Patient Organisations' contribution to drug development

This document describes where Patient Organisations (PO) or Patient Experts (PE) should be involved as a minimum during drug development[1]. The document also includes a list of questions (source: PFMD) to check whether the patient perspective is sufficiently included in the drug development process. This list is aimed more at researchers, but Patient Experts could also use it as a reference.

For completeness, here is an overview of a typical drug development flow. The sections below highlight what a patient organisation can do at each stage.

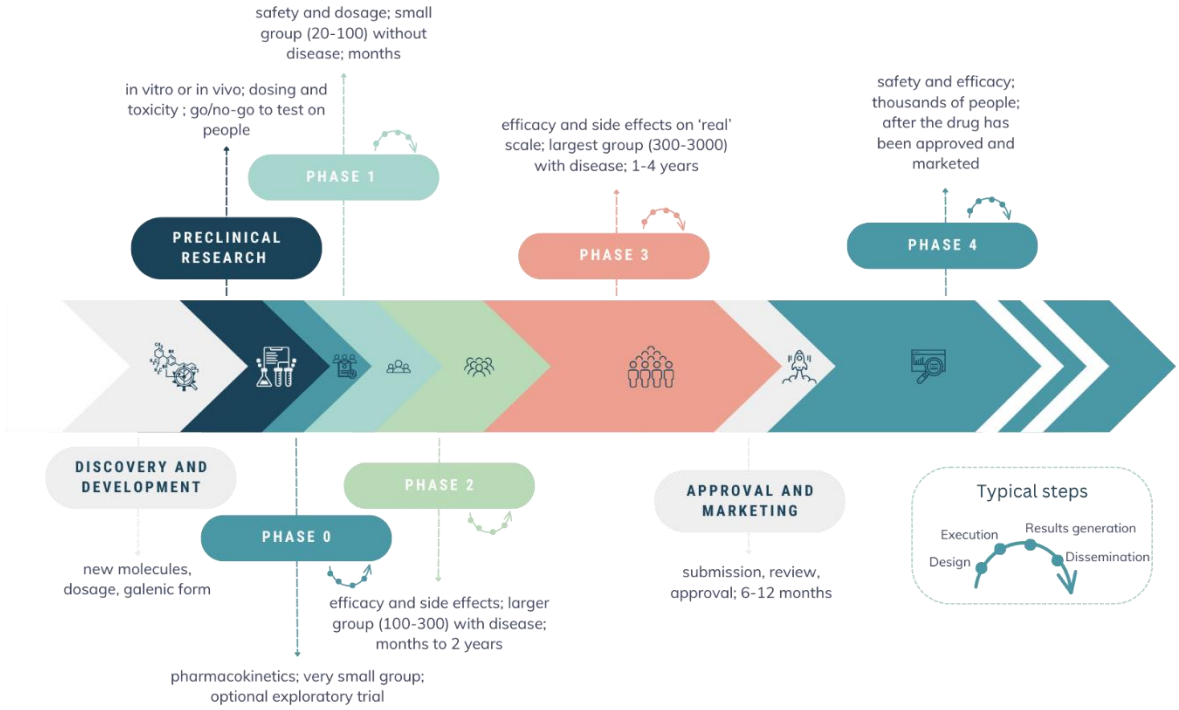

Figure 1: drug development flow[2]

Priority Setting

Priority setting happens before any drug development and it ensures that health research funders are aware of the issues that are most important to the people who need to use the research in their daily lives.[3] Although priority setting could be aimed at policy makers, it is also interesting to involve clinical researchers or companies developing treatments.

Some insights POs can provide:

1. What are the unmet needs from patient perspective?
2. What is the current social/professional situation of patients that can be improved?
3. What is important to the patient in the treatment/ maintenance of their condition?
4. What would the patient like to see a drug/device to do to make living with the disease easier?

[1] Medical device development follows a different approach
[2] Based on FDA "Drug Development Process": https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process consulted 02/08/2023 and Wikipedia https://en.wikipedia.org/wiki/Phases_of_clinical_research
[3] James Lind Alliance https://www.jla.nihr.ac.uk/

Discovery and Development

Apart from giving input for priority setting, there is no PO engagement in this phase of a drug development.

Preclinical research

There seems no interest in involving patients in this phase of therapy development.

Phase 0 – 3 clinical trials[4]

Study Design

During the design of a clinical trial, patients should be involved in writing or – at least - reviewing the study protocol. A list of questions for each chapter of the protocol is given in the table at the end of this document and can be used as a reference when reviewing a protocol.

