D1.2 Criteria to assess how patient engagement expectations are met

777450 - PARADIGM

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

WP1 – Defining stakeholders' preferences, needs and expectations

Task 1.2 Co-Prioritize minimal expectations for patient engagement across key stakeholders

Task 1.3: Develop a set of criteria to assess patient engagement practices and processes against minimal expectations

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Due date	30/05/2019
Delivery date	20/05/2019
Deliverable type	R
Dissemination level	PU

Description of Action	Version	Date
	V1.1	XXX

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Document History

Version	Date	Description
V0.1	01/04/2019	First Draft
V0.2	08/04/2019	Comments from experts panels
V0.3	06/04/2019	Comments from first round reviewers
V0.4	20/05/2019	Draft edited based on comments
V1.0	30/05/2019	Final Version

Partners of the PARADIGM Consortium are referred to herein according to the following codes:

- **EPF**. EUROPEAN PATIENTS FORUM (Luxembourg) – **Project Coordinator**
- **EURORDIS**. EUROPEAN ORGANISATION FOR RARE DISEASES ASSOCIATION (France)
- **EATG**. EUROPEAN AIDS TREATMENT GROUP (Germany)
- **AE**. ALZHEIMER EUROPE (Luxembourg)
- **AIFA**. AGENZIA ITALIANA DEL FARMACO (Italy)
- **HTAi**. HEALTH TECHNOLOGY ASSESSMENT INTERNATIONAL (Canada)
- **IACS**. INSTITUTO ARAGONES DE CIENCIAS DE LA SALUD (Spain)
- **FSJD**. FUNDACIO SANT JOAN DE DEU (Spain)
- **VU-ATHENA**. STICHTING VU (The Netherlands)
- **UOXF-CASMI**. THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (United Kingdom)
- **EFGCP**. EUROPEAN FORUM FOR GOOD CLINICAL PRACTICE (Belgium)
- **SYNERGIST**. THE SYNERGIST (Belgium)
- **SYNAPSE**. SYNAPSE RESEARCH MANAGEMENT PARTNERS SL (Spain)
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- **VFA**. VERBAND FORSCHENDER ARZNEIMITTELHERSTELLER EV (Germany)
- **SARD**. SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT (France)
- **NOVARTIS**. NOVARTIS PHARMA AG (Switzerland)
- **COVANCE**. COVANCE LABORATORIES LTD (United Kingdom)
- **ALEXION**. ALEXION SERVICES EUROPE (Belgium)

- **Consortium.** The PARADIGM Consortium, comprising the above-mentioned legal entities
- **Consortium Agreement**. Agreement concluded amongst PARADIGM participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

1. Publishable Summary

This report describes the work that was done as part of PARADIGM's[1] work package 1 (WP1), which aimed to identify and define stakeholders' preferences, needs and expectations in patient engagement (PE) through an online survey and focus group consultations that were conducted in 2018[2].

The objectives of this work were two-fold: firstly to prioritise those needs and expectations identified, and secondly, with the help of topic experts, turn those prioritised needs into a set of criteria for a good PE activity.

The Delphi methodology[3] was used as the main tool to reach these objectives. Three expert panel groups were formed to match the three decision-making points Paradigm project focuses on [setting research priorities (SRP), the design of clinical trials (DCT) and early dialogues with Health Technology Assessment (HTA) bodies and regulators (ED)][4].

Each expert group went through two online survey rounds, and a subsequent meeting in Brussels where experts (who completed both online rounds) discussed to reach consensus on the final criteria to assess PE practices. The format, procedure and methodology of all three meetings were identical.

Each group produced a set of weighted criteria and categories for their dedicated decision-making point. The weights allocated represent the relative importance of the criteria in the set to assess PE practices.

Key outcomes:

The outcomes of the three Delphi groups showed some similarities. Some convergence can be seen at the level of themes as *aims and objectives*, and *selecting the right target population to engage with* scored as top criteria, and *sustainability* which scored the lowest in two Delphi groups (SRP and DCT), while the third Delphi group (ED) dropped sustainability in its final meeting.

Some criteria were debated more than others due to differences in interpretations of the terminology. For example, conflict of interest (COI) was understood as 'managing', 'disclosing' or 'avoiding' by the different stakeholders. Additionally, some bias in interpretation could have also come due to the EU and US perspective.

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1 PARADIGM is an Innovative Medicines Initiative (IMI) - a public-private partnership co-funded by the European Commission and EFPIA (the European Federation of Pharmaceutical Industries (and Associations). For more information about IMI projects, please visit: https://www.imi.europa.eu/about-imi. For more information about PARADIGM, please visit www.imi-paradigm.eu

[2] To learn more about WP1's online survey and focus group consultations, please see the report: https://imi-paradigm.eu/wp-content/uploads/2019/03/D1.1-Survey-analysis-report.pdf

[3] The Delphi methodology originates from the US and is meant to estimate the likelihood of future events. (RAND Corporation, 2019. Internet source, available here: https://www.rand.org/topics/delphi-method.html). In health research, it is widely used as a tool to obtain consensus on group opinion (Trevelyan, 2015. *European Journal of Integrative Medicine.* Available here: https://www.sciencedirect.com/science/article/abs/pii/S1876382015300160)

[4] , "PARADIGM focus[es] on three decision-making points, during which integration of the patient perspective is critical (if not essential) for the medicine lifecycle" as requested by the IMI call (PARADIGM, 2018). More information here: https://www.imi.europa.eu/projects-results/project-factsheets/paradigm.,

These results will be used in other PARADIGM work packages (i.e. WP2) in order to co-create questions for the gap analysis tool. In addition, the authors propose a way the results of the Delphi could be operationalized as a tool to assess PE practices in each of the three specific decision-making points to determine whether they meet the expectations for a good PE practice.

2. Introduction

PARADIGM, which stands for Patients Active in Research and Dialogues for an Improved Generation of Medicines, is an EU project funded by the Innovative Medicines Initiative (IMI) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). It is a 30-month project that involves 34 partners. Its mission is to develop a Patient Engagement (PE) framework that allows structured, meaningful, sustainable and ethical patient engagement focused on the three key decision-making points in the lifecycle of a medicine, i.e. research priority setting, design of clinical trials and early dialogue with regulators and Health Technology Assessment (HTA) bodies. The framework will include recommendations on processes, tools (with the creation of templates) and methods to measure and demonstrate the added value of innovative and effective approaches to patient engagement.

This work is part of work package 1 (WP1: Defining stakeholders' preferences, needs and expectations) deliverables and is a continuation of the online survey and focus group consultations created in 2018[5] that intended to map out the range and frequency of needs, expectations and desired outcomes for PE. To achieve a consensus for stakeholders' expectations and needs, a Delphi methodology was chosen to address the levels of specificity and in-depth information obtained from the survey and focus groups. The Delphi expert panels determined which priority and relative value (weights) each need and expectation for PE would get in each of the three decision-making points; how they relate to each other to form "good practice"; and which are more likely to predict desired outcomes.

3. Methodology

The Delphi methodology (Fig. 1) was used to firstly prioritize the stakeholders' needs and expectations and then to turn them into a set of criteria to assess PE practices and processes.

The Delphi process is a consensus technique, widely used in healthcare research[6] that meets the requirements of scientific methods[7]. This technique helps to identify and prioritise the expectations and preferences regarding a specific issue. The results obtained from the interaction of a structured group of experts are more solid than those from individuals[8]. In using this technique, all participants accept or at least have no strong disagreements regarding the criteria and categories[9] developed. Within PARADIGM, the Delphi modified technique

[5] For more information, see the report from the survey analysis here: https://imi-paradigm.eu/wp-content/uploads/2019/03/D1.1-Survey-analysis-report.pdf

[6] Eubank BH, Mohtadi NG, Lafave MR, Wiley JP, Bois AJ, Boorman RS, et al. Using the modified Delphi method to establish clinical consensus for the diagnosis and treatment of patients with rotator cuff pathology. BMC Med Res Methodol [Internet]. 2016;16(1):1–15. Available from: http://dx.doi.org/10.1186/s12874-016-0165-8

[7] Hutchings A, Raine R, Sanderson C, Black N. A comparison of formal consensus methods used for developing clinical guidelines. J Heal Serv Res Policy. 2006;11(4):218–24.

[8] Black N, Murphy M, Lamping D, McKee M, Sanderson C, Askham J, et al. Consensus development methods: A review of best practice in creating clinical guidelines. J Heal Serv Res Policy. 1999;4(4):236–48.

[9] Criteria refer to the attributes of PE practices. Categories are elements that describe the characteristics and nuance of each criterion in which

gathers the relevant issues in PE within each of the three decision-making points in medicines development.

