinating or co-leading such work packages or subprojects.

- **Coordinator of an Advisory Board.** Patients can also take a chairing role of project advisory boards of research projects, e.g. the patient advisory board or the ethics board. Coordination of such boards go beyond the advisory role, given the chairs of those boards usually have an institutionalized role in the governance of a research project.

2.2.2 Project member partner and paid contributors

Patient organisations or patient advocates can become full project members of a project. IN that role, they are responsible for delivering part of the paid project work to implement the project, e.g. by delivering specified contributions and deliverables of work packages or subprojects, based on defined tasks, milestones, output and budgets.

Here are some examples of contributions that patient organisations and patient advocates may provide as project members and contributors:

Co-creation of the research design

- Coordinate pre-involvement planning
- Coordinate, implement and analyze patient preference studies
- Selection of outcome measures and how and when to measure them during the research phase
- Co-creation (joint development) of research design and related documents
- Pilot testing of research elements like surveys, focus groups etc.
- Assessing the inclusion and exclusion criteria for prospective participants in research
- Produce a lay summary of the research project

Coordination of overall patient community engagement

- Coordinate the involvement of the wider patient community (e.g. additional patient advocates, patient experts or patient organisations) in activities, work packages, subprojects or advisory boards of the research project. Typical examples are acting as a Patient Involvement Hub, running Patient Advisory Boards,

Co-creation and interpretation of evidence and data

- Coordinate, conduct and analyze pre-activity research, e.g. patient preference studies, surveys of patients and caregivers on unmet patients' needs or expectations
- Coordinate or facilitate focus groups
- Collect additional registry data
- Support recruitment into a study, trial, or other engagements
- Contribute to data analysis and/or interpretation of data/preliminary findings
  Conduct analyses of survey or registry data
  Community review - review of data analyses, articles and presentations from the patient community's perspective

2.2.3 Communication and dissemination of project outcomes and recommendations

- Presentation about the patient perspective on project work or outcomes at international conferences, meetings, symposia
- Authoring or co-authoring scientific publications on outcomes of the project
- Collaborate on communication activities or awareness campaigns
- Disseminate project outcomes in lay friendly language to non-scientific communities

2.3 Advisory roles

Patients can provide advisory roles in the design and implementation of a collaborative research project. Typical examples are being members of project advisory boards, scientific advisory boards or ethics advisory boards that meet in regular intervals to provide advice on project plans, project outcomes, ethical dilemmas, safety issues.

Involvement as advisors may be implemented at different time points, may be time limited, or may cover the entire project duration.

2.4 Reactor roles

Patients can act as reviewer of research work and propose modifications and can provide individual patients' or caregivers' perspectives through surveys, focus groups or interviews. This role is different from any co-creation roles mentioned before because patients mainly react to or review concepts and/or study documents that have been developed by others, rather than consulting patients directly about their ideas before a study design has been created and almost completed or after important outcomes have been completed.

2.5 Trial or study participant role

The enrolment of patients as trial participants into a clinical study is not considered as patient involvement or involvement and is mentioned here only for completeness. The patient community can support participant recruitment by disseminating trial information in lay language.

Care is required if a patient is engaged in a double role as both a study participant and as a contributor to the design and implementation of a research project. There may be a conflict of interests and possible bias in the study results if the patient works as an expert and is also enrolled in the study. We do not advise this double role but are aware that by example in rare diseases it can be difficult to avoid.

3. Choice of models of patient involvement in research projects

This section will help the patient community to develop and agree on a meaningful model on patient involvement for a specific research project. It is based on the classification of patient roles and contributions above. Examples are also added from previous research projects which include relevant patient involvement and input.

3.1 Choosing suitable models of patient involvement in research projects

Applicant teams are encouraged to think carefully about the activities across the whole project lifecycle that the patient community could undertake. Short term activities are easy to define upfront, but it is more challenging to think about sustained involvement across the entire project. The same is recommended for patients and patient organizations, preferably in close cooperation with the applicant teams.
Therefore, it is important to think about the most suitable **model of patient involvement** in a clinical or other research project. The choice may depend on the particular research project and the specific tasks required.

The table below gives examples for the different roles described here. Patient involvement is organized in a systematic way by placing patients into different leadership or advisory roles for a given research project. The table also provides information on the level of impact and resources required. The more complex the role and the greater the degree of responsibility, the higher the workload and more intensive effort required. Some benefits and limitations of particular models are also outlined. Choosing the right model will depend on the nature of the project, the intended outcomes, the available resources, and the time when patient involvement becomes an active part of the project. Here, the basic rule of “the earlier the better” always applies, especially when basic research is considered.

The different examples in the table confirm that it is possible to devise a theoretical framework for patient involvement as described in Section 2 above. However, many actual solutions are implemented as hybrids or mix of more than one model. The ideal model may be determined by the purpose and conditions of the project. The recommended models should be treated with a degree of flexibility depending on some key factors:

- Objectives of the research project
- Capacities and level of expertise of the patient organization and/or the patients involved
- External / third party requirements about patient involvement in research
- Clear definition of work processes and workflows
- System readiness of the applicant and the patient organization to be able to work together

3.2 Involvement models in research projects: roles, impact, effort, pros and cons

From an organizational standpoint, there is a number of different effective models how patient involvement can be established and implemented in collaborative research project. Each model has perceived benefits and drawbacks that have been observed in existing projects, e.g. in terms of influence, impact and workload of the contribution from the patient community.