The table below contains some actions a Patient Organisation or Patient Expert can take to answer some of the questions. Be aware that these actions will require a reasonable investment of time and resources.

Protocol section	**Topic**	**How**
Study design and endpoints	Understanding current standard of care environment *Deliverable:* description of the current standard of care, mentioning room for improvement	Survey among members of patient organisation/patients recently treated in hospital, on • health economic challenges for patients, patients' family (or for government) • what keeps patients awake?
	Identification and discussion of primary & secondary endpoints *Deliverable:* report on the patient relevant endpoints	Focus group/Individual interviews or questionnaire with relevant patient experts - including on QoL, PROMS, PREMS[5]
	Identification of risk perception and weighing of risks *Deliverable:* description on the risks levels patients are willing to accept	Interviews with patients about risk acceptance levels (can be different than investigators')
	Feasibility of study protocol from patient's point of view *Deliverable:* a review report of the protocol or study design	Review of study protocol by patient experts
Study recruitment	Recruitment materials *Deliverable:* score of and/or points of improvements for the recruitment materials	Reviewing material on legibility, comprehensiveness, form (video, leaflets, …), communication channels (PO, internet, physical distribution, …) [F-RecruitmentMaterialReview]

[4] Most patient input is expected for phase 2 or phase 3 clinical trials, but as the structure of phase 0 and phase 1 trials is similar, they are also mentioned.

[5] QoL: Quality of Life; PROM: Patient Reported Outcome Measurement; PREM: Patient Relevant Outcome Measurement

	Lay Person Summary *Deliverable:* score of and/or points of improvements for the lay person summary	Review of summary by patient experts to ensure completeness, accuracy and clarity. [F-LayPersonSummaryReview]
	Informed Consent Forms *Deliverable:* score of and/or points of improvements for the ICF	Review of ICF by patient experts to ensure completeness, accuracy and clarity. [F-ICFReview]

Table 1: example actions of a PO or a PE

Study Execution

Patient Organisations can play an important role in some practical aspects of the study execution by organising patient discussions (focus group) on

- Recruitment: informing patients about the trial
- ICF: helping patients understanding the ICF
- *Others?*

Results generation

Patient Organisations are not involved in generating the results (i.e. consolidating and analysing the data, drawing conclusions, writing the report) but they can be engaged in reviewing the presentation of the data , interpreting the results, translating the conclusions to patients' point of view, … This can be done in a focus group with patient experts.

Deliverable: an interpretation of the results of the trail from a patient's point of view.

Dissemination of results

Patient Organisations should review the communication materials (legibility, clarity) and discuss ways of distributing the results of a trial to the patients participating in the trial and the patient population.

[F-ResultsCommunicationReview] – this document can be made if desirable.

Approval and marketing

Patient experts can play an important role in the approval and marketing phases of drug development. This is described in [P-MarketAccess].

Phase 4 clinical trial

As with phase 0-3 clinical trials, patient organisations can play an important role in phase 4 clinical trials. Apart from reviewing the study design and the ICF, the added value of patient engagement is in monitoring the real world, keeping track of patients' questions or identifying new – unmet – needs.

Protocol section	What is addressed in this section	Questions and considerations
Objectives and purpose	This section of the protocol provides a detailed description of the primary (and secondary) objectives of the study. The objective is based on the scientific questions to be answered and the reason for performing the clinical trial.	• Why is there a need for the study? What is the current standard of treatment? • Do the study objectives address an area of unmet need? • What is important to the patient in the treatment/ maintenance of their condition? • What would a patient (or carer) hope to get out of study participation? • Is it a novel treatment? • What would the patient like to see a drug/device bring to them to make living with their disease easier? • What is meaningful for the patient for treatment/maintenance of their condition? • Is the therapeutic area one that may provoke sensitivities?
Study design and endpoints	The design of the study (e.g. type of study, phase, single, multicentre or decentralised) and the study primary, secondary (and exploratory) endpoint(s) should be drawn up based on the study objective(s).	<u>Overall Study Design</u> • Is the study design appropriate? • Is the risk for the patients acceptable from a patient's perspective? • Is there a need for a 'study partner' (carer or family member)? If so, is their role and responsibility during visits explained clearly? • Are there specific considerations that may impact a clinical trial participants' life (e.g. frequent travel to hospital, hospital stays, privacy impacts)? • What changes to the design could be implemented to minimize the burden on the patient participant? • Are there special considerations where children or vulnerable populations are involved? <u>Investigational product/placebo/standard care</u> • Does the clinical trial have a placebo? Does the trial have different randomization strata? If so, what considerations are needed for explaining these to the clinical trial participant? • Is the use of the comparator treatment or placebo justified? • Assuming this is a blinded clinical trial, it is Important that patients do not unintentionally unblind it. Sharing study-specific information on social media is probably not advisable. <u>Study Endpoints</u> • Is the study endpoint meaningful to the patient population? • Which study outcomes are most important to the patient? Do the primary/secondary endpoints in the protocol map to this? • How important are patient-relevant endpoints? Are the current measurement approaches appropriate? Or is there a lack of patient-relevant endpoints? • What patient-reported outcomes or other patient experience measures are appropriate? • Are the patient-reported measures captured in a practical way (i.e. on paper, tablet, etc.)? • Will any study endpoints be related to patient reported outcomes data? <u>Progress and results</u>

