PATIENT EXPERT CENTER

Clinical Research

Trial Design Collaboration

Value/Why

The aim of collaborating with patient organisations is to optimise study designs, clinical endpoints, data generation, clinical trial procedures and study execution. A well-designed clinical trial, including the patient perspective, will have a positive impact on patient recruitment and retention. Patient experts should not give any scientific nor methodologic input, but input about which results are important for patients or suggestions for practicalities of the trial organisation.

A complementary objective is to ensure that the target populations perceive the clinical trial as valuable and responsive to their needs and preferences (e.g. practicalities, logistics, unmet needs, safety, ethics), while also supporting subsequent regulatory and reimbursement discussions (where applicable).

This document describes the process of setting up and executing a collaboration. The document does not provide details on the contents of the collaboration. Possible topics for collaborations are explained in [D-POContributionToDrugDevelopment].

Initiators

Trial initiator or sponsor. This can be a CRO, a Pharmaceutical Company, a Medical Device Company, an Investigator of a (academic) hospital ...

PATIENT EXPERT CENTER: Imperiastraat 16 | 1930 Zaventem
info@patientexpertcenter.be | www.patientexpertcenter.be

1 Process

This process follows the structure of the *How-to Guide on patient engagement in Clinical Trial Protocol Design*[1], developed by PFMD, available on https://pemsuite.org/. This document can be seen as a short summary of the full 46 pages document. The How-to Guide can be consulted to find out more about each step.

The process boils down to a project management workflow, with particular emphasis on preparing and organising the collaboration. If the project is conducted correctly and sufficient attention is paid to follow-up, a new project could be started following the same phases. The responsibility for following these steps is shared between the trial sponsor or investigator and the PO. The conduct of the clinical trial itself is, of course, the sole responsibility of the investigator or sponsor.

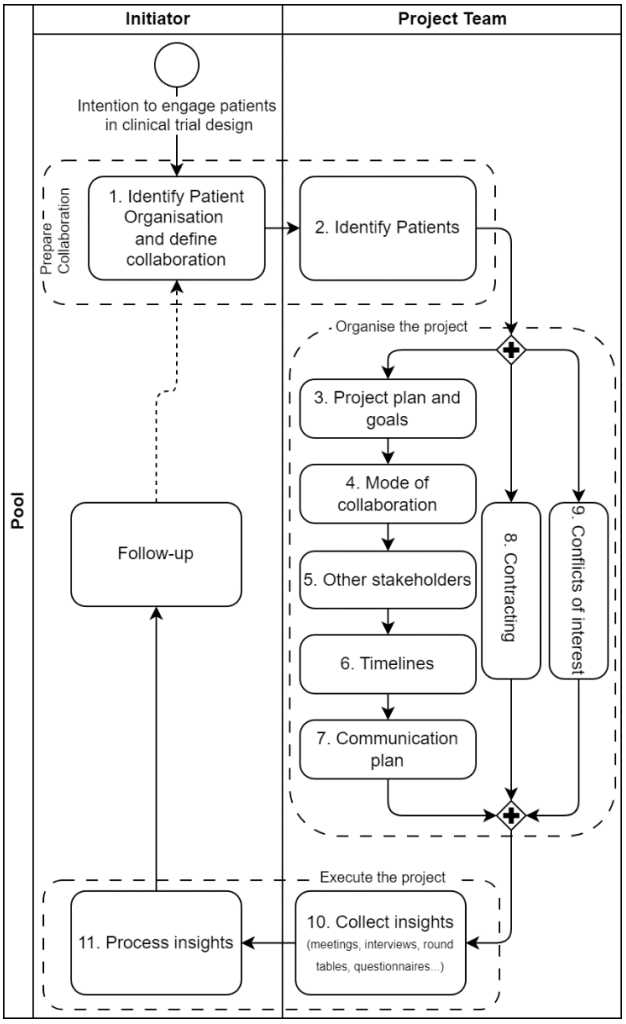
The process map and the table below give short descriptions of each step. A more detailed explanation is included in section 5 Details.

[1] https://pemsuite.org/How-to-Guides/Patient-engagement-in-clinical-trial-protocol-design.pdf

Trial Design Collaboration

Detailed step description

1. First, identify the patient organisation(s) that is (are) closest to the disease of the clinical trial you are considering. Once the organisations have been identified, each party should explain its reason for working together. [F-TrialCollaborationDefinition] If deemed necessary a CDA can be created at this point.



