



PATIENT FOCUSED  
MEDICINES DEVELOPMENT

made  
with  
patients



# The PFMD Book of Good Practices

1<sup>st</sup> edition | 2018

 @The\_Synergist  
@PFMDwithPatient

#PEQualityGuidance  
#PEQualityCriteria

 [www.PatientFocusedMedicine.org](http://www.PatientFocusedMedicine.org)  
May 2018



# Message from PFMD

Dear reader,

Patient Focused Medicines Development (PFMD) was established in 2015 out of a need that was expressed by many stakeholders in various roundtable discussions. This need was eventually translated into a dedicated organisation that aims to drive systematic patient engagement and involvement forward in the research, development and delivery of medicines.

Today we are very proud that you are reading the Book of Good Practices, as this too was born from a need expressed by many stakeholders. As patient engagement is becoming a norm instead of an exception or a one-off practice, there was a need to share knowledge about

- how other organisations have involved patients in their activities,
- what can be considered as high quality patient engagement, and
- how can different organisations reach the level of patient engagement that is both meaningful to patients but also to the research and development processes so that the output or outcomes will serve the end users better.

The PFMD Patient Engagement Quality Guidance, that was launched in 2018, introduces 7 Quality Criteria for good patient engagement that can be used to plan patient engagement activities, or to assess the level of patient engagement in ongoing or completed activities. Where the Patient Engagement Quality Guidance serves as a tool to help you to do patient engagement, the Book of Good Practices serves as a set of real life cases from a variety of organisations, that illustrate in detail how they have done it. These cases have been chosen from a big pool, assessed by an external group of reviewers and chosen to be included because they exemplify exceptionally well the 7 Quality Criteria. For detailed descriptions of the criteria and explanations for icons used, check the annexes at the end of the book.

The Book of Good Practices will be growing year by year with new cases. To contribute to this work, you can also submit your patient engagement experiences to the PFMD team.

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We hope this book will inspire and help you in your patient engagement journey. We encourage you to explore all the tools at your disposal within PFMD and Synapse - the mapping and networking tool, and connect with us for more guidance if needed.

We'd like to extend our thanks to all the reviewers, all case owners and all readers for making the Book of Good Practices possible.

PFMD Team



PATIENT FOCUSED  
MEDICINES DEVELOPMENT



# Develop AKUre - Patient-led clinical trial

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Organisation: AKU Society

## The PFMD Book of Good Practices

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**THE BOOK OF GOOD PRACTICE INITIATIVES ARE ALSO AVAILABLE IN SYNAPSE.**

**TO DOWNLOAD THE FULL BOGP, PLEASE VISIT:**

<https://involvement-mapping.patientfocusedmedicine.org/book-of-good-practices>

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# Develop AKUre - Patient-led clinical trial

Organisation: AKU Society

## Basic Information

**DevelopAKUre**



AKU Society led a project to start clinical trials on repurposing an existing medication to a rare disease. “It aims to study a potential new drug, called nitisinone, and assess its potential effectiveness in treating the rare disease, alkaptonuria (AKU)”. The project started in 2003 and got European Commission’s funding in order to develop and run the clinical trials. The project is ongoing until 2019.

Which phases of research, medicines development, lifecycle or disease management does this PE project cover?





## Which stakeholders does this PE project involve?



**Patients  
and carers**



**Polymakers**



**Health technology  
assessment  
organisations**



**Research funders**



**Patient advocates,  
patient organisations  
and associations**



**Regulators**



**Pharmaceutical  
companies or  
industry**



**Other**



**Healthcare  
professionals**



**Payers**



**Researchers**



# The quality of patient engagement

## 1. Shared purpose



AKU Society aimed to develop AKU re-discussion with patients (who were involved a long time) before the clinical trials (CTs) started; AKU meetings, communication towards patients. After visits, personal experience patient feedback is aggregated and presented to consortium members. Feedback is generated through a google sheets survey. ([Attached is an example of the survey and how it is presented to consortium members](#)).