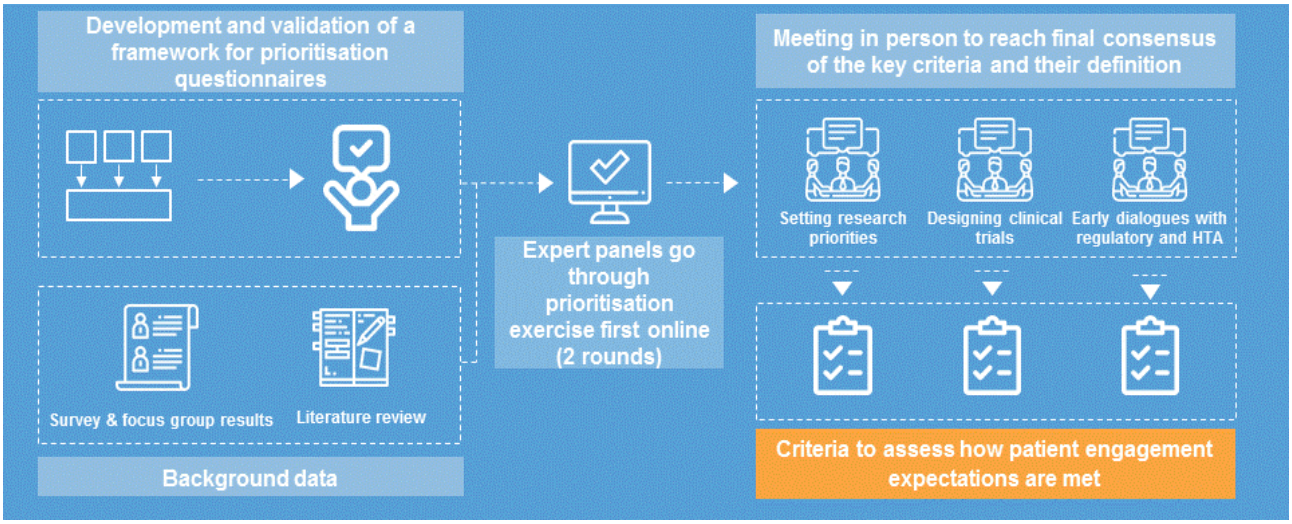


Figure 1: Overview of the PARADIGM Delphi process

This technique uses qualitative and quantitative data sequentially by combining two online surveying rounds to elicit responses in a systematic manner, and a subsequent meeting in person that allows expert panels to interact, discuss, debate and justify their viewpoints. Following the two on-line survey, a face to face meeting was held to achieve consensus on a set of criteria to assess PE practices in medicines development.

Using this technique, expectations and preferences for PE can be identified and prioritised in the three specific points in time. The technique is based on the assumption that the convergence of "good practice" elements and their relative value, steered by structured interaction among a group of individual experts on PE processes, yields more accurate results than those from individuals; thus the consensus produced is more likely to lend credibility within each of the decision making point in medicine development.

Procedure

1- Developing Delphi Questionnaires

First, the Delphi questionnaires were developed for the two online surveying rounds (Fig. 1). A separate questionnaire was created for each of the three decision-making points. These questionnaires were built on the basis of the information obtained from various sources:

- The previous work carried out within WP1:
    - Results from the *Survey analysis report on stakeholder-specific preferences, needs and expectations* carried out within WP1 (task 1.1)

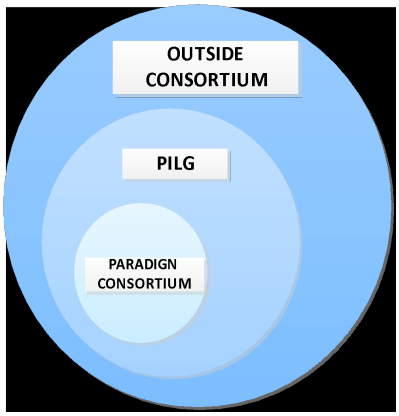
is included

- Three focus Groups by Alzheimer Europe, San Juan de Deu (paediatric group) and HTA bodies.
- Patient Focus Medicine Development (PFMD) PE Quality Guidance (https://patientfocusedmedicine.org/)
- Literature review from National, European and International public and private institutions and organisations, academics, regulatory bodies, HTA bodies, patient's organisations etc. The types of documents consulted and reviewed were those related to PE in the three decision-making points[10].

Followed the search, all gathered information was analysed; those elements deemed relevant for the questionnaire were retrieved and organized into criteria with their categories, to anticipate the potential structure of the questionnaires for assessing PE practices[11]. The PARADIGM consortium was involved throughout the development of the questionnaires.

2- Experts' recruitment for the three Delphi panels

The recruitment process began (see Figure 1) at the same time as the questionnaires were being constructed. The objective was select participants who share and bring a variety of perspectives and expertise and have the potential to provide relevant, key and rich information about PE for each of the Delphi. To select the experts, first the Delphi team (WP1 leaders and IACS) defined stakeholder and participant profiles for each panel. The main requirement to participate was to have recognised expertise, experience and knowledge within their topic group[12]. Additionally the selection criteria took into account the type of stakeholders, as well as country and gender diversity, to avoid bias and support global applicability.



For the recruitment process (Figure 2), the PARADIGM consortium was invited to propose candidates from within or outside the consortium. Members of the PARADIGM International Liaison Group (PILG) were also invited to participate. To ensure adequate representativeness of views as well as to complement the level of expertise in the expert panels, the Delphi team recruited other relevant expert (outside the Consortium) whose profile was still missing ensure representativeness in the panel groups.

Figure 2: Experts recruitment and outreach process

[10] See annex 1 for the list of sources

[11] See annex 2 for the questionnaires

[12] See Annex 3 for the panel stakeholder profile

3-Delphi first and second online round (R1 and R2)

The finished questionnaires were created and distributed on an online platform and access to it was given to expert panellists individually (see figure 1). This platform provides participants the survey information in real-time (i.e. how many have already scored each category and the corresponding median score). During the survey periods, the system allowed users to stop and resume the task (including modifying the previous responses) as many times as they needed. Participants could also add comments and suggestions for the questions presented in the platform in both rounds. These comments were used to prepare the final meeting and suggest to the experts possible merging and rephrasing of some of the criteria and categories. A glossary was included, to help experts understand the concepts used in the questionnaires[13].

During the first and second rounds, experts had to rate each question based on their knowledge and expertise in PE. Concretely during the first round, experts were asked to assess how relevant was each question when assessing PE practices using a Likert-scale[14] [from 1-3 (not relevant at all) to 9 (highly relevant)]. The Mean, Median, Coefficient Variation (CV), Interquartile range (IQR), Quartile 1 (Q1) were calculated along the vote distribution. Agreement was reached and kept for priority setting in the second round for those questions when Q1≥7, IQR ≤ 1, CV <20%; and when the median and the votes fitted within the same bracket (agreement converged around 'relevant') by the experts. Questions were dropped when Q1≤ 6, IQR ≥ 2, CV < 20% and there was agreement when the median and votes fitted within the irrelevance or not clearly relevant bracket. The rest of the questions that did not reach any agreement were kept for reassessment for the second round

For the second round, participants were asked to individually re-score the categories. In this round, questions that experts had agreed on as relevant for assessing PE practices during the first round were again presented for prioritisation (from 1=lowest priority to 9= highest priority). The analysis focused on the Mean, Median, Coefficient deviation (CV), and Interquartile range (IQR), Quartile 1 (Q1) as well as the vote distribution to determine whether experts agreed on the level of priority (1-3 low priority; 4-6 moderate priority; 7-9 high priority). Questions that reached no agreement in the first round were presented again in the second round to the experts to re-rank using the proposed relevance scale from the first round (from 1= 'not relevant at all' to 9= 'highly relevant').

4- Meeting in person

After the two online survey rounds finished, only those experts who completed the first and second round were eligible and invited to participate in the third round meeting in Brussels to reach consensus about the final criteria to assess PE practices. There was one specific meeting organised for each Delphi panel group. The format, procedure and methodology of all three meetings were identical.

13 See Annex 4 for the glossary
14 See Annex 4 for the glossary

A facilitator (from the IACS who was not part of the expert panel), helped conduct the discussions following a structured consensus methodology. Two rapporteurs (from IACS who were not part of the panel of experts either) provided support in recording voting processes and modifications in phrasing and allocation according to experts' consensus. During the group discussion, experts were able to discuss and elucidate their point of view.

The objectives of these meetings were to

- identify similarities within the different criteria and categories,
- resolve eventual redundancies, decide the final set of criteria and categories,
- allocate the corresponding weight to each criteria and category.

In the first part of the process, questions prioritised during the second round were presented to the experts; those questions that failed to reach agreement during the first and second rounds were also presented to experts who were asked to decide if the questions were relevant to assess practices of PE, and whether to keep or drop them. Merging, rephrasing and reallocating the categories across each criterion were allowed at this stage. Once full consensus was reached, the panel spent the remainder of the meeting voting.