The following list describes potential involvement models that have been implemented frequently. These are practical examples we are most used to - there may be adapted modalities of patient involvement that are more informal, or more creative, innovative, or inclusive.

Model	Description	Impact, Effort, Pros, Cons
Project coordinator	Patient organization leads and coordinates the whole project	Impact: very high Effort level: very high + Most influential role, e.g., patient-led research project – Highest workload, skills, experience and commitment required Example: European Patients' Forum in EUPATI, https://www.imi.europa.eu/projects-results/project-factsheets/eupati
Steering committee member	Patient organization / advocate is member of the governing committee of the project - and may be funded for the work delivered	Impact: very high Effort level: very high + Patients are part of all relevant strategic decisions – High workload, skills, experience and commitment required – Often not funded for the work delivered. Example: ART CC, HIV cohort collaborations, http://www.bristol.ac.uk/art-cc/
Work package leader	Patient organization / patient advocate coordinates a specific work package in the project	Impact: high Effort level: high + Patients with responsibility to coordinate and deliver defined elements of the project e.g., a work package on patient involvement, needs assessment, external communication + Patients organizations (sometimes) funded for the work delivered – High workload, skills, experience, and commitment required Example: LeukaNET in the IMI HARMONY Big Data project, https://www.harmony-alliance.eu/patient-cluster, or Myeloma Patients Europe in SISAQOL-IMI, https://event.eortc.org/sisaqol/
Research project member	Patient organization/patient expert is a full member of the research project	Impact: medium Effort, skills, experience level: medium + Full participant of the overall project team + Patient organizations (sometimes) funded for the work delivered – Limited influence on decisions, usually only through project meetings of work packages and annual assembly Example: Association Française du Gougerot Sjögren – AFGS in H2020 NECESSITY, https://www.necessity-h2020.eu/patient-involvement/

Role	Description	Impact, Effort, Pros, Cons
Patient involvement hub	Patient organization/patient expert is a full research project member, coordinating contribution from other patient organizations outside of the project team, e.g., indication specific	Impact: high Effort, skills, experience level: high + Full participant of the overall project team + Patient organizations funded for the work delivered +/– Does the administration and coordination workload for the wider patient community Example: LeukaNET in the IMI HARMONY Big Data project, https://www.harmony-alliance.eu/patient-cluster, or Myeloma Patients Europe in SISAQOL-IMI, https://event.eortc.org/sisaqol/
Associated project partner	Patient organization has a partnership agreement with the research project	Impact: low Effort, skills, experience level: medium + Patients may prefer as it may take less time + Easier to combine with other activities – Patient organization usually not funded for the contributions and work – Usually not much influence on decisions of the project – Usually no compensation for time, so little time investment possible Example: Patient Advisory Group of four patient organizations in IMI PREFER, coordinated by ECPC, https://www.imi-prefer.eu/stakeholders/patients/
Advisor / advisory board member	Membership of ethics committee, scientific advisory board, project advisory board, data safety monitoring board.	Impact: low Effort, skills, experience level: medium + Patients' expertise provided into specific committees, but no participation in active work – Usually no compensation for time, so little time investment possible – Advice only – frequently little influence on decisions and no accountability whether advice is actually used and implemented by project Example: Patient Advisory Group of four patient organizations in IMI PREFER, coordinated by ECPC, https://www.imi-prefer.eu/stakeholders/patients/

3.3 Developing an organizational structure and terms of reference

The composition and process of patient involvement differs based on the nature of the project and the engagement model chosen. However, the expectations from all involved parties

always need to be clear and realistic. Patient involvement should be recognized by all partners as an integral and equal part of the project.

To make sure meaningful patient involvement actually happens, it is recommended to provide a **clear organizational structure and terms of reference for patient involvement** from the start of the project. Also, **tasks, rights, and responsibilities as well as timelines** should be agreed in writing.

Given patient community members may be connected as individual experts and not necessarily through a professional organization, it is helpful if a patient organization or other project partner is being assigned as **patient involvement coordinator** of the collaborative project. Their responsibilities are to define who should coordinate meetings, to develop terms of reference on patient involvement, and to ensure that the project infrastructure is accessible to the patient partners and the patients are equipped with the required know-how. The patient involvement coordinator will also ensure regular communication with the overall project management and the patient partners. They should also ensure that involved patient partners do not become detached from the situation, especially when patient partners are not directly connected to the research being conducted.

4. Patient engagement in calls for proposals

Issues covered in this section include:

- **Patient engagement in the definition of research questions and calls for proposals (CFP)** to ensure calls for proposals address patient-focused[4] questions or areas.

- **Patient engagement in the dissemination of published Calls for Proposals in the patient community**, to raise sufficient interest to collaborate with researchers in applications.