Workshops are a valuable tool to report back to patients about the progress of the trial and enables the AKU Society to address any issues if they arrive. International workshops are attended by the majority of consortium members who can address patients directly.

Communication with patients happened naturally, listening to their concerns in these discussions helped in the design and planning of the CT and making it adapt to patients' needs. A few things were changed in the design, some were compromised and some couldn't be changed based on the feedback (E.g. non treatment group).

## 2. Respect and accessibility



Patients' needs were taken into consideration in the design of the CT. This includes reducing the amount of time participants spend in each of the trial sites. Based on feedback from the project's first clinical trial, we explained to other stakeholders the importance of patients having 'down time' and not staying in hospital as if they were unwell. Due to this, for the second phase of the project's clinical trial, patients stayed in a nearby hotel. Feedback from this move was overwhelmingly positive and has led to patients from across Europe seeing their visit as a holiday. They take ample opportunity to use the trip as an opportunity to explore Liverpool and its tourist sites, as well as extending their trip to holiday in the UK (Feedback is attached [here](#)).

It was also noted that due to the nature of the disease, patients may have severe mobility issues. As a reflection of this, and with feedback from the patient group, it was decided that those patients will be accompanied by a chaperone who is fully reimbursed. Normally this is a family member who acts as a carer. This is vital, as patients communicated they would not come without one and allows for continuity of care.

Recruitment was efficient because patients were helping in the discussions as well (finding patients outside of AKU Society's network). Understand that patients can be very motivated and a useful partner in recruiting and finding new patients. Patients understood the benefit of the trial for themselves and the patient community now and in the future. This was shown to them with reference to existing research and by a simple and accessible explanation on the trials website.

Researchers and doctors across Europe who may have patients affected by the disease were made aware of the trial by a series of email campaigns aimed either directly at them or through membership societies. Informed patients, however, would often tell their physicians about the CT. Due to the relatively low number of patients globally, these doctors are often highly specialised and have other patients with the disease who were then informed in turn. These would become 'patient champions' who would go onto disseminate to their own national patient groups.



Ongoing surveying allows us to track how patients are feeling in regards to all aspects of the trial. Monthly individual contact also adds to ongoing changes in areas that patients are concerned about based on their responses.

For example, the AKU Society took over the paying of personal and travel expenses and booking flights for patients enrolled at the city trial site, in the middle of the trial based on feedback in regards delays in reimbursement and issues over flights. The vast majority of patients when contacted directly saw this as positive and have commended the consortium on the positive impact this has had for them.

Almost half the patient population was recruited using the steps above. Due to the nature of the recruitment, it was integral that they keep the conversation with those enrolled open at all times throughout the trial. This is reflected by the decisions taken, which are highlighted above, and by their continuing high level of retention, which is almost 95%. Very high for this type of CT.

### 3. Representativeness of stakeholders



Aiming to get everyone possible - eligible over 16 yrs old, able to travel to the site.

Some patients didn't attend due to other conditions. Approx. 60 patients from the UK couldn't join the CTs because they had taken the drug previously as unlicensed drug (National Specialised Services) >> however, they did participate in the design of the study.

Representativeness of data:

- Benefit: two different data sets (60 patients from NAC) and 140 from the CT.
- As per the majority of other CT's, pregnancy or imminent pregnancy was an automatic bar to enrolment due to lack of scientific understanding of how the drug affects unborn children.

The AKU Society knows of only 500 patients throughout Europe. This meant diversity was almost guaranteed. All study materials were professionally translated and the website was installed with a translation service so that it was accessible to everyone.

### 4. Roles and responsibilities



- AKU Society was accountable to the patients > workshop actions were followed up by patients
- Getting EU Commission funding made the Society accountable to proceed with the application process> having the actual EU funding held us accountable
- Within the project, partners held each other accountable (12 partners: 2 PGs, 1 Industry, 3 hospitals, 1 CRO, rest research teams >> 5 different countries represented)

Regular project meetings by teleconference, face to face meeting once a year, progress reports every six months.