In the second part, the experts voted on the final hierarchy of the elements for the decision-making point to obtain relative weights for the consolidated criteria and categories.

Experts proceeded to prioritise the categories by weighting them by sharing 100 points among them. The final weight for each category was calculated by averaging total points by the number of voters (dividing total points by number of experts and multiplying by 100, so the sum of categories' weight within a criterion was always 100).

The experts were then asked to prioritise and weight the criteria in the same way - by sharing 100 points among all criteria. In both cases, the process was anonymous and prioritisation was conducted using a document that included all final categories and criteria previously agreed on by the experts.

The experts voted on the final hierarchy of elements of good PE practices for the corresponding decision-making point

4. Results

4.1. Representativeness of the three Delphi Expert Panels

The composition of the Delphi expert panels is described in Figure 3. The main requirement was that the participants hold relevant knowledge and experience in the field of PE they are involved in to have the potential to provide relevant information about patient engagement.

Participants	Initially	Round 1	Round 2	Round 3 F2F	Profiles in the F2F meeting
DELPHI					
Setting research priorities	24	20	16	10	Patient/Patient advocate/ Patient representative, Regulator, Pharma company, professional, Research Funder (public or private), Healthcare professionals, Academic, researcher, other
Design of clinical trials	31	29	26	18	Patient/Patient advocate/ Patient representative, Academic, researcher, Healthcare professionals, Pharma company professional, HTA Body, Research Funder (public or private), other
Early Dialogues with HTA and Regulators	26	20	18	12	Regulator, Pharma company professional, Academic, researcher, Patient/Patient advocate/ Patient representative, HTA Body, other
TOTAL	81				

Figure 3: Representativeness of the Delphi experts groups

No specific information was collected regarding the specific reasons for the dropouts during the process. However, some reported to be unable to attend the meeting in Brussels due to work commitments. Some others informed that the reason for their dropping out was due to their institution rules and regulations; they were not allowed to attend any meeting with private companies present to avoid potential conflict of interest.

The reliability of the results could be compromised if many experts drop out of the study before it is completed, putting at risk some stakeholders' representativeness. Accordingly, the Delphi team analysed the dropouts in each of the Delphi rounds to check for stakeholders' participation to make sure that representativeness was not compromised. It was concluded that, despite the dropouts, response rate has remained high and the dropouts did not affect any stakeholder groups' representativeness. Thus the final results of the Delphi can be considered valid with the existing participation.

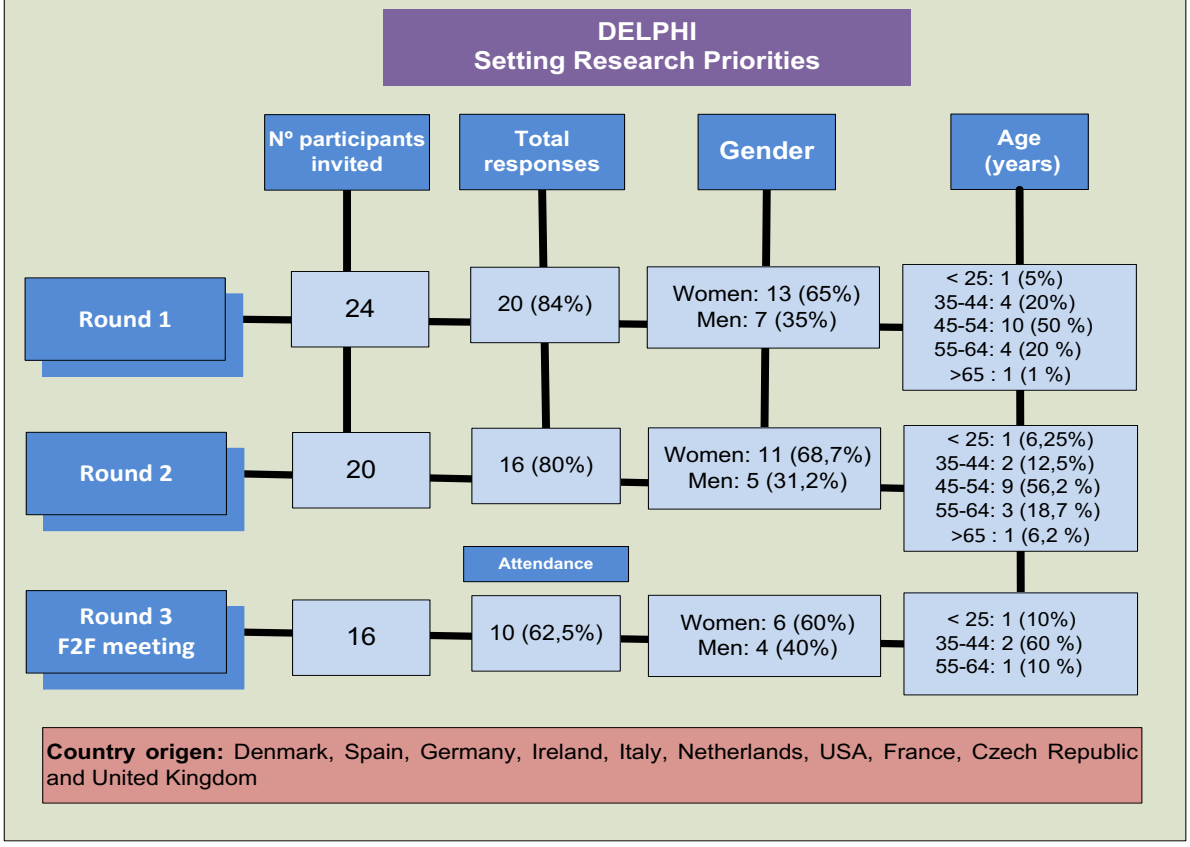
4.2. Delphi on Patient Engagement in Setting Research Priorities

Expert panel for the Delphi in PE in Setting Research Priorities

The socio-demographic characteristics of the respondents in this Delphi for the three rounds are displayed in Figure 4.

Figure 4: Demographic of the Delphi experts in the group for setting research priorities

Figure 4: Socio-demographic characteristics of the participants for the Delphi in SRP



Round 1 (Online) – Relevance Assessment

The first round lasted three weeks (November 12th 2018 – December 3rd 2018).

From the initial 56 categories [49 categories and 7 PE impact (PEI) sub-categories] that made up the list to be assessed, agreement was reached on 20 categories (17 categories + 3 PEI sub-categories, (table 2 in Annex 5). No consensus was reached on 32 categories (28 categories and 4 PEI sub- categories), (table 3 in Annex 5) and 4 were dropped, (table 4 in Annex 5).

Round 2 (Online) – Relevance Assessment and Prioritization

The second round lasted three weeks (January 1st 2019 – January 18th 2019).

Regarding the 32 categories (28 categories + 4 PEI sub- categories) on which no consensus was reached in the first round, 7 (5 categories + 2 PEI sub- categories) were deemed relevant (table 5 in Annex 5).

As for the rest of the categories, in 14 categories (13 categories + 1 PEI sub- categories) still no consensus was reached about the level of relevance, so they were retained for discussion at the face-to-face meeting (table 6 in Annex 5) and 11 (10 categories + 1 PEI sub- categories) were dropped (table 7 in Annex 5).

From the 20 categories (17 categories + 3 PEI sub- categories), agreed as relevant in Round 1, 14 were considered a high priority and 5 were considered medium priority and 1 was low priority on Round 2. They were kept for discussion at the face-to-face meeting. The scores obtained for each category and the corresponding criteria are summarized in table 8 in Annex 5.

Round 3 (Meeting in person) – Discussion and Final Prioritization

PE in Setting Research Priorities Expert Panel

The expert panel took part in round 3 meeting in two half days in Brussels. The final set of criteria with their weights recommended for assessing PE process in setting research priorities are detailed in Table 9 in Annex 5.