2. The patient organisation should identify which patients and/or patient experts are best suited to join the collaboration.
3. The goal of this step is to agree on the shared purpose of the project, establish communication, define the responsibilities of each contributor, identify leaders for the collaboration and identify the needs for additional support or training.
4. Engaging patients in clinical trial design can happen at several intensities: Surveys or questionnaires - Interviews or focus groups - Patient Advisory Boards or Community Advisory Boards.
   A variety of these approached can be combined to design a trial.
5. Other collaborators of the sponsor of the project should be considered as involved or informed about the patient engagement activities.
6. Building the timelines of the collaboration (long-term or short-term).
7. Agree on the communication with the POs, the Patient Experts and the patients involved in the project: meetings, status updates, SPOCs, external updates
8. A contract between the sponsor and the PO(s) is necessary for any collaboration. It is a good practice to agree on (the outlines of) a contract before considerable work is performed for the project by any of the partners.
9. While setting up the project, it is important to consider how conflicts of interest will be avoided or managed.
10. There are multiple ways of collection insights. [D-POContributionToDrugDevelopment] serves as a starting point.
    This is the actual “execution” of the collaboration: collecting input through surveys, focus sessions, interviews etc.
11. The insights gathered should be incorporated into the study protocol, which will improve recruitment because aspects valued by the patient population will be included.

2 Definitions

Patient Experts (PE)

Patients that have expertise in living with their disease but also have the necessary knowledge about clinical trials, the organisation of healthcare etc. For example patients that have followed the training of Patient Expert Center.

Patients

Patients that are involved in the development of the clinical trial design.

These patients anywhere on the scale form “naïve” patients to Patient Experts, or even relatives/carers of patients.

PO

Patient Organisation

CDA

Confidentiality Agreement

SPOC

Single Point Of Contact

3 Roles

Patient Organisation

The patient organisation for the specific disease. If there are several organisations (regional, language-based) for a disease, preferably all of them are involved in the process.

Project Team

The project team consists of the people preparing the project and should contain at least (collaborators from) the initiator, a representative from the patient organisation and a Patient Expert.

4 Requirements

There are multiple requirements for these collaborations to be successful.

The patient organisation needs to have

- Patients (experts) with basic knowledge about clinical research
- Patient experts that are fluent in English
- A list of candidate patients or patient experts to join the collaboration
- Some guidelines or questionnaires to review clinical trial related documents
- A way to communicate efficiently with the involved patient experts
- A (digital, online) system to run surveys among patients

Clinical trial initiators should

- Contact the PO in time, since it can take time to set up the collaboration
- Be open to input that contradicts prior beliefs

5 Details

Prepare the collaboration

Identify patient organisation and define purpose of collaboration

First, identify the patient organisation that is closest to the disease of the clinical. If the disease is covered by more than one patient organisation, all should be contacted.

Once the organisations have been identified, **each party should explain its reason for working together**. For example, a company may be seeking patient input on a particular project, while a PO may want to shape the direction of drug development. All parties involved should agree on the purpose of the collaboration. [F-TrialCollaborationDefinition]

Identify, select and invite patients

The patient organisation should identify **which patients and/or patient experts are best suited to join the collaboration**. Some examples of selection criteria are[2]:

- The type of patient profile needed (i.e., 'naive' patient, patient advocate, patient expert, carer or family member, patient community).
- The level of research expertise the patient should have (and if any training or education may be needed).
- The role the patient will take and how complex it is. (See the description of the four levels of patient contribution below)
- The patient's medical condition profile.
- The patient's ability to mobilize their community. For example, what is the size, scope, and geographical footprint of their network; how good is the relationship with the Patient Organisation?
- Other capabilities and competencies needed from the patient.
- The expected project timelines, duration, frequency of interactions, technology

When initiating contact selected patients, a brief description of the patient's role should be prepared, outlining the expected level of contribution.

The **four levels of contribution**, each increasing in complexity:

- Patients provide insights into the **disease burden:** *the patient pathway, patient needs and preferences for clinical trials/research methodology*;
- Patients provide **generic insights on the study:** *assessing if the clinical visit schedule is too heavy and if there could be transportation issues*;
- Patients provide input on **study design**: *inclusion/exclusion criteria and endpoints, co-creating patient interview guides and plain-language summaries*
- Patients with **vocational backgrounds** relevant to medicines development.