These meetings and continued teleconferences were used to ensure that each member of the consortium knew what was expected and were accountable to everyone else.

As a patient group, we are tasked with the dissemination of all the project's ongoing achievements and how it was reaching its goals. This meant that all partners had to feed back to them in regards to how these goals





were being met. This was then disseminated to the patient group via our website. If these weren't being met, we held the relevant partners to account based on patient questions generated at face to face meetings.

Each partner was involved in the trial design at earlier stages and throughout. This involvement wasn't limited to the areas that they would be responsible for. This inclusivity has led to mutual ownership of the trial and where members are responsible to each other and the wider patient group.

## 5. Capacity and capability for engagement



Capacity was built almost by accident over time - AKU Society learned about the CT process alongside with patients.

Big questions from patients:

- Patients had their own explanations about the randomisation/group
- Placebo group problem - what's the point in it if the drug is known to already work
- CT phases/ process clarified

Suggestions from both researchers and patients were discussed openly and agreed mutually. A few workshops together, having a statistician helped in clarifying some of the questions patients had.

\* The EUPATI programme is good for patient education. Educating patients on clinical research and how they are involved- 3 representatives did a EURORDIS summer school.

## 6. Transparency in communication and documentation



Communication:

- Comms (related to CT) to patients has to go through the ethics committee
- Advice received from CRO on transparency and communication with patients (documents needed, what can be said and not, how to explain things)
- Ongoing discussions about patient support after the trial is over

Documentation is part of the EC grant requirements - every 18 months.

- Making sure patients know what's going on to ensure retention (interim communications after phase 2, midway phase 3)
- Every month all patients emailed for questions or update with information.
- For the CRO, this level of communication was unusual.
- Partners happy to have discussions about how much can be shared.
- Need to understand different stakeholders' motives to keeping some of the information confidential.



## 7. Continuity and sustainability



Continuity:

- EC project requires study reports, documentation for licensing
- Patient survey for patients taking the drug on why they're taking this drug should help in discussion with payers

As a patient group, we have a vested interest in the continuation of the search for an effective treatment for alkaptonuria. If this trial is successful we will liaise with all concerned in regards to licensing of the drug and reimbursement across the world. We will assist patients enrolled on the study to find healthcare and treatment after the study. Any further discussion on this isn't appropriate at this stage.

## Results and outcomes

### Positive impact for specific medicines development phases

**Discovery and research:** identifying unmet medical needs, prioritise research agenda.

**Clinical development phases:** improving study design (e.g. fewer protocol amendments), accelerating patient recruitment, improved retention of the patients during clinical studies, reduced time of the clinical development of the medicine, financial impact.

**Registration:** quality of registration dossier, timing to registration.

**Post launch - life cycle:** patient solutions increasing patient adherence to medication, extension to new patient groups, adapted formulation, enhanced quality of AE monitoring and reporting, etc.

- First treatment to AKU
- No major amendments to the study protocol.

**Efficiency:** Faster recruitment (under 1 year vs. 2 years) due to prepared patients

### Direct or indirect positive impact for patients

Finding treatment for AKU patients.

- Recruitment rate 50% of eligible patients across Europe
- Retention rate over 95%

### Direct or indirect positive impact for stakeholders involved in the project (other than patients)

**Researchers:** understanding patients' unmet medical needs, PE helps in focusing and prioritising research efforts, research funding process is empowered with patient insights.

**Patients/ Carers:** influence/ impact to research prioritisation agenda, easier access to novel therapeutic options (e.g. new medicine in clinical trials phase), influence on outcomes of clinical trials, enhanced understanding of disease conditions and treatment options, better compliance to treatment.

**Wider community:** more effective medication leading to reduced health services, health/ condition related education of one individual is shared beyond that individual.

**Patient Advocates/Patient Organisations:** increased knowledge about being involved in collaboration with other stakeholders.

**Industry:** more effective research prioritisation efforts, acceleration of clinical development, faster registration process, etc.

**HCPs:** better understanding of patients' health conditions and expectations, quality of clinical trials, adherence to medication is increased, etc.