- **Patient engagement in the definition of the expected roles for patients in the selected Calls for Proposals**

4.1 Patient engagement in the definition of research questions

There is a strong need for patient communities to be involved at the earliest stages while research priorities and objectives are being defined and set.

From a patient organization's perspective, this means defining terms and conditions for a Call for Proposals which ensure patient involvement truly happens. Mechanisms and procedures are proposed that ensure patients' needs (unmet medical needs and first-hand experiences) are adequately reflected in the setting of research priorities and objectives. For this, it is essential that patients and patient organizations can communicate these needs and experiences in a reliable and credible way, relying on the techniques and principles of evidence-based patient advocacy[5].

Some patient organizations already participate in this type of work. However, their participation may be to a limited extent and their involvement is often informal. Good personal relationships may be maintained by key patient opinion leaders and patient experts with researchers and

[4] https://www.fda.gov/media/131230/download
[5] https://wecanadvocate.eu/academy/evidence-based-advocacy/

clinicians. This relationship may be the basis for becoming partners or even initiators of research ideas and projects. We propose targeted development and some formalization of such relationships.

4.2 Patient engagement in defining Call for Proposal topics

Patient engagement should be the goal when defining topics for Calls for Proposal of funding programs. This ensures the Call for Proposals addresses patient-relevant questions or areas. To achieve patient relevance, the patient community should be involved in the process the same as every other expert group like clinicians.

Typical patient input could be elicited through the following mechanisms:

- Input into the **scientific strategy** of the funding body (annual research priorities, topic development etc.).
- Definition of the **overarching goals, aims, scope and structure** of a specific Call for Proposals topic.
- Description of **the patient relevance of the expected** outcomes of funded projects, e.g., how the Call for Proposals' projects intend to address the unmet needs of patients**.**
- **Definition of patient roles in the research topic.**
- Review of related documents of a Call for Proposals to ensure they are accessible and understandable to patient advocates. Also, in language or jargon that does not exclude patients **when it comes to patient engagement** at later stages.
- Definition of the **evaluation criteria** of grant applications, e.g., on patient relevance of the research, and the patient engagement plan of the applicant.
- After the decisions: criteria for evaluating patient engagement and evaluating research as part of the annual assessment of the research progress.

Specific questions can be collected from different reviewers. Establishing a small team of patient/public expert reviewers with experience of the specific indication could be a promising strategy. Another way to get involvement in the earliest stages is the organization of partnering meetings as described in a later section. It might also be achieved through fostering and promoting more open and better relationships between research and patient communities. The following sections provide further recommendations for this type of work.

4.3 Promotion of Calls for Proposals in the patient community

The patient community should be made aware of Call for Proposals, so they are more likely to engage in collaborative research projects.

There is a general problem regarding the accessibility and availability of information about planned or ongoing research initiatives and calls for patient communities. This was highlighted in January and February 2021 by the funding body Rising Tide who conducted a series of interviews with a panel composed of expert patients, representatives of funders and academia. In these interviews, 12 respondents from all stakeholder groups expressed concerns that the earlier the stage of a research initiative, the less information was available. It was increasingly more difficult to learn about these initiatives as one moved to the earlier stages. While efforts to obtain this information can be expected from the patient organizations to a reasonable extent (pull), there should also be more proactive dissemination and outreach activities from the funders and applicants (push).

The ways in which academic institutions and funders disseminate information on the content of research initiatives tend to be erratic, informal, and unreliable. The processes described below use a multi-pronged strategy:

- **Building an inventory of ongoing research with researchers, academia and patient organizations:** Proactively contact academic communities and research groups (including patient organizations) to make an inventory of their research initiatives and to increase awareness of an upcoming Call for Proposals.

- **Systematic communication with patient communities:** Contact patient communities to inform them about engagement opportunities and deadlines in their areas of interest. They can assist in the compilation of lay language versions.

5. Bringing researchers and patient communities together

This section recommends how funders can facilitate researchers to identify relevant patient partners for the application, and for implementing the project should it be granted.

Different ways how this could be implemented are:

- **Setting up and using a patient partner database** which could be used to suggest patient partners for potential applicants of a Call for Proposals.

- **Partnering meetings, information days and matchmaking services** could be set up once a Call for Proposals has been published to give researchers and patient community members the opportunity to discuss a research collaboration.

- **Providing pre-application grants to patient contributors** could eliminate one of the main barriers to the involvement of patient organizations in the pre-application phase: the lack of funding and the resulting risk of non-participation.

To support these approaches, a **platform** could be set up so that it registers information about calls, research initiatives, and potential partners in research and patient advocacy (i.e. a **"clearing house"**). This platform would support matchmaking between the different potential partners, thereby **linking the partner database with the clearing house** of research information.

5.1 Setting up and using a Patient Partner Database

It is possible to start by **setting up and using a Patient Partner Database** to interact with experienced patient advocates and patient organizations in research or funding institutions. This database could be used during the definition phase of a call topic to recommend patient partners to potential applicants to a Call for Proposals. It could also be used to involve patients as review panel members for working on proposals, and on ongoing and completed projects.