[2] PFMD How-to Guide on patient engagement in Clinical Trial Protocol Design p. 8

Trial Design Collaboration

Initiating the patient-sponsor partnership should take place as early as possible, since it can take a while for patients to acquire the necessary knowledge about clinical trials or for sponsors to be trained on the value of patient engagement[3]*. Collaborating with patient experts reduces the need for training, since they are trained already and know how to represent their disease objectively.*

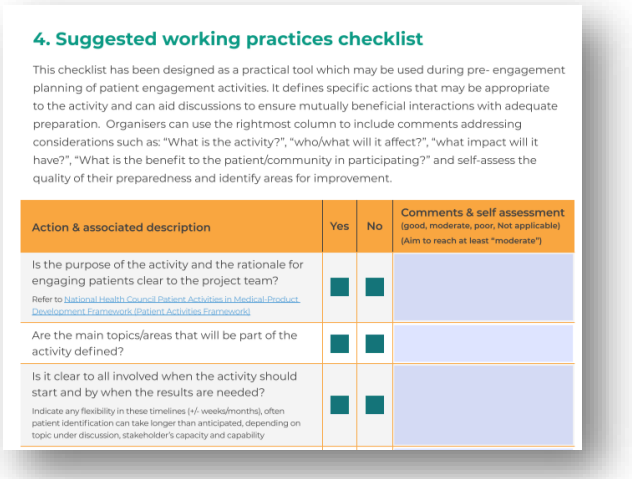
Setup the project

Project plan and goals

If a project is carefully set up, this can lead to a long-term relationship that can effectively support project communication, the recruitment and retention plan, and the dissemination of study results. Long-term partnerships with the patient community can also have a positive impact on a company's reputation, public trust in the company, and community's overall willingness to partner.

The goal of these steps is to agree on the shared purpose of the project, establish communication, define the responsibilities of each contributor, identify leaders for the collaboration and identify the needs for additional support or training.

imi-Paradigm has developed a checklist to help cover all the issues that need to be agreed between the parties working together for patient engagement in a clinical trial. Use of this checklist will help ensure that all issues are addressed.



4. Suggested working practices checklist

This checklist has been designed as a practical tool which may be used during pre- engagement planning of patient engagement activities. It 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.

Action & associated description	Yes	No	Comments & self assessment (good, moderate, poor, Not applicable) (Aim to reach at least "moderate")
Is the purpose of the activity and the rationale for engaging patients clear to the project team? Refer to National Health Council Patient Activities in Medical-Product Development Framework (Patient Activities Framework)	■	■	
Are the main topics/areas that will be part of the activity defined?	■	■	
Is it clear to all involved when the activity should start and by when the results are needed? Indicate any flexibility in these timelines (+/- weeks/months), often patient identification can take longer than anticipated, depending on topic under discussion, stakeholder's capacity and capability	■	■	

Figure 1: screenshot of imi-paradigm checklist

http://imi-paradigm.eu/PEtoolbox/EUPATI/PARADIGM-Suggested-Working-Practices.pdf

Mode of collaboration

Engaging patients in clinical trial design can happen at several intensities:

- Surveys or questionnaires
- Interviews or focus groups
- Patient Advisory Boards or Community Advisory Boards

A variety of these approached can be combined to design a trial.

[3] Patient Engagement Training, an innovative learning program that will concretely help you start your patient engagement journey or take it to the next level. Available here: https://pemsuite.org/patient-engagement-training/

Trial Design Collaboration

Sponsors should consult internal knowledge and secondary patient-focused data sources, as well as insights from previous patient engagement activities, before engaging with patient organisations to avoid duplication of effort and to build on previously identified insights and gaps.

Patient organisations should do internal research on insights gathered in previous engagement activities with other sponsors (or even the same sponsor) and share these insights in a transparent dialogue.

Including all stakeholders

Other collaborators of the sponsor of the project should be considered as involved or informed about the patient engagement activities.

For example: patient advocacy/engagement team, medical affairs, clinical operations, market access, regulatory affairs, health economics, psychometricians, PRO methodologists, epidemiologists, statisticians, legal and compliance teams.

Timelines

The next step is building the timelines of the collaboration (long-term or short-term). Some considerations for resources and time required are listed below:

- Selecting the right patients or patient experts or establishing contracts takes considerable time and resources from patient organisations.
- Sponsors might be struggling with tight deadlines which in turn might translate into unrealistic timeline expectations towards patients and patient engagement activities
- Ensure that the findings collected from patients are collected and processed before the study protocol is finalized. This can happen in parallel with the collection of site feedback.
- Consider whether it is necessary to organise a basic training about clinical trials. Patient Experts do not need this training, although a refresher can be useful.
- Research might take time and resources and projects might extend beyond the original estimates
- Sponsors need to ensure that they have the necessary resources required to support patient engagement activities. Do not underestimate the amount of time needed for administrative aspects, such as agreeing on contracts, and compliance processes.

It should be possible to voice any concern (about timelines, resources or other issues) at any time during the project; either to the sponsors or patient organisations involved.

Plan communication

Agree on the communication with the POs, the Patient Experts and the patients involved in the project.

- Meetings: frequency, location, virtual/in-person, number of participants
  - Preparation time
  - Travel time
- Status updates: frequency, medium, content
- Language: English?
- SPOC for POs, PEs and patients: specific e-mail address, phone…

Trial Design Collaboration

Do not forget a way to keep all partners informed about the progress of the trial and the impact of their involvement. Even – especially – if the trial has a negative outcome and does not progress to the next clinical stage. The patient community needs to know whether or not their contribution has made a difference.