**Regulators:** patients' voice is embedded in decision-making, ensuring the quality of the regulatory file etc. Reducing the time that patients had to spend at the site

**Funding:** all partners received funding from EC in this project. The pharmaceutical company hopefully will end up with an approved product at the end of the study

**Hospital site:** Came up a new method to measure HGA (chemical in AKU patients) and therefore monitor progression of AKU → Papers/ research articles published





## Lessons learned

Since the beginning of the project, we have shared what we have learnt across a myriad of media, from articles to talks. This is due to the rarity of projects like this. We were learning every step of the way. Luckily with the help of the pharmaceutical company the clinical sites and the CRO, along with our drive to represent patients, we believe we have designed a remarkable CT.

As AKU Society lead on patient identification, recruitment and support for all patients enrolled at the three clinical sites across Europe and also leads on dissemination of the project, we were in a unique position to give advice to others in a similar situation.

- Relationships: it's integral to build relationships with patients, to help them understand everything about the trial and feel able to ask the difficult questions. This is the key reason for including patient groups in clinical trials. Pharma companies have to keep their distance from patients, and so patient groups can fulfil that role.
- 61% of patients said feeling part of a community was an important part of deciding to take part in a trial. Rare disease patients are so spread apart, communities have to be online to get the discussion going with the most patients.
- 30% of clinical timelines is to recruit patients for research and 90% of clinical trials are delayed because of patient recruitment problems; this is made even more difficult in rare diseases. However, in this project they reached target of almost 150 patients in under 9 months. Through hard work, and collaboration, media campaigns across Europe, attendance at scientific conferences, and email campaigns to 7,000 specialist doctors.

## References

1. <http://patientfocusedmedicine.org/wp-content/uploads/2018/05/Attachment.xlsx>



## Appendix 1 (2016 Feedback -Liverpool)

### Clinical trial 2

**Overall experience?** Average of 4.5

**The travel organisation?** Average of 4

**The accommodation?** Average of 4

**The interpreter?** Average of 4.5 (four answered this question)

**The organisation of tests and Assessments?** Average of 4

**Communication with staff prior to visit?** Average of 4

**During visit?** Average of 4.5

**After visit?** Average of 4

### Comments

#### Negative

- Patients prefer the Liner over other hotels.
- Some patients wish to go home on early and feel like they are not needed for the whole time.
- Taxis being late/not turning up in Liverpool.
- Expenses issues.
- Having to go back to departments due to mistakes.
- Mixed reviews of interpreters in Liverpool.

#### Positive

- The staff in Liverpool are widely praised by patients, especially Emily and Ranga.
- High score for overall experiences staff and organisation
- High praise for communication before during and after visit.

### Observational study \*

\*Only three patients responded.

**Overall experience?** Average of 4.5

**The travel organisation?** Average of 4

**The accommodation?** Average of 4.

**The interpreter?** N/A

**The organisation of tests and Assessments?** Average of 4

**Communication with staff prior to visit?** Average of 4

**During visit?** Average of 4.5

**After visit?** Average of 4.5

### Comments

#### Negative

- Ear Biopsy did hurt. One patient said it hurt a lot, the other two thought it was an acceptable level of pain. Suggestion strong painkillers are provided.
- Slight delay in expenses.

#### Positive

- High score for overall experiences staff and organisation
- High praise for communication before during and after visit.
- Liverpool staff and Patient Organisation are highly praised
- "Everyone was great! Which eased a lot of my concerns."
- "Thanks you guys, seriously. It means a lot to be treated like a human being especially during trials."



## About AKU Society

The AKU Society is a patient led charity that offers life-changing support to AKU patients and their families. We provide patients with personalised care and home visits along with the latest information from specialist workshops, our website, social media and online patient communities. We have also pioneered and funded research into the diseases whilst looking for an effective treatment: a drug called nitisinone is working, drastically lowering the build-up of the harmful acid.