Similar patient pools and databases have previously been built by: the Innovative Medicines Initiative (IMI Pool of Patient Experts, https://www.imi.europa.eu/get-involved/patients/imi-pool-patient-experts), the European Medicines Agency (EMA Experts' Stakeholder Database, https://www.ema.europa.eu/en/partners-networks/patients-consumers/getting-involved) and the Swiss National Science Foundation's (SNF) Patient/Public Reviewer Pool. The IMI and SNF databases can be used as models but are not openly accessible. The EMA database is currently accessible to third parties.

A more sophisticated matchmaking service or partner database may become available in the future from the European Patients' Academy **(**EUPATI) or Patient Focused Medicines Development (PFMD). Alternatively, it has been proposed to discuss building a joint patient partner/expert pool with other funding institutions to perform these tasks.

5.2 Who would be in a Patient Partner Database?

Patients, caregivers, patient organizations, patient advocates or patient representatives could apply to be listed in the database for a call for applications. The database would be accessible to the funding body (e.g., Rising Tide) but only for the specific purpose of engagement in the funding program, and not publicly or for marketing purposes. The available information enables the funder's office to rapidly identify patient experts with the most suitable profile for a specific task.

To be eligible as a patient partner they should:

- Be a patient, a family member or taking care of a patient (caregiver), or a patient representative of a patient organization in a specific therapeutic area.
- Have a specific interest in one of the disease areas.

In their application, the patient experts may state:

- Their individual experience as patient and caregiver, if any.
- Their motivation for applying for membership in this patient partner database and participating in the funding activities.
- Their knowledge and/or experience of clinical research and innovation activities in general, the clinical development cycle, and research ethics.
- Their prior experience of working/interacting with different stakeholders in clinical development e.g., with academic researchers, industry Research and Development, clinical institutions, and regulatory bodies.
- Their prior experience of patient engagement in research projects or with funding institutions.

A check of all applications may first be carried out to make sure all the minimum criteria listed above have been fulfilled. Applying patients that meet the eligibility criteria can become part of the patient expert database. From this pool, the funding institution will draw individual experts for specific assignments and activities as and when needed.

Data protection and withdrawal
All data captured must be obtained and stored according to the EU's General Data Protection Regulation (GDPR) rules. Any individual may request to be removed from the database at any time. A contact address must be given.

Third party databases
Building and maintaining a patient partner database requires considerable effort. The most effective way might be to rely on locally available resources. Partnering with the EUPATI Foundation could be an option in Europe and contacting the National Health Council in the US is worth considering.

5.3 Partnering meetings and information days

Partnering days of the funding institution
Once topics of a Call for Proposals have been published, **information days, partnering/matchmaking meetings and webinars** provide different ways to ensure potential

applicants understand the CFP content. Potential applicants should understand the topics of the Call for Proposals, the funder's rules and procedures, and the expectations and requirements of applications. The partnering events also give researchers and patient community members the opportunity to meet and discuss research collaboration.

The funding institution should invite the patient community to the meetings or establish a consultation process to ensure that funded projects are relevant. It should be emphasized at the meeting that the patient community is able to contribute value in terms of their unique insights, knowledge, and resources. Researchers are often unaware that early and systematic patient engagement increases the likelihood of a successful application and clinical research project.

In addition, **the funding institution should identify and make relevant patient organizations aware** of published calls and partnering days that may cover specific research in their area of interest. Patient organizations do not usually follow scientific funding institutions and may be unaware that a call topic in their area of interest has been published and they may be unaware about a funding program's specific deadlines.

It is therefore recommended for patient organizations (and even individual patients) to **proactively monitor such announcements** and invitations, and to attend the meetings through representatives that are knowledgeable about the given research topics.

The organization of regular online and face-to-face events on specific topics will gradually create a lively and vibrant "marketplace" for the exchange of ideas, initiatives and needs. Although results may not always be immediately measurable, longer term benefits will become apparent. Benefits will include research projects that are more relevant to patients (hence the end users) and an easier, more welcoming interaction across different communities. Communities such as researchers and patients may otherwise be confined to silos.

Academic project leaders should understand the different roles patients can play in the project life cycle. Depending on the role, there will be specific criteria for finding the most suitable patient partners. Lay patients can play an important role in focus groups and are informative at the project planning and implementation stages. Research-experienced patients may be active as implementation partners and can contribute to work packages. Very advanced patient experts may also be suitable for advisory roles from the application and planning phase to publications and dissemination. **Training of patients in efficient patient engagement processes could be provided** in close collaboration with research institutions and funders active in the field of training or by patient organizations themselves.