Contracting

A contract between the sponsor and the PO(s) is necessary for any collaboration. It is a good practice to agree on (the outlines of) a contract before considerable work is performed for the project by any of the partners.

In some instances, a Confidentiality Agreement (CDA) is required before sharing any details about the project, if the topics covered in the patient engagement activities are commercially sensitive to the sponsor.

Please consider the *Guiding Principles on Reasonable Agreements between Patient Advocates and Pharmaceutical Companies*, developed by the Workgroup of European Cancer Patient Advocacy Networks (WECAN), Myeloma Patients Europe and PFMD when creating contracts:
https://wecanadvocate.eu/wp-content/uploads/2019/03/Guiding-Principles_final-document6.2_clean.pdf

The checklist below can serve as guide[4]

- Has my organisation worked with this PO before?
  If yes:
  - Can the previous contract speed up this contracting process?
  - Is a CDA needed or can this be covered within the contract?

  If no:
  - Ask the legal, compliance and privacy teams about the time it takes to set up contracts
  - Share this information with the PO
  - Are the new contracts understandable? Check the guidelines (e.g. WECAN https://wecanadvocate.eu/wp-content/uploads/2019/03/Guiding-Principles_final-document6.2_clean.pdf)
  - Is a CDA needed or can this be covered within the contract?
- Is there internal guidance for reimbursing and compensating POs?
  If no, refer to the National Health Council's Fair Market Value Calculator[5] and the Guiding Principles on Legal Agreements[6]. Discuss with the PO
  - reimbursement and compensation
  - the potential costs and how they will be reimbursed (e.g. is a lump sum foreseen for travel or for each travel separately?)
  - the time and effort required to be involved in the project (e.g. preparation time, meetings, travel, independent work, reporting, and other communication as relevant)

---

[4] PFMD How-to Guide on patient engagement in Clinical Trial Protocol Design p. 14-15
https://pemsuite.org/How-to-Guides/Patient-engagement-in-clinical-trial-protocol-design.pdf
[5] For more information: NHC. Patient Engagement Fair-Market Value Calculator. Available from: https://nationalhealthcouncil.org/fair-market-value-calculator/
[6] See section 8 on WeCAN. (2018) "Financial compensation and reimbursement of expenses" Available at: https://wecanadvocate.eu/wp-content/uploads/2019/03/Guiding-Principles_final-document6.2_clean.pdf

Trial Design Collaboration

- Have the lead times and deadlines been defined and agreed with the PO(s)?
- Have the roles and responsibilities and other rules of collaboration been defined with the PO(s)?

Conflicts of interest

While setting up the project, it is important to consider how conflicts of interest will be avoided or managed. Patients (experts) who contribute to the design of a clinical trial may also be interested in and eligible to participate in that clinical trial at a later stage. Consider how potential conflicts of interest can be avoided from the outset (e.g. by keeping patients anonymous or communicating with patients indirectly through a patient organisation).

Execute the project

Collecting insights

There are multiple ways of collection insights. The document [D-POContributionToDrugDevelopment] serves as a starting point. More tips and tricks at TransCelerate website: https://www.transceleratebiopharmainc.com

Processing insights

The insights gathered should be incorporated into the study protocol, which will improve recruitment because aspects valued by the patient population will be included.

In addition to using the insights for the protocol, it is good practice to

- Create a 'knowledge library' of patients' insights, with their consent, so that learnings can be shared more widely and used in future clinical trials.
- Summarise the repository of patient insights for regulatory submissions.
- Communicate with Patient Organisations throughout the study duration; this may include sharing press releases, clinical trial updates and published data, including any reasons for study discontinuation.
- Inform Patient Organisations when their contributions to a single clinical trial protocol will be applied to other related clinical trials or clinical development programmes.

Feedback and follow-up

Maintaining the contact with the POs is important to ease future collaborations and to increase the efficiency of patient engagement activities. POs can also help articulate the right messages to the relevant patient communities.

Once the trial protocol has been completed, the sponsor should share where the contributions were incorporated and how the clinical trial protocol or other study elements have been influenced by the contributions. Equally important is sharing why certain insights could not be incorporated.

The collaboration can continue and information should be exchanged once a clinical trial has started:

- Share information about the progress of the clinical trial, including recruitment, completion and/or publications
- Invite patient organisations to contribute to the plain language summary (lay language) of the clinical trial
- Involve patient organisations in the writing and/or reviewing of the manuscript/abstract
- See [D-PatientOrganisationsInDrugDevelopment]