Protocol section	What is addressed in this section	Questions and considerations
		• How will the sponsor communicate the progress of the trial in terms of enrolment of clinical trial participants, active clinical trial sites, and timelines? • Is there a clear commitment from the sponsor to share the study results in an understandable format (leaflets, brochures, ad hoc communication at conferences) and in lay language? How will the results of the trial be communicated to the participants?
Study enrolment and withdrawal	This section of the protocol encompasses the study population, the inclusion and exclusion criteria, and the recruitment and retention approaches of the study, and how participants may withdraw or be discontinued from the study.	<u>Inclusion/Exclusion criteria</u> • Is the study population appropriate (also in terms of diversity: gender, age, sex, ethnicity)? • Are we excluding certain populations, for safety, for instance? • Do the inclusion/exclusion criteria present a barrier to recruitment? <u>Patient Screening/Recruitment</u> • Is there a recruitment strategy and recruitment tools for patients, sites, clinics? • Are there any geographic, cultural, age, gender, race, language, socio-economic status specific considerations that we need to address when we identify participants for the clinical trial? • Are the geographical locations and number of sites enrolling participants appropriate? • What are the considerations when choosing study sites, testing, accessibility, and diversity of the patient population? • Have we considered all possible clinical trial sites, or can we consider new sites? Depending on the scope of the study (international, regional, country-specific), the specific considerations may be tailored and adapted with the support of the patient partners. • Are the patient-facing documents, such as recruitment materials and Informed Consent Forms (ICF), clearly written and understandable for patients? • Will there be lay language materials (e.g. brochures, booklets, videos, etc.) to help clinical trial participants understand the clinical trial and the Informed Consent documents? • Are the benefits and risks clarified in the ICF? If not, have the potential benefits and risks of participation been identified for the patient? And for their caregivers? • Will the sponsor implement electronic Informed Consent for the clinical trial (e.g. eConsent or ePRO) and are there any special considerations needed? • Are support services offered during the screening process? • What happens if, following screening, a potential clinical trial participant is not eligible? • What kind of support services would be helpful when participating in the clinical study? • What type of information would patients like to receive as part of a clinical trial, and from whom? (e.g. peer, doctor, patient organization, family member) • What value does the patient see from the clinical trial for them and other patients with the condition? <u>Participant withdrawal</u> • Are the procedures for withdrawing from the study clearly communicated?

Protocol section	What is addressed in this section	Questions and considerations
		• How will patients be appropriately followed up if they discontinue the study? <u>Patient Compensation</u> • Are any clinical trial participation costs reimbursed? And are their other financial or non-financial incentives for participation (e.g. vouchers, medical or technological devices, etc.)? • How will the burden on the clinical trial participant and carers be alleviated (e.g. clinical assessment and travel, meals, accommodation reimbursement, child care, if applicable)? <u>Management of care</u> • How will the study impact the patients' current care? • What are the other conditions of participation? • When will the study begin, and how long will it last? <u>After the trial</u> • What are the procedures when a clinical trial participant needs to leave the study (e.g. withdrawal or termination), and how will they be followed-up? • What will happen from the clinical trial participants perspective when the study ends? • Will the study drug be provided after the trial? If so, for how long? Is there an added cost or how? • What happens to the patient data during the study or when the clinical trial is completed/discontinued? • How will the results of the trial be communicated to the participants? <u>Other</u> • What study assurance is needed in case of medical problems due to the study? Are the risks mentioned and explained to the study participants? • What are the barriers and motivators to participating in a particular study?
Study agent (if applicable)	The study agent is the intervention being studied (e.g. drug, device). The dosing and administration schedule should be described (e.g. dose, time of day and interval, route of administration) and should include conditions for dose adjustments/modifications/ delays and the duration of the therapy.	<u>Dosing</u> • What is the daily dose? • How might participants feel about dose escalations or scheduling changes? • How will possible dose adjustments/delays affect the patient? <u>Mode of Administration</u> • How will the study agent be delivered? (e.g. oral, intravenous, etc.) • Are there practical considerations around the administration (e.g. length of visits, suitable formulation for study population)? <u>Treatment duration</u> • What is the expected duration of treatment? <u>Other relevant questions</u> • How does the treatment differ from the current (if any) standard of treatment? • Is there a process for patients to ask questions about the agent?