Identifying patient partners on patient engagement platforms and at events using **existing platforms, partnering meetings and services** may also provide the opportunity to bring together researchers and patient organizations. These approaches may also make good platforms to create awareness about the topic of the Call for Proposals. For example:

- **PFMD SYNaPsE patient engagement hub:** The global multi-stakeholder initiative on patient engagement, Patient Focused Medicines Development (PFMD), provides SYNaPsE, PFMD's Global Mapping and Networking Tool. The user-populated platform categorizes and maps over 500 patient engagement initiatives, over 900 organizations active in patient engagement, and more than 2400 individuals active in patient engagement. SYNaPsE may allow identification of individuals or organizations that may be interested in a specific call topic. https://synapse.pfmd.org/

- **Patient Engagement Open Forum (PEOF):** The PEOF is an annual event held by PFMD, EUPATI and European Patients' Forum (EPF), that brings together all stakeholders across the patient engagement ecosystem. The event covers

frameworks, tools, recommendations, and good practices. The PEOF may be a good opportunity for researchers to identify patient organizations. https://patientengagementopenforum.org/

- **Pan-European patient advocacy organizations:** Many pan-European patient advocacy organizations run annual conferences, workshops or open forums focused on patient engagement. These events present a good opportunity to identify patient organizations interested in a specific research program. Contacting the EPF (www.eu-patient.eu) or the Workgroup of European Cancer Patient Advocacy Networks (WECAN, www.wecanadvocate.eu) or EURORDIS (www.eurordis.org) may help.

- **EUPATI matchmaking service:** EUPATI is currently developing a “matchmaking service". It facilitates collaboration between the graduates of the EUPATI Patient Expert Training Course and researchers in regulatory agencies, academia and industry. EUPATI can assist in connecting with the right person for the task. https://collaborate.eupati.eu/home/matchmaking/

In the future, the funders' database of suitable and available patients and patient experts could be linked to the clearing house that registers information about calls and research initiatives. The semi-automated and non-commercial database could build on automatic matchmaking processes and informal deliberations on the proposed matches. However, such a solution is not yet available.

6. Patient involvement during the project application phase

6.1 Patient contributions during the project application phase

A collaborative research project usually starts with a core team of experts that already know each other well and that have developed an idea for a collaborative research project. The decision to collaborate on a research project may be sparked by a public Call for Proposals of a funding institution. The core team then usually identifies additional partners, institutions or experts that may complement the core team by bringing in additional competences, resources or other characteristics that will be required to implement the research project successfully, or that may be defined as a requirement in the Call for Proposals.

During the pre-submission phase in which the collaborating partners compile a thorough and complete proposal to for submission to the funding institution, key decisions on the research question, the objectives and intended outcomes, the overall project structure, its governance as well as tasks and responsibilities of all involved partners are taken.

To ensure that collaborative research projects not only focus on scientific or structural questions, but on true needs of the patients as the ultimate user of healthcare services, research programs or institutions increasingly suggest or require to involve the patient perspective in the design, planning and conduct of those collaborative research projects. This is frequently the reason why the applicant teams then contact patient organisations to join the team in one of the other forms (see chapter “Models of patient involvement”).

As it is usually difficult to change the set-up and budget of a project after submission of the research proposal, it may be very important for the patient community to be involved already during this pre-submission stage. During the pre-submission stage, the patient community can contribute e.g. on:

- Pre-activity research (e.g. evidence on patients' unmet needs, patient preferences, gaps in care that supports the need for the research projects)
- Generation and refinement of the research hypothesis and objectives
- Co-creation (joint development) of research design, protocol, inclusion/exclusion criteria for potential patient participants in studies
- Selection of outcome measures, and how and when to measure them during the research phase
- Pilot testing of research elements like surveys, focus groups etc.

However, the work in this preparatory phase is usually not funded and the likelihood of a successful bid may be low. Therefore, the workload and expenses for participating in preparatory meetings and teleconferences of the applicant tram may create an undue burden to potential patient partners.

6.2 Funding the application efforts through pre-application grants to patient contributors

Patient organizations struggle to cover the costs arising during the application phase of a new project. This is because funding is not yet available, and members of the applicant team are usually investing time and resources into the application. While some patient organizations may be ready to absorb these costs on their part, this is not always the case.

To facilitate patient engagement during the design phase of collaborative research projects, funding institutions may choose to provide **pre-application grants** that would support patient organizations during this early phase with a budget. The budget could cover e.g. travel costs to preparatory meetings and the work time invested by staff, patients or consultants. A working contribution from these groups is required while the application is being prepared and/or submitted. Examples include: the authoring or iteratively reviewing (giving regular feedback) sections of the applications, generating, and providing required documentation, and attending coordination calls and sub-workgroups of the applicants. Such an approach could also improve the relevance of the application to the patients concerned.

A pre-application grant may not be an incentive for an organization to participate in an application. However, their participation helps to ensure the applicant is able to plan a meaningful patient engagement during funding and implementation of the project.

7. Patient involvement in the assessment of applications

Patient experts may engage with funders and researchers as review panel members when assessing grant applications that were submitted on a specific Call for Proposals. The patient reviewer's role needs to be clearly defined. For example, in the Swiss National Fund review team, patient reviewers focus on patient/public involvement aspects in submitted applications, similar to the biostatistician focusing on statistical aspects of an application.

Three steps are described in this section:

- Metrics to be used for assessing the level and quality of patient engagement of applications.
- How to identify and train patient reviewers.
- Fair compensation and acknowledgement of patient reviewers.

7.1 Metrics to assess patient engagement

The following potential assessment questions could be used to score applications for the level and quality of patient engagement. These questions should be listed in the application guide to help applicants in developing their patient engagement plan for their grant application.