4.3. Delphi on Patient Engagement in Designing Clinical trials

Expert panel for the Delphi in PE in Designing Clinical Trials

The socio-demographic characteristics of the respondents in this Delphi for the three rounds are displayed in Figure 5

Figure 5: Socio-demographic characteristics of the participants for the Delphi in DCT

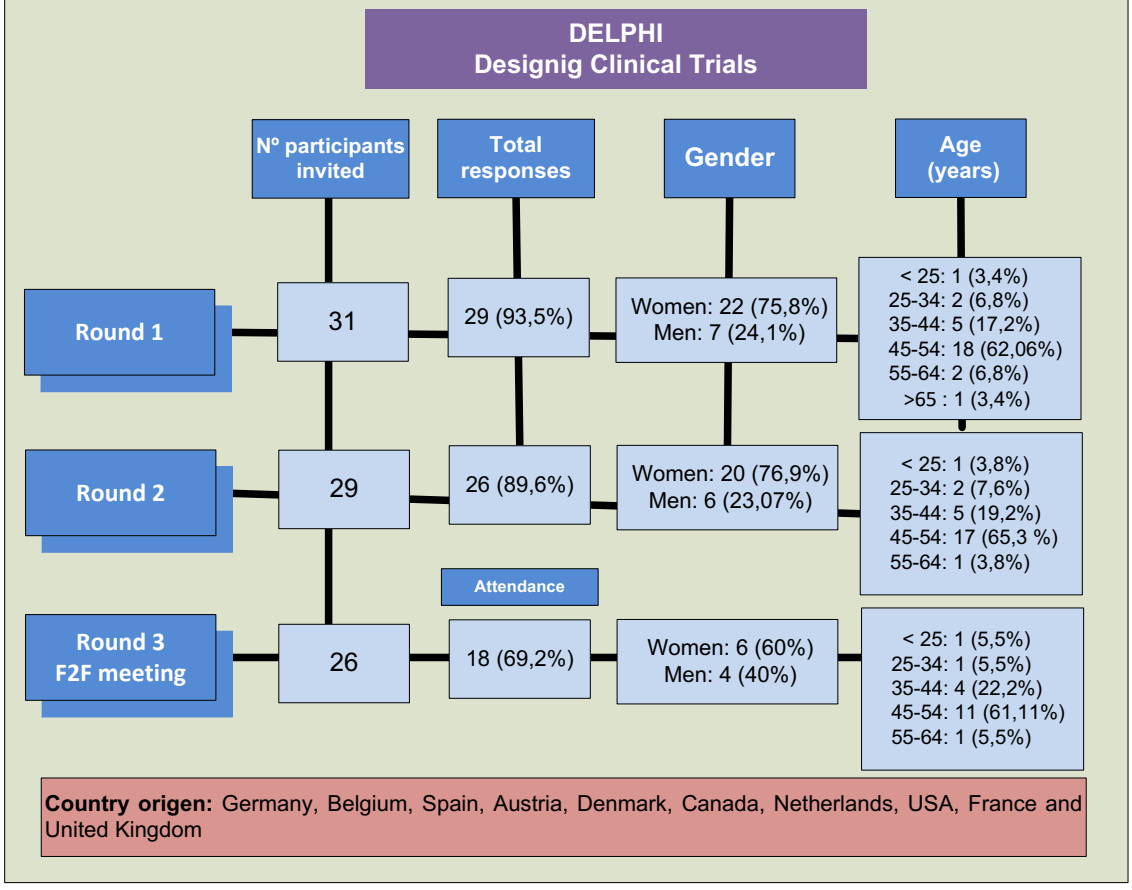


Figure 5: Demographic of the Delphi experts in the group for designing clinical trials

Round 1 (Online) – Relevance Assessment

The first round lasted three weeks (November 12th 2018 – December 3rd 2018).

From the initial 58 categories [48 categories + 10 PE impact (PEI) sub- categories] that made up the list to be assessed, agreement was reached on the relevance of 26 categories (21 categories + 5 PEI sub- categories), (table 10 in Annex 6). No consensus was reached on 22 categories (19 categories + 3 PEI sub- categories), (table 11 in Annex 6) and 10 (8 categories + 2 PEI sub- categories) were dropped, (table 12 in Annex 6).

Round 2 (Online) – Relevance Assessment and Prioritization

The second round lasted three weeks (January 1st 2019 – January 18th 2019).

For this second round, experts suggested incorporating two new categories (1 category under the Criterion 7: Involvement and participation and 1 as PEI sub-category; both are indicated in the tables) as they considered important and they were not initially included in the questionnaire of the first round.

Regarding the 22 categories (19 categories + 3 PEI sub- categories) on which no consensus was reached in the first round, 16 (13 categories + 3 PEI sub- categories) were deemed relevant (table 13 in Annex 6).

As for the rest of the categories, in 2 categories and 1 of the new categories still no consensus was reached about the level of relevance, so they were retained for discussion at the face-to-face meeting (table 14 in Annex 6) and 4 categories were dropped (table 15 in Annex 6).

From the 26 categories (21 categories + 5 PEI sub- categories), agreed as relevant in Round 1, 12 were considered as high priority and 11 were considered medium priority and 3 was low priority on Round 2 (table 16 in Annex 6). They were kept for discussion at the face-to-face meeting.

Round 3 (Meeting in person) – Discussion and Final Prioritization

PE in Designing Clinical Trials Expert Panel

The expert panel took part in round 3 meeting in two half days in Brussels. The final set of criteria with their weight recommended for assessing PE process in in designing clinical trials are detailed in Table 17 in Annex 6.

4.4. Delphi on Patient Engagement in Early Dialogues with HTA & Regulators

Expert panel for the Delphi in Early Dialogues with HTA and Regulators

The socio-demographic characteristics of the respondents in this Delphi, for the three rounds, are displayed in Figure 6

Round 1 (Online) – Relevance Assessment

The first round lasted three weeks (November 12th 2018 – December 3rd 2018).

From the initial 62 categories [51 categories + 11 patient engagement impact (PEI) sub-categories] that made up the list to be assessed, agreement was reached on the relevance of 30 categories (23 categories + 7 PEI sub- categories) (table 18 in Annex 7). No consensus was reached on 20 categories (18 categories and 2 PEI sub- categories) (table 19 in Annex 7) and 12 were dropped (table 20 in Annex 7).

Figure 6: Socio-demographic characteristics of the participants for the Delphi in ED with HTA and Regulators

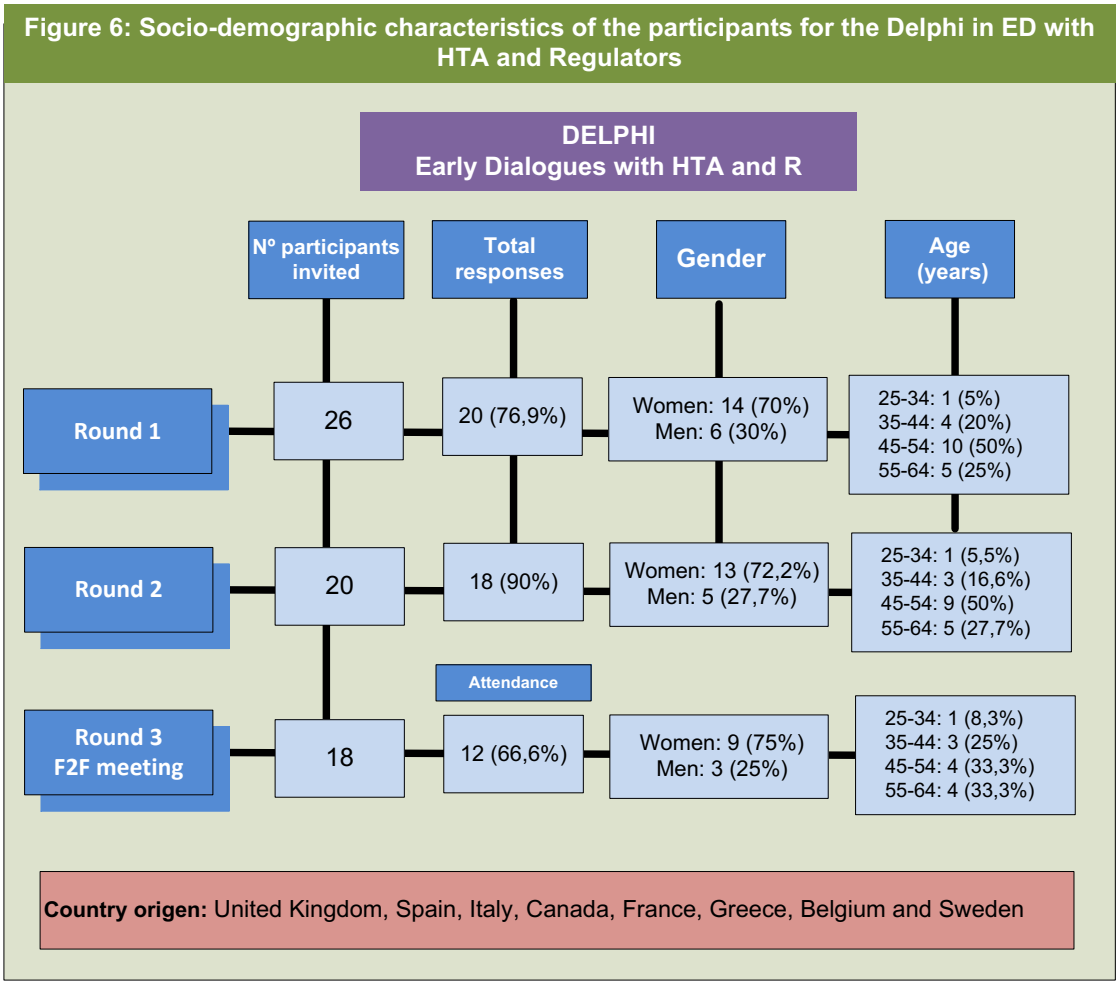


Figure 6: Demographic of the Delphi experts in the group for early dialogues with regulators and HTA

Round 2 (Online) – Relevance Assessment and Prioritization

The second round lasted three weeks (January 1st 2019 – January 18th 2019).