Protocol section	What is addressed in this section	Questions and considerations
		• Are there specific considerations that may impact the clinical trial participants (e.g. drug packaging or the use of (unfamiliar) devices for administration)?
Study procedures and schedule (if applicable)	Procedures and scheduling for the collection of data (medical history, height, weight, BMI , sex, age, demographic group, health status of participants), including clinical, laboratory and imaging results, and questionnaires, should be defined.	<u>Schedule</u> • Is the schedule of events feasible in terms of screening, enrolment/baseline, and follow-ups? • Is the visit schedule feasible (e.g., frequency of visits, length of visits, at-home requirements)? • Is the order of the tests and procedures during visits realistic for patients (e.g., urine testing isn't the first test if people have a long distance to drive to the site or have a bladder control issue and cannot hold it for their travel distance)? • Could the timing/volume of procedures have negative practical implications for participants or disrupt their quality of life? If so, can the schedule and/or operational set-up of the clinical trial be redesigned to address this? What does taking part mean to the patients: 'What's going to happen to me and what impact will it have on my life?' • Is the frequency of the tests and procedures realistic? (e.g., minimize the number of lumbar punctures, propose optional sub-groups for specific tests and procedures) <u>Procedures - medical</u> • Will the clinical trial include any invasive procedures? Could these have a negative effect on willingness to participate? • Are there requirements in the study that may add additional burden? (e.g. colon prep agents) • Would alternatives to study visits (nurse home visits or telemedicine) would improve patient participation? • Are the tests and procedures included needed to answer the study objectives? Or are they more 'exploratory' in nature? <u>Procedures – data collection</u> • Are any new technologies being used in the study (e.g. smartwatch, tablet, smartphone, etc.)? Are there practical implications (e.g. training needed)? • How are you going to gather patient feedback, specifically on patient-reported outcome questionnaires (e.g., clarity of language, comprehension, appropriateness of questions asked) and on devices used (e.g., whether the use of a hand-held device is easy or difficult)? • How many questionnaires will participants need to complete at each visit? • How long are patients willing to spend on answering questionnaires (e.g., are there multiple PROMs/ questionnaires each visit)? • How and when will patients receive their test results? • Does the patient need to attend the clinic, or can they complete the questionnaires at home? • Is there a questionnaire for the caregiver? (if yes, the same questions as above would be applicable)

Protocol section	What is addressed in this section	Questions and considerations
Assessment of safety	This section of the protocol outlines the assessments and procedures related to risks and safety, and the steps that will be taken to ensure the safety of clinical trial participants and minimize risk.	• What information is provided to clinical trial participants to help them understand possible side effects? • How will adverse events be classified and reported? • Are there any risks to individuals other than the clinical trial participants (e.g., carers or close contacts)? • Is the process for reporting side effects clear for patients? • How will the patient contact the study coordinator throughout the study with concerns, worries, or side effects, including during evenings and at weekends?
Ethics	This section of the protocol outlines the ethical considerations, including, among many considerations, information on the Informed Consent procedures and participant and data confidentiality.	• What are the Informed Consent procedures? • Are there supplemental materials available to help clinical trial participants (and carers) understand the study and the Informed Consent Form(s)? • What considerations are needed around Informed Consent or assent in paediatrics or those who cannot consent for themselves? How to inform them correctly? • Will any of the data or samples collected in the clinical trial be used elsewhere? • Will an independent review board approve the study protocol?
Data handling and recording Keeping	This section of the protocol outlines the data handling and record-keeping for the clinical trial, including study records retention.	• Who is responsible for the collection and management of the clinical trial participants' data? For how long will it be retained? • Will clinical trial participants be able to request their data at a later date? • Is the personal data used in accordance with GDPR (in Europe)?

Table 2: Questions and considerations relevant to each section of the clinical trial protocol[6]

[6] Based on PFMD How-to Guide on patient engagement in Clinical Trial Protocol Design p. 21 - 28 https://pemsuite.org/How-to-Guides/Patient-engagement-in-clinical-trial-protocol-design.pdf