Patient-centric design:

- How were patient advocates involved in the design and development of the application and of the project?
- Have the applicants assessed patients' unmet **needs, goals, concerns, or preferences**, and whether the research question reflects an unmet need within the patient population?
- Have the applicants described how the input from the patient community has influenced the **research design**?
- Were patient advocates involved in planning the **research question**? Have the applicants assessed if their **endpoint** is meaningful from a patient perspective, i.e. with regards to
    - health improvement
    - improvement of quality of life
    - improvement of societal participation and self-reliance
    - improvement of the care in general?
    - how can patients benefit from the research? Is this a "game-changer"?
- Does the study consider **patient subpopulations and patient diversity** to ensure the results from the research are useful and applicable to all relevant patients?
- Did the applicants consult with patients or representatives to see if patients would be **willing to take part** in the clinical trial? How will **study participants benefit** if they decide to enroll? / How attractive is it for patients?
- Does the study discuss a **"patient retention"** strategy and how will the applicant deal with patients leaving the trial for other reason than adverse effects?
- Is the research plan **feasible** from the perspective of the study participants with regard to:
    - the burden for the participants (questionnaires, tests, treatment)
    - the overall burden for participants during the entire study (number of contacts, time invested, logistics)
    - potential objections of study participants to participation (e.g. preference for a particular treatment)
- Is the **lay summary** for the general public written in a way that someone unfamiliar with research could understand the general scope of the study?

Patient engagement during the project:

- **In which ways and when** will the patient representatives be involved (member of safety board, steering committee, leader of a work package)? Is the model chosen likely to be **adequate, meaningful, feasible and effective** in the proposed project?
- How will engagement of patients be **supported and resourced**?
- Will the applicants consult with patient groups, care givers, patient organizations and/or patient advocacy groups for **recruiting** purposes?
- **How much training** does the project provide for patient partners? Are patient partners involved in determining which training is required and how it should be offered to the involved patient partners?
- Are patient representatives informed when endpoints (also secondary) or other parameters are **adjusted**?

- How will the patient community be involved in the **dissemination** (notification to other parties) of the project's results? Is there a proactive **dissemination plan** beyond scientific journals, e.g. conferences, the patient community and the public?
- How do the researchers ensure that everyone for whom the results are relevant (including care providers, professional associations or health insurers) can be informed of the results?

Evaluation of patient engagement:

- How will the applicant **evaluate the impact and outcomes of patient engagement** during and after the research project (e.g., surveys, interviews)?

7.2 Identifying and training patient reviewers

Qualified and knowledgeable expert patients could act as reviewers when reviewing research applications to funding institutions. For example, they could assess patient-related relevance of the research questions and intended outcomes or evaluate the patient engagement strategy of the applicant. These patient reviewers should be fully integrated into the multidisciplinary review panels and have equal weight and rights.

To ensure that reviews are consistent, all applications should be assessed based on the same criteria for patient engagement, patient relevance, and the use of metrics.

Some criteria that may help to choose a suitable patient expert for a given task are[6]:

- **Being a patient expert, patient advocate and/or representative of a patient organization** and having a deep insight into the patient community in a relevant therapeutic area. Insights into the unmet needs of the wider community is more important than having personal disease experience.
- **Having expertise in the processes of clinical research and innovation**, the clinical development cycle, and ethics.
- **Having prior experience of working/interacting with different stakeholders** in clinical development e.g., with academic researchers, industry research and development, clinical institutions, regulatory bodies.
- **Having prior experience of patient engagement in research projects or with funding institutions.**

It is also helpful if patient reviewers are prepared and trained in these assessment criteria. They should also receive training about the system of assessment and how to collaborate with other reviewers on a review panel. The patient organization, together with the funding body, should implement a training program and an onboarding process to acquire knowledge and skills for patient reviewers.

7.3 Compensation of patient expert reviewers

An organization needs to have a clear policy on reimbursement and compensation of patient experts. This also applies to patient organizations: their internal policies should include consistent guidance on the compensation of patients for their work.

Unless they decide otherwise, invited **patient experts should be entitled to a time-based honorarium, plus reimbursement of expenses** when invited to carry out reviews (e.g., for

[6] https://imi-paradigm.eu/PEtoolbox/identification-of-patient-representatives.pdf

travel, accommodation, and subsistence expenses). Allowances may be increased for experts with disabilities.

Compensation for patient reviewers should be in line with compensation for any other professional. However, exceptions may include healthcare professionals expected to act as scientific reviewers. For example, clinical experts and other members of the scientific community may review the applications in the context of their paid job. Patient expert reviewers may also qualify for compensation for their time.

Patients and patient advocates living with a chronic condition often must stop paid work. Sometimes patients have a lot of volunteer commitments in addition to their normal job. They may also have increased costs due to additional medical care, childcare, or other support needs. It is sometimes forgotten that patients and patient advocates do not usually receive a salary to cover the time they spend on advocacy work or research. If only travel costs and some other expenses are reimbursed for patient involvement, this is usually insufficient and will lead to a very limited availability of patients who may be able to contribute. Even patients and patient experts who are still working cannot do this work within the context of their paid job because they work in very different environments and in very different roles.