Regarding the 20 categories (18 categories + 2 PEI sub- categories) on which no consensus was reached in the first round, 7 (6 categories + 1 PEI sub- categories) were deemed relevant (table 21 Annex 7).

As for the rest of the categories, in 7 categories (6 categories and 1 PEI sub-category) still no consensus was reached about the level of relevance, so they were retained for discussion at the face-to-face meeting (table 22 in Annex 7) and 6 categories were dropped (table 23 in Annex 7).

From the 30 categories (23 categories + 7 PEI sub- categories), agreed as relevant in round 1, 9 were considered a high priority and 16 were considered medium priority and 5 was low priority in this round and were kept for discussion in round three (table 24 in Annex 7).

Round 3 (Meeting in person) – Discussion and Final Prioritization

PE in Early Dialogues with HTA & Regulators Expert Panel

The expert panel took part in the round 3 meeting in two half days in Brussels. The final set of criteria with their weight recommended for assessing PE process in early dialogues with HTA and Regulators are detailed in Table 25 in Annex 7.

5. Discussion

It is acknowledged that the differences in the outcomes (Table 1) of the three Delphi groups result from differences in interpretation of the questions by the experts within each group. Thus, all three Delphi outputs are not necessarily directly comparable (i.e. each expert panel group and their questionnaires were different for each decision making point), but key similarities also exist.

Setting Research Priorities		Designing Clinical Trials		Early Dialogues with Regulators and HTA	
CRITERIA	WEIGHT	CRITERIA	WEIGHT	CRITERIA	WEIGHT
Key Elements of Practice Design	19.5	Aim and objectives	14	Aim and objectives	17.9
Resources	16	Patient engagement impact	14	Target participants involved in patient engagement	15.3
Evaluation of the PE Practice in Setting Research Priority	12	Target patients involved	12	Involvement and participation	14.7
Capacity Building	12	Legal and ethical consideration	11	Code of conduct	11.3
Patient Engagement Impact	11.5	Involvement and participation	11	Capacity building	11.1
Involvement and Participation	11	Resources	10	Resources	10.9
Code of Conduct	10	Capacity building	10	Patient Engagement Impact	10
Sustainability	8	Evaluation of the PE practice in the Design of Clinical Trials	10	Evaluation	8.8
		Sustainability	8		
TOTAL	100	TOTAL	100	TOTAL	100

Table 1: Summary of final output from the three Delphi panel groups

Some of the key findings discussed throughout the face-to-face meetings as follows. Some convergence can be seen in the outputs of the three Delphi groups. For example, Aims and

Objectives of a practice ranked high, which shows the general agreement by the experts that this criterion is relevant for a good PE practice. The aims and objectives should be agreed on and understandable by all stakeholders involved in the PE practice. At this stage of the design, the PE practice should also contemplate to define and agree on the roles and responsibilities among all participants and to include mechanism to ensure that that all participants understand each other's roles and responsibilities.

For all decision-making points, there was a major discussion about the difficulty in selecting the right patients ("…involve patients as individuals too no only patients' organisations"), with specific characteristics and circumstances to engage with, which reflect the diversity of the target population. Establishing a clear method to select patients was also deemed relevant to ensure the engagement is not meaningless and incomplete.

Establishing a regular feedback system to inform patients about outcomes or changes that may happen in each phase of the involvement was debated during the meetings. However, in the discussion experts pointed out the difficulty sometimes of giving feedback without breaking confidentiality requirements, due to the nature of some information. It was also highlighted that patients should be able to provide feedback on the information received related to the results, documents, final output, etc. The experts agreed that feedback is essential after the completion of the process and that giving regular feedback closes the loop of patients' involvement in the implementation of a practice.

Likewise, the criterion related to conflict of interest was extensively discussed in the three separate meetings. The communication and management of potential conflicts of interest, especially those referred to patients and healthcare professionals was largely discussed. It was pointed out that "…conflicts of interest must be avoided, not just managed or disclosed" in a PE practice. However, as this is not always possible; and if the involvement of some healthcare professionals is avoided because of their conflicts of interest, experts with strong knowledge in the field would be excluded; therefore, a valuable contribution could be missed. The discussion also revolved around payments and funding for participants involved in some PE practices. There was a diversity of opinions and views. On one side, some experts considered, neither patients nor professionals should collect payments for their participation because of the potential conflicts of interest that these payments could imply. Other views considered that any activity should be remunerated to any stakeholder involved (i.e. healthcare professionals and patients) because they are contributing with their knowledge, expertise, time and effort. There was a range of opinions depending on the type of stakeholder (private or public sector) and by their country of origin.

Finally, another key criterion discussed during the meetings was related to sustainability. Although this criterion was considered relevant by the experts, during the voting process it reached the lowest score in the Delphi groups of SRP and DCT. In the Delphi group of early dialogues with HTA and Regulators sustainability was included in the first two online rounds but dropped in the final meeting. For some HTA bodies it is already very difficult to start a process like PE so "long term sustainability is not yet considered in the early dialogues". Thus

sustainability should not be an element to be evaluated in PE practices in this decision-making point. It was also recognized that sustainability of PE for vulnerable populations is key and that these populations are experiencing resource, process and cultural barriers to sustainability.

Another major element debated within sustainability was related to fostering alliances with private and/or public institution to facilitate sustainability in the PE practices. There were opposing points of view; on one side, some experts from public entities or patients organisations seek partnerships in order to ensure long-term and sustainable practices, which might not be so necessary for the private sector (i.e. one explanation for this was that sometimes the continuity of a project was decided by the institution's already set plans).

Biases in the Delphi results may come from two known sources. The assumptions that definitions of PE and patient and public involvement (PPI) relate to only English speaking interpretations were acknowledged as a caveat. Additionally, many respondents in the DCT Delphi group were from North America, hence some bias in interpretation of responses and weightings is inevitable from an EU vs. US perspective.

6. Proposal for Utilising the Criteria

Translating Delphi outputs into a tool to assess implemented PE practices

In this section, we suggest how the results of the Delphi groups could be translated into a tool that can be used to assess PE practices to assess and determine whether they meet the expectations for a good PE practice in these specific decision-making points. With this tool, we propose a way to operationalize the output of this work, namely the co-prioritised set of minimum criteria that derived from stakeholder's needs and expectations for PE. The results of the assessment could help users to firstly identify successful practices and secondly to replicate them into their own setting.

It should be noted, that these proposed tools are not within the scope of this work and thus have not been further developed. However, as we have been part of producing the criteria, these tools are our suggestion of how the criteria could be operationalized.

How the criteria has been operationalized

This proposed tool provides an approximate score for each category (0 to 100) within each criteria and a final score (0 to 100) for the practice. The scores of each category within the criteria have been weighted accordingly to the results of the prioritisation done by the Delphi panels. These weights represent the importance given by the expert panel with regards to the completion of each criterion in the PE practice design or implementation.

To convert the weights into a global score, the weight of each criterion is calculated by adding the weight of its categories.

How to use these tools

The tool uses a weighted 5-item Likert-scale to assess PE practices, however, it should be noted

that it cannot fully counter the subjectivity of the user with regards to the interpretation of how each criteria addressed in the PE practice.

When assessing a PE practice, the user should choose within the likert-scale a score from 0 (minimum score) to 5 (maximum score) based on the degree of fulfilment of the practice against each of the category within each criterion of the tool. Once the assessment process is done, the scores are added up to give a final score that can be used to demonstrate how well a practice has been designed or implemented according to the criteria.

To establish a threshold that will determine if a practice is good or not (based on the final score) could be decided by the user prior to the assessment process.