The DevelopAKUre programme was a series of three major international clinical trials, run by a consortium of 12 European partners. It aimed to study a drug, called nitisinone, and assess its effectiveness in treating AKU. Nitisinone is not licensed for AKU but is being used by many patients off- label and at the National Alkaptonuria Centre (NAC) in Liverpool.

DevelopAKUre ended in January 2019, and the consortium then worked on analysing the data. SOBI announced in July that the data was positive and that they would apply to the European Medicines Agency (EMA) for a marketing authorisation license for nitisinone for AKU.



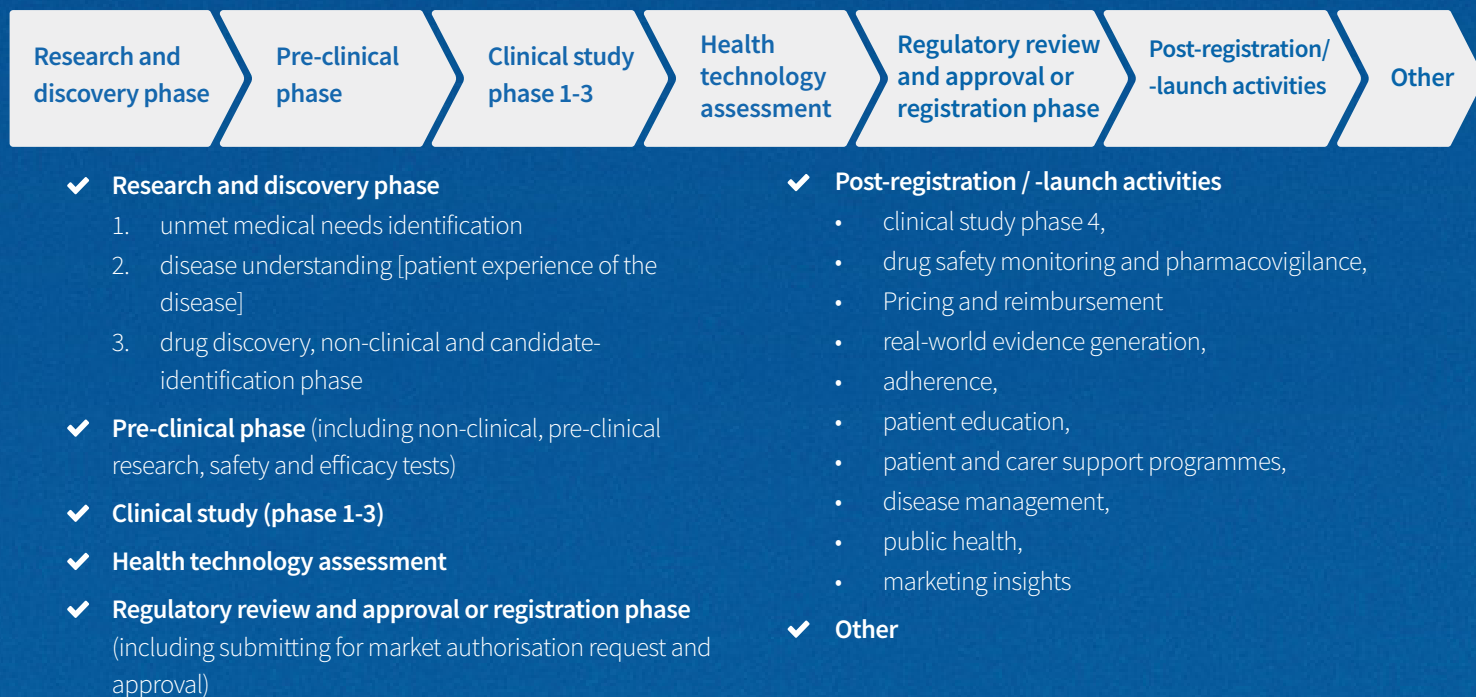
Picture of the consortium



# Annex 1: How to read the Book of Good Practices

The Book of Good Practices cases are all structured in the same way as the Patient Engagement Quality Guidance. You will find that each case has a basic description, followed by icons to show in which phases of medicines continuum they fit in and which stakeholders they have involved in their work (see description of icons below). In section 2 these cases will describe how they reached each of the 7 Quality Criteria. You will see from the wheel in the beginning, which of the Quality Criteria they exemplified in (judged by an external group of reviewers). Finally, you will find the results and outcomes of each case and the lessons learned.