A common **"fair market value rate"** for the work of patient experts has not yet been established. However, an hourly non-governmental organization (NGO) rate in the range of 55-100 EUR has been observed as compensation for the work of patient experts on review panels or clinical research projects. Bigger funding institutions such as the Swiss National Fund use daily rates. Typical rates for patient experts' contributions to industry-sponsored research are up to three times higher. Fair market value rates usually consider individual expertise, level of training and education, total amount of time invested, complexity of tasks, country of origin, and other contributing factors. Review and research work is usually rated at the upper rate limit in terms of expertise.

An important consideration in compensation for patient experts is that the individual situation of the patient expert can be very different. It is important that the individual situation of each patient expert is assessed, and this assessment forms the basis of if and how they receive compensation.

For additional information see e.g. https://nationalhealthcouncil.org/fair-market-value-calculator/

7.4 Evaluation of patient expert reviewers' contribution

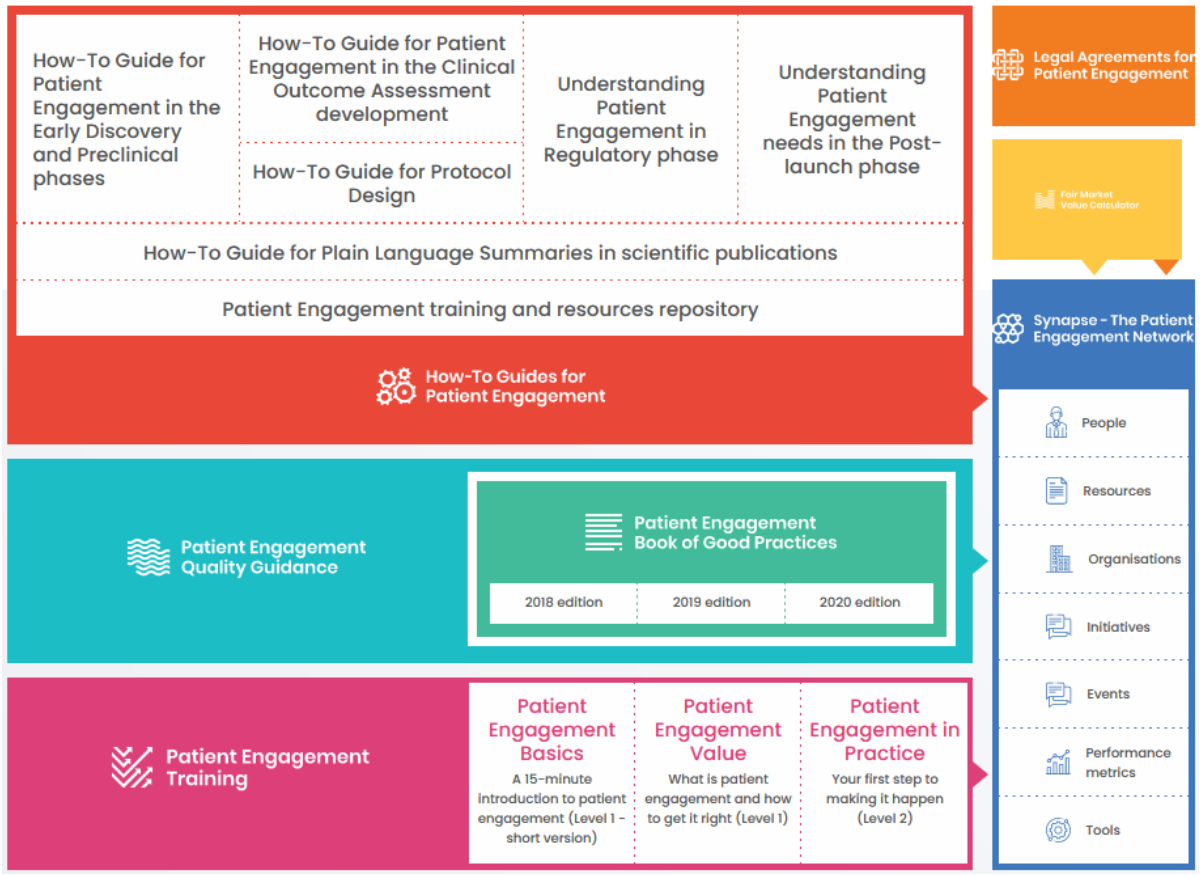
Implementing patient reviewers within assessment planning requires careful planning. A scientific assessor could act as mentor for patient reviewers in case they have questions. After a round of assessment, a thorough evaluation of the patient reviewer contribution is recommended. When onboarding new patient reviewers, already experienced fellows should be involved in the process.

8. Additional references and further reading

Here are some additional external resources where you can find examples, templates or other reference materials on patient engagement in clinical research projects.