To access the proposed tool for *Patient Engagement in Setting Research Priorities* please follow this link: https://imi-paradigm.eu/wp-content/uploads/2019/06/Assessment_tool_PE-in-Setting-Research-Priorities.xlsx

To access the proposed tool for *Patient Engagement in Designing Clinical Trials* please follow this link: https://imi-paradigm.eu/wp-content/uploads/2019/06/Assessment_tool_PE-in-Design-Clinial-Trials.xlsx

To access the proposed tool for *Patient Engagement in Early Dialogues with HTA bodies and Regulators Tool* please follow this link: https://imi-paradigm.eu/wp-content/uploads/2019/06/Assessment_tool_PE-in-Eary-Dialogues-with-HTAR.xlsx

Annex 1. List of sources

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PPI Guidance for researchers supported by the BPSU

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CADTH

Patient Input Template and Integrating Companion Diagnostic Assessment Into CADTH's Drug Review Programs (2017)

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Template for Patient Group Input to CADTH Common Drug Review and pan-Canadian Oncology Drug Review

https://www.cadth.ca/pcodr

Durham University Centre for Social Justice and Community

Action Community-based participatory research A guide to ethical principles and practice

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academics and their organisations. EMA 2017

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The patient's voice in the evaluation of medicines How patients can contribute to assessment of benefit and risk. EMA. 18 October 2013

https://www.ema.europa.eu/documents/report/report-workshop-patients-voice-evaluation-medicines_en.pdf

EMA-Incorporating patients' views during evaluation of benefit risk by the EMA Scientific Committees. 23 October 2014 https://www.ema.europa.eu/documents/other/incorporating-patients-views-during-evaluation-benefit-risk-european-medicines-agency-scientific_en.pdf

The role of patients as members of the EMA Human Scientific Committees

https://www.ema.europa.eu/documents/other/role-patients-members-european-medicines-agency-human-scientific-committees_en.pdf

EPF

Patient Involvement in Health Technology Assessment in Europe (Results of the EPF Survey)

http://www.eu-patient.eu/globalassets/projects/hta/hta-epf-final-report2013.pdf

Fastercures

Patient Perspective Value Framework

http://www.fastercures.org/programs/patients-count/patient-perspective-value-framework/

FDA

Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making. Guidance 1: collecting comprehensive and representative input. https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm610279.htm

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PATIENT-FOCUSED DRUG DEVELOPMENT PUBLIC WORKSHOP ON GUIDANCE COLLECTING

COMPREHENSIVE AND REPRESENTATIVE INPUT DISCUSSION DOCUMENT Workshop Date: December 18, 2017 (FDA)

https://www.fda.gov/drugs/newsevents/ucm574725.htm

HQIP

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HTAi

Patient Group Submission Template for HTA of medicines (2014)

https://htai.org/interest-groups/pcig/resources/for-hta-agencies-and-policy-makers/

Patient Group Submission Template for HTA of non-medicines

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RESOURCES TO INVOLVE PATIENTS AND PATIENT GROUPS IN HTA: Patient Group Submission Templates Generic patient submission templates for an HTA, with useful prompts in English and French (Medicine's HTA)

https://htai.org/interest-groups/pcig/resources/for-patients-and-patient-groups/

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Public involvement in clinical trials: Supplement to the briefing notes for researchers

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Beresford P. Beyond the usual suspects, towards inclusive user involvement https://www.invo.org.uk/beyond-the-usual-suspects-towards-inclusive-user-involvement/

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(M-CERSI) Assessing meaningful patient engagement in drug development: a definition, framework, and rubric. University of Maryland

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MEDICAL DEVICE INNOVATION CONSORTIUM (MDIC)

Patient centered benefit-risk project report

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National Health Council (NHC)

Dialogue / Advancing Meaningful Patient Engagement in Research, Development, and Review of Drugs September 22, 2015

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National Institute for Health Research

National Standards for Patient Involvement

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Parent Project Muscular Dystrophy (PPMD)

Key considerations for developing & integrating patient perspectives in drug development: examination of the Duchenne case study.

https://www.bio.org/sites/default/files/BIO_PPMD_Paper_2016.pdf

Patient-Centered Outcomes Research Institute (PCORI)

Engagement in health research

https://www.pcori.org/engagement

https://www.pcori.org/literature/engagement-literature

Patient Focused Medicine Development (PFMD)

Patient Engagement Quality Guidance Tool [Planning a PE project] [Assessing an ongoing or completed PE project]

http://patientfocusedmedicine.org/peqg/patient-engagement-quality-guidance-scenario-2.pdf

Spanish Ministry of Health, Consumption and Social Welfare

Patient Involvement in the Development of Clinical Guidelines. Methodological handbook. (Implicación de Pacientes en el Desarrollo de Guías de Práctica Clínica. Manual Metodológico) Grupo de trabajo de implicación de pacientes en el desarrollo de GPC. Implicación de Pacientes en el Desarrollo de Guías de Práctica Clínica: Manual Metodológico. Ministerio de Sanidad, Servicios Sociales e Igualdad. Instituto Aragonés de Ciencias de la Salud-IACS. Guías de Práctica Clínica en el SNS: IACS Nº 2010/01.

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Annex 2. Delphi questionnaires

Questionnaire-DELPHI ON PE IN SETTING RESEARCH PRIORITIES

Criterion 1: Aim and objectives

R1. The aim and objectives of the practice on PE in research priority are agreed with all stakeholders (i.e patients, academics, researchers, pharmaceutical companies etc) involved.

R2. The aim and objectives of the practice on PE in research priority are related to patients' needs and interests.

R3. The aim and objectives of the practice on PE are clear and understandable for all participants.

Criterion 2: Contextualization of the practice on PE in Research Priority

R4. The practice is based on an assessment of the patients' needs and preferences who will be engaged in setting research priority processes.

R5. There is a clear understanding of contextual factors that could affect the outcomes of involving patients in setting research priority (e.g funders, policy makers, industry, research promoters…etc).

R6. Any existing policy directives, legal (governance requirements) and/or regulatory framework about how to engage patients in setting research priority have been considered

Criterion 3: Target participants involved in patient engagement

R7. The profiles of the patients engaged in setting research priorities reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc) and includes gender sensitive information.

R8. The profiles of the patients engaged in setting research priorities are selected to represent relevant patients' circumstances (e.g., former patients, patients who are at risk for a disease, but do not yet have the disease, severity of the disease, patients' advocates, patients' representatives, patient organizations, level of experience in setting research priority, patient's scientific knowledge/ background).

R9. The practice includes methods to identify individuals who have the necessary scientific background or expertise, "lived" experience to participate in setting research priority (e.g., patient's networks, health care professionals' networks, public advertise etc.).

R10. The practice supports patients to engage and/or reach out to vulnerable groups to involve them in setting research priorities, as well as to mentor other patients.

R11. The practice includes relevant points of view other relevant stakeholders (e.g., carers, tutors, researchers, health care providers, decision-makers, policy makers, funders).

R12. In the PE practice, the roles and responsibilities of all participants involved, including patients, are clearly defined and agreed.

R13. There is clear guidance about how to assign roles among all participants involved in setting research priority.

R14. The practice display flexibility and open-mindedness in assigning the roles for the patients, according to the profile, interest and background of the patient (e.g. as sources of

information, as consultants or as collaborating partners of the process).

R15. The practice includes specific tools (e.g., roles and responsibility charts, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), to ensure that all participants understand their own and other's roles and responsibilities.

Criterion 4: Code of conduct

R16. The practice includes a code of conduct, which clearly states the rules and mechanism of participation in setting research priority for all stakeholders involved.

R17. The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way, and adapted to the target population involved.

R18. The practice contains mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).

R19. The practice contains procedures (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidating, and unethical behaviours resulting from their participation in the research priorities process.

Criterion 5: Resources

R20. All participants involved in the setting research priority practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.

R21. The practice includes an equitable financial compensation framework for all participants (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).

R22. Funding is allocated to cover all the elements of the practice (e.g., human resources, material resources), and is adequate for the intended work.

R23. The adequate infrastructures needed for patients' and other stakeholders' involvements are in place (e.g., technological support, working space, information and communication technologies) adapted to specific circumstances of participants (e.g possible physical, mental, cognitive or any impairments etc.)

R24. The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.

Criterion 6: Capacity building

R25. The practice identifies the competencies required by all participants involved in setting research priority (e.g knowledge and skill such as how to perform patient engagement in setting research priority, etc).

R26. The practice includes specific training programs about setting research priority processes and methods to all participants (e.g., written information, in-house training, online, personalised assistance, and webinars).

R27. The training material is adapted, comprehensible and accessible to all participants taking into consideration impairments, literacy levels, cultural background and the circumstances of vulnerable patients involved in setting research priority.

R28. The training program specifies time when training needs to be provided, duration and

frequency of the sessions (e.g., on demand, once, twice a month/year).

R29. The practice includes training for patients and other stakeholders involved in different areas (e.g legal and regulatory concepts and challenges in research or deliberative processes, concepts, terminology etc).

R30. The practice incorporates training/coaching for stakeholders, other than patients (e.g researchers, healthcare professional, funders etc) regarding the participation of patients in research priority setting.

Criterion 7: involvement and participation

R31. The type of interaction among different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.