## Which phases of research, medicines development, lifecycle or disease area does this PE project cover?



## Which stakeholders does this PE project involve?



# Annex 2: Descriptions of the Patient Engagement Quality Criteria

## 1. Shared purpose



This refers to the project's aims and outcomes that all stakeholders taking part should agree on before starting the project. Consider putting in place processes to help facilitate discussions between all stakeholders to identify each other's values, expectations and objectives, and review and discuss priorities in the planning of the project. It can be valuable to enable stakeholders to exchange views openly to understand the scope and objectives of the project, acknowledging that some of their objectives may differ. All parties concerned should also have a shared written description of the common goals of the project.

## 2. Respect and accessibility



This refers to (1) respecting each other, and respectful interactions within the project to be established among partners, and (2) openness to and inclusion of individuals and communities (to the project) without discrimination. Considerations to ensure good conditions to implement the project should be made from the beginning. For example:

- simplification of wording
- budget and payment considerations
- cultural adaptations to procedures
- practicalities such as meeting timing, location and format
- accessibility of project materials
- written co-developed rules of conduct

Accessibility to participate may be facilitated by enabling multiple ways to involve stakeholders who could benefit from and/or contribute to the project. For example, patients with cognitive impairment might need more time to go through project material, or need printed versions rather than electronic documents or PDFs for easier reading.

## 3. Representativeness of stakeholders



This refers to the mix of people you involve, which should reflect the needs of the project, and the interests of those who may benefit from project outputs (for example, target population). Consider diversity in expertise, experience, demographics, and other relevant criteria for inclusion. When selecting PE stakeholders, patients, attention will be given to awareness of the diversity required to achieve visible representative voice.

## 4. Roles and responsibilities



This refers to the need for clearly agreed, and ideally co-created roles and responsibilities, in writing, addressing that all aspects of project needs will be established upfront and revisited regularly.

## Annex 2: Descriptions of the Patient Engagement Quality Criteria

### 5. Capacity and capability for engagement



This refers to (1) capacity as having relevant and dedicated resources from all stakeholders (for example, providing a dedicated point of contact by the sponsor and having allocated sufficient time by all stakeholders to allow genuine engagement); and (2) capabilities for all stakeholders to enable meaningful engagement. (For example, the level of knowledge, expertise and training stakeholders might need to deliver PE activities throughout the project).

Consider supporting stakeholders to build the required capacity and capabilities for this project in different forms of training both with sponsor organisations and with each stakeholder (for example, helping to understand the context, processes, involved terminology etc.).

Both capacity and capability building are intended to facilitate participation and lower barriers to collaborate. Stakeholders can be given access to learning resources and given dedicated support (if needed). Capability needs may vary depending on the project needs, but also e.g. personal circumstances of PE representatives.

### 6. Transparency in communication and documentation



This refers to the establishment of communications plan and ongoing project documentation that can be shared with stakeholders. Communication among stakeholders must be open, honest and complete.

In addition, adequate up-to-date documentation must facilitate communication with all stakeholders throughout the project. Consider proactively and openly sharing progress updates throughout the project externally. In addition, communicating outcomes of the project to all stakeholders and how their contribution was of value to the success of the project is critical.

### 7. Continuity and sustainability



This refers to the smooth progression of the project, as well as efforts to maintain ongoing relationship with stakeholders. Consideration should be given for the role of stakeholders beyond a single project. When starting the project, consider including in your project plan the actions needed for maintaining expected flow of the project from beginning to end.

Create a plan to nurture relationships with your partners and stakeholders involved during the project, and when needed and requested, beyond the project as well. For all stakeholders successful planning and personal and organisational resilience should be anticipated.