8.1 Patient Focused Medicine Development (PFMD)

Patient Focused Medicines Development (PFMD) is a global multi-stakeholder initiative on patient engagement in research and development, established in 2015. PFMD provides a Patient Engagement Management Suite (PEM Suite), featuring practical tools to plan, assess and execute patient engagement initiatives. It includes “How-to Guides” on early discovery and preclinical phases, protocol design, clinical outcome assessment development, regulatory and post-launch phases, and a "Patient Engagement Quality Guidance" and various e-Learning modules on patient engagement.
See https://patientfocusedmedicine.org/pemsuite/



8.2 European Patients' Academy (EUPATI)

The European Patients’ Academy (EUPATI) is a patient-led, multi-stakeholder partnership focused on education and training on patient engagement in medicines research and development. It runs an annual "EUPATI Patient Expert Training Course" and an open-access multilingual "EUPATI Toolbox on Patient Engagement in R&D" that has served more than 4 million users around the world to date.
The EUPATI Toolbox is available in multiple languages at https://toolbox.eupati.eu/
Specifically, relevant articles and case studies in the EUPATI Toolbox include:

- **EUPATI Guidance Documents on Patient Involvement in R&D, Ethics Review, Regulatory and HTA:**
- https://www.frontiersin.org/research-topics/7005/the-european-patients-academy-on-therapeutic-innovation-eupatiguidelineson-patient-involvement-in-re#articles
- **Patient experts on Bioethics Advisory Panels:** https://toolbox.eupati.eu/resources/patients-involved-patient-expert-on-external-bioethics-advisory-panel/

- **HIV case study: Between sponsors and participants:** https://toolbox.eupati.eu/resources/patients-involved-between-sponsors-and-participants/
- **Patient engagement in Patient-reported outcomes (PRO) assessment:** https://toolbox.eupati.eu/resources/patient-reported-outcomes-pros-assessment/
- **Patient engagement in a rare disease registry:** https://toolbox.eupati.eu/resources/patients-involved-patient-organisations-input-on-a-rare-disease-registry/
- **EUPATI Patient Engagement Roadmap in medicines R&D:** https://eupati.eu/patient-engagement-roadmap/?lang=de
- **Being developed: Patient engagement in medical device development** (should be available beginning 2022)

8.3 PARADIGM Patient Engagement Toolbox

This toolbox centralizes all PARADIGM's co-created recommendations, tools and relevant background information to make patient engagement in medicines development easier for all. Browse from the sections below for the tools you might need, hover over to see a quick preview and click on the tool to access all related resources. Let us know how you've used these tools; we'd love to know how they've helped you in your patient engagement activities! https://imi-paradigm.eu/petoolbox/

8.4 INVOLVE (UK)

INVOLVE is a key public participation charity in the UK with a mission to put people at the heart of decision-making in healthcare and research. INVOLVE UK has developed a knowledge-based resource with guidance on how to plan participatory processes end-to-end, e.g., planning participation, preparing scope, purpose, outputs and outcomes, and whom to involve:
https://www.involve.org.uk/resources/knowledge-base
https://www.nihr.ac.uk/documents/ppi-patient-and-public-involvement-resources-for-applicants-to-nihr-research-programmes/23437

8.5 Macmillan "Building Research Partnerships" (UK)

The UK charity Macmillan Cancer Support runs a free course called 'Building Research Partnerships' which outlines the different types of research methods and terminology. It also explains how the public can get involved as well as exploring the issues related to becoming and being a consumer involved in cancer research.

https://learnzone.org.uk/downloads/Building%20Research%20Partnerships%20-%202013%20Report%20-%20Macmillan%20NIHR%20CRN.pdf

8.6 Journal of Research Engagement and Involvement

Research Involvement and Engagement co-produces a journal involving academics, policy makers, patients and service-users, with a unique governance structure. They welcome articles from anyone involved in or engaged with research in supporting, encouraging or delivering the patient/public voice in research processes or structures. This certified Patients Included journal publishes articles on and with patient engagement and involvement in an open access format.
https://researchinvolvement.biomedcentral.com/

8.7 Patient Engagement for the Life Sciences

Patient Engagement for the Life Sciences written by Guy Yeoman and Mitchell Silva is a practical handbook for anyone striving to incorporate patient value in the delivery of medicines from Research and Development into a practical healthcare setting. This book provides a tangible framework of how this can be achieved with and for patients.

Any profits generated from book sales will be donated to International Health Partners UK, Europe's largest coordinator of donated medicines, to support patients around the world.

https://www.amazon.com/Patient-Engagement-Life-Sciences-Yeoman-ebook/dp/B07GTQLRFJ

8.8 Patient and Public Engagement Toolkit

Now that patient and public involvement is in the mainstream of healthcare, professionals at all levels from postgraduate trainee to consultant need to understand the issues and be able to collaborate with patients on joint initiatives.

The “Patient and Public Engagement Toolkit” written by Julia Cartwright, Sally Crow, Carl Heneghan, Rafael Perera and Douglas Badenoch answers questions about setting up a project and seeing it through successfully. In the concise, easy to follow format so popular in the Toolkit series, it guides through the process step-by-step. A seemingly complex project will become straightforward once the principles outlined there are grasped.

https://www.amazon.com/Patient-Public-Involvement-Toolkit-EBMT-EBM-ebook-dp-B005D7EHAY/dp/B005D7EHAY/ref=mt_other?_encoding=UTF8&me=&qid=