R32. Patients receive timely, clear, accessible and appropriate information about their involvement (i.e what will be addressed, what is expected from them, what their participation will entail, how the practice will be organised etc)

R33. The timing requirement of the engagement in setting research priority is appropriately planned, taking into account patient's needs, and based upon the requirements of the engagement process (e.g time of the day, duration etc).

R34. Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc).

R35. A regular feedback system to inform patients about the outcomes / changes is included for each phase of the involvement.

R36. The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into consideration potential impairments (e.g., impaired vision, blindness, deafness and cognitive problems), low literacy levels , cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).

R37. The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in setting research priority.

R38. Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.

Criterion 8: Evaluation of the PE Practice in Setting Research Priority

R39. An evaluation framework is included (structure, process and results) and it enables regularity evaluation (frequency, timing…).

R40. The evaluation framework is shared and agreed among the participants to foster collaboration.

R41. Methods, tools and monitoring system are in place to evaluate the PE practice.

R42. The evaluation outcomes are linked to the aim and objectives of the PE practice in setting research priority.

R43. The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.

R44. The practice includes procedures by which the conclusions of the evaluation of the practice on PE are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or the current one with a continuous improvement process).

Criterion 9: Patient Engagement Impact

R45. The practice identifies relevant outcomes and impacts regarding the involvement of patients in setting research priority.

R46. Assess the relevance of the following possible outcomes and impacts for patient engagement in setting research priority:

46.1 Research topic and priorities become more appropriate, based on patients' needs

46.2 The product profile (drug, technology) become more relevant and usable for patients.

46.3 Research questions and outcomes/endpoints become more relevant for patients.

46.4 Increased probability of ending the study during the research process (reduced failure of the project).

46.5 Research proposals submitted to public funders have more options to be financed (e.g. enhanced credibility).

46. 6 Resource allocations when engaging patients within industry become more appropriate and are based on patients' needs.

46. 7 Funded studies will provide more useful information for patients and decision-making processes

Criterion 10: Sustainability

R47. The continuation of the practice is ensured through ownership and it is embedded in the institution or organisation.

R48. Human and financial resources required for the long-term continuity of the practice on PE in setting research priority are identified and secured.

R49. The practice identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity.

R50. There is a dissemination and communication plan/strategies of the results in PE in setting research priority through culturally appropriate and accessible mechanisms.

Questionnaire -DELPHI ON PE IN THE DESIGN OF CLINICAL TRIALS

Criterion 1: Aim and objectives

D1. The aim and objectives of the practice on PE in the designing clinical trials are agreed with all the stakeholders (i.e patients, academics, researchers, pharmaceutical companies, etc.) involved.

D2. The aim and objectives of the practice on PE respond to patient's needs and interests.

D3. The aim and objectives of the practice on PE are clear and understandable for all participants.

Criterion 2: Contextualization of the practice on PE in the Design of Clinical Trials

D4. The practice is based on a pre-assessment of patients' wants and needs when participating in the design of clinical trials.

D5. A clear understanding of contextual factors that would affect the outcomes of involving patients in the design of clinical trials is demonstrated (e.g. funding, health system and coverage, characteristics of the population, socioeconomic environment).

D6. Any existing policy directives, legal (governance requirements) and/or regulatory framework (e.g EMA) about how to engage patients in clinical trials' design have been followed.

Criterion 3: Target participants involved in patient engagement

D7. The patient profiles engaged in the design of clinical trials reflect the relevant diversity of the population targeted (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc) and includes gender sensitive information.

D8. The target participant's profile who participate in the design of the clinical trials represent the target population that will be recruited to the clinical trials (e.g., former patients, people who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organisations, level of experience in the design of clinical trials).

D9. The practice of PE includes methods to identify individuals eligible to engage in the design of clinical trials (e.g., patient's networks, health care professionals' networks, public advertise etc).

D10. Practices on PE in the design of clinical trials consider the inclusion of other relevant points of view separated to that of the patients (e.g. carers, tutors, research and academia, healthcare professional, pharmaceutical/biotechnology/medical technology industry, policymaker, regulator, HTA agency, funder, payer…).

D11. The role and responsibilities of all participants involved in the design of clinical trials, including patients, are clearly defined and agreed.

D12. There is clear guidance about how to assign roles among all participants involved in the design of clinical trials.

D13. The practice displays flexibility and open-mindedness in assigning the roles for the patients, according to the profile and background of the patient (e.g. as sources of information, as consultants or as collaborating partners of the process).

D14. The practice includes specific tools (e.g., roles and responsibility charts, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), to ensure that all participants understand their own and other's roles and responsibilities.

Criterion 4: Code of Conduct

D15. The practice includes a code of conduct, which clearly states the rules and mechanism of participation in design of clinical trials for all stakeholders involved.

D16. Efforts are made to ensure that all individuals involved know the rules of participation in clinical trials design (e.g., workshops, meetings).

D17. The terms and conditions of confidentiality agreements are adequate, written in a clear and

accessible way, and adapted to the target population involved.

D18. Potential conflicts of interest are addressed and managed (e.g., policies that require full disclosure, transparency, and accountability).

D19. The practices contains mechanisms (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidation, and unethical behaviours resulting from their participation during the design of the clinical trials process.

D20. Funding resources for the practice on PE in the design of clinical trials are clearly explained to all stakeholders involved prior to involvement, and any changes that occur during the practice are communicated up-front.

Criterion 5: Resources

D21. All participants involved in the design of clinical trials practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.

D22. An appropriate and equitable financial compensation framework is in place for all participants (e.g. professionals, patients etc.) invited to participate in the PE practice in the design of clinical trials (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care).

D23. Funding is allocated to cover all elements of the practice (e.g., human resources, material), and is adequate for the intended work.

D24. The adequate infrastructures needed for patients' and other stakeholders' involvement in the design of clinical trials practice are in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g possible physical, mental, cognitive or any impairments etc.)

D25. The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.

Criterion 6: Capacity building

D26. The practice includes comprehensive and accessible training or induction material and programs to respond to the needs of the people involved in the design of clinical trials.

D27. The training program specifies time when training needs to be provided, duration and frequency of the sessions (e.g. on demand, once, twice a month/year).

D28. Training for patients includes areas, such as legal and regulatory concepts and challenges in clinical trials or deliberative process, concepts (e.g basic statistics etc), terminology etc.

D29. Practices on PE in design of clinical trials incorporate training/coaching for stakeholders, other than patients, regarding how to incorporate patients in the design of clinical trials.

Criterion 7: Involvement and participation.

D30. The type of interaction among the different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.

D31. Consideration has been given to specific participants' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).

D32. The timing requirement of the engagement in the design of clinical trials is appropriately planned, taking into consideration patient's needs, and based upon the requirements of the engagement process (e.g time of the day, duration etc).

D33. Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc).

D34. A regular feedback system to inform patients about the outcomes/changes is included for each phase of the involvement.

NEW CATEGORY: When engaging patients in the Design of clinical trials, patient-oriented outcomes are obtained through valid instruments

D35. The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats and taking into account potential impairments (e.g., impaired vision, blindness, and deafness and cognitive problems), low literacy levels, cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).

D36. A single point of contact for or a named person to whom patients can reach out to when needed for information and/or support, throughout their involvement in the design of clinical trials.

D37. Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.

Criterion 8: Evaluation of the PE Practice in Setting Research Priority

D38. An evaluation framework is included (structure, process and results) and it enables regularity of the evaluation (frequency, timing…)

D39. The evaluation framework is shared and agreed among the participants to foster collaboration.

D40. Methods, tools and monitoring system are in place to evaluate the PE practice.

D41. The evaluation outcomes are linked to the aim and objectives of the PE practice in the design of clinical trials.

D42. The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.

D43. The practice includes procedures by which the conclusions of the evaluation of the practice on PE are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or the current one with a continuous improvement process).

Criterion 9: Patient Engagement Impact

D44. The practice identifies relevant outcomes and impacts regarding the involvement of patients in the design of clinical trials.

D45. Assess the relevance of the following possible outcomes and impacts for patient engagement in the design of a clinical trial:

D45.1 Improved recruitment of study participants

D45.2 Increased retention (i.e lower drop out) of study participants

D45.3 Increased diversity of study participants

D45.4 Better adherence to the research protocol, less amendments

D45.5 Improved study participants' trial experience

D45.6 Faster study completion as a result of improved recruitment and adherence to the protocol

D45.7 Decrease costs as a result of improved recruitment, retention and positive trial experience

D45.8 More appropriate, inclusive, sensitive and ethical trial design

D45.9 More appropriate wording and timing of research instruments (e.g. questionnaires and interventions)

D45.10 Improved patient information accessibility (e.g. lay summaries, information sheets, consent form, recruitment material)

NEW CATEGORY: Identification clinical trial endpoints that better reflect functional outcomes/benefits for patients from using a given therapy compared to traditional/standard regulatory endpoints

Criterion 10: Sustainability

D46. The continuation of the practice is ensured through ownership and it is embedded in the institution or organisation.

D47. Human and financial resources required for the long-term continuity of the practice on PE in the design of clinical trials are identified and secured.

D48. The practice on PE in the design of clinical trials identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity, as long as confidentiality is respected.

D49. There is a dissemination and communication plan/strategies of the results in PE in the design of clinical trials through culturally appropriate and accessible mechanisms.

Questionnaire -DELPHI ON PE IN EARLY DIALOGUES

Criterion 1: Aim and objectives

E1. The aim and objectives of PE in Early Dialogues reflects patients' needs, experiences and expectations in the early dialogues process.

E2. The aim and objectives of the practice on PE in early dialogues are co-designed and agreed with all the stakeholders involved.

E3. The aim and objectives of PE in Early Dialogues are clear and understandable for all participants.

Criterion 2: Contextualization of the practice on PE in Early Dialogues

E4. In the practice on PE in early dialogues, the process is based on the assessment of the patient's preferences and needs.

E5. A clear understanding of contextual factors that inform the process of patient engagement is demonstrated so that the quality of dialogue when involving patients in early dialogues with HTAs and regulators is improved.

E6. Any existing policy, legal (governance requirements) and regulatory framework (e.g EMA) about how to engage patients in early dialogues with HTA and regulators have been followed.

Criterion 3: Target participants involved in patient engagement

E7. The profiles of patients engaged in early dialogues with HTA and regulators reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc) and includes gender sensitive information.

E8. Patients engaged in early dialogues with HTA and regulators are selected to represent relevant patients' circumstances (e.g., former patients, patients who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organizations, level of experience in early dialogues with HTA and regulators, patient's scientific knowledge/ background).

E9. The practice of PE in early dialogues includes methods to identify patients who match the clinical criteria needed for a particular dialogue (e.g., patient's networks, health care professionals' networks, public advertise etc.).

E10. The practice supports patients to engage and/or reach out to vulnerable groups to involve them in early dialogues with HTA and regulators, as well as to other patients.

E11. Relevant points of view other than patients (e.g. carers, parents etc.) are considered.

E12. In the practice, the role and responsibilities of all participants involved, including patients, are clearly defined and agreed.

E13. There is clear guidance about how to assign roles among all participants involved in early dialogues.

E14. Guidance, training adequate is provided to ensure that all participants understand their own role and responsibilities, as well as the responsibilities and roles of others.

Criterion 4: Code of Conduct

E15. The practice includes a code of conduct, which clearly states the rules of participation in early dialogues with HTA and regulators for all participants involved.

E16. The practice on PE in early dialogues includes mechanisms, adequate and adapted to the target population to ensure that all individuals involved know the rules of participation in early dialogues with HTA and regulators (e.g., workshops, meetings).

E17. The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way, and adapted to the target population.

E18. The practice on PE in early dialogues incorporates mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).

E19. The PE practice contains procedures (e.g., personalized meetings advocacy figure clearly identified) to identify and address potential discriminatory, coercive, intimidating, and unethical behaviours resulting from the participation in the early dialogue process.

E20. Funding resources for the practice of PE in early dialogues are clearly explained to all stakeholders involved, prior to involvement, and any changes that occur during the practice of PE in early dialogues are communicated up-front.

Criterion 5: Resources

E21. All participants involved in early dialogues with HTA and regulators are informed in clear and accessible way, of the resources available to support their tasks during the process.

E22. The practice includes an equitable financial compensation framework for all participants (e.g. professionals, patients etc.) invited to participate in the early dialogues with HTA and regulators (i.e reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).

E23. Funding is allocated to cover all the elements of the practice (e.g., human resources, material resources), and is adequate to the intended work.

E24. Adequate infrastructures needed for PE in early dialogues are in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g. possible physical mental, cognitive or any impairments etc.).

E25. The practice includes guidance, and ready-to-use tools and templates material that facilitate effective patient engagement implementation in a clear and accessible way.

Criterion 6: Capacity building

E26. The practice on PE in early dialogues identifies the competencies required by all stakeholders involved in early dialogues with HTA bodies and regulators (e.g knowledge and skill such as how to perform patient engagement in early dialogues, etc.).

E27. The practice on PE in early dialogues includes training programs on HTA/Regulatory processes/clinical trial design and methods to patients (e.g., written information, in-house training, online, personalized assistance, and webinars).

E28. The practice includes comprehensive and accessible training or induction material and programs to respond to the needs of the participants involved in early dialogues with HTA and regulators.

E29. The training program specifies time when training needs to be provided, duration and frequency of the sessions (e.g., on demand, once, twice a month/year).

E30. The practice on PE in early dialogues incorporates training/coaching for all stakeholders, other than patients, regarding how to incorporate patients in early dialogues with HTA and regulators.

Criterion 7: Involvement and participation

E31. The mechanism of interaction among the stakeholder is adapted to their needs. (e.g. meetings, online, skype, etc.).

E32. Patients receive timely, clear, accessible and appropriate information about their involvement (i.e what will be addressed, what is expected from them, what their participation will entail, how the practice will be organized etc)

E33. The practice considers specific patients' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).

E34. The timing of the engagement in early dialogues with HTA and regulators is appropriately planned, based upon the requirements of the review process.

E35. The practice on PE in early dialogues sets mechanisms to ensure a proper deliberative process (e.g meetings, interviews, focus group, workshops…).

E36. A regular feedback system to inform patients about the outcomes/changes is included in each phase of the involvement.

E37. The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into account potential impairments (e.g., impaired vision, blindness, and deafness), low literacy levels, cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).

E38. The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in early dialogues.

E39. Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.

E40. The practice on PE in early dialogues fosters discussion and agreement with patients about identifying and selecting preferences about the ED process with HTA bodies and regulators.

Criterion 8: Evaluation of the PE Practice in Setting Research Priority

E41. An evaluation framework is included (structure, process and results) and it enables regularity evaluation (frequency, timing…).

E42. The evaluation framework is shared and agreed among the participants to foster collaboration.

E43. Methods, tools and monitoring system are in place to evaluate the PE practice.

E44. The evaluation outcomes are linked to the aim and objectives of the PE practice in early

dialogues.

E45. The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to participants' characteristics and needs.

E46. The practice includes procedures by which the conclusions of the evaluation of the practice on PE are used (e.g. mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process

Criterion 9: Patient Engagement Impact

E47. The practice identifies relevant outcomes and impacts regarding the involvement of patients in early dialogues with HTA and regulators.

E48. Assess the relevance of the following possible outcomes and impacts for patient engagement in early dialogues with HTA and Regulators:

48.1 Better understanding of technologies' impact in real life context and the quality of life aspects.

48.2 More practical and better designed development plan for medicines.

48.3 Higher accuracy in measuring needs and preferences of patients.

48.4 Better quality of the evidence assessed during the later HTA assessment.

48.5 More useful advice given to aid company decisions.

48.6 Higher relevance of the advice given to the local context of application

48.7 Increased public knowledge and awareness of HTA and regulatory processes

48.8 Transparency of HTA/regulation processes.

48.9 Acceptability of regulatory decisions/HTA reports for stakeholders

48.10 Inclusion of patients' relevant outcomes and end-points in clinical trials data collection and analysis.

48.11 Mutual understanding between all involved stakeholders including the patient community about the regulatory and HTA process.

Criterion 10: Sustainability

E49. The continuation of the practice is ensured through ownership and institutional or practice organization anchoring.

E50. Human and financial resources required for the long-term continuity of the practice on PE in early dialogues are identified and secured.

E51. The practice on PE in early dialogues identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure the continuity of the PE in early dialogues as long as confidentiality is respected.

E52. There is a dissemination and communication plan/strategies of the results of the process of PE in early dialogues through culturally appropriate and accessible mechanisms.

Annex 3. Expert panel stakeholders' profiles

	Stakeholder categories	Individuals working on or with experience in	Rationale of their contribution
Delphi 1 *PE in Setting Research Priorities*	Research Funders (public and/or private)	* Responsibility in management and/or design of Public funding schemes for research (government agencies, public organizations, funding programs at universities, etc.). * Responsibility in management and/or design of Private funding schemes for research (research and development departments in companies, scientific societies, charities and other private organizations, etc.).	*Views on how patient engagement fits into their decisions and processes to set priorities for the research to be funded. Suitability of engagement practices in place. How it shapes results*
	Regulators	Health authority at national or regional level (end user of evidence to inform its decision making)	*Views on the impact of patient engagement on the research agenda and how it affects the usability of research findings for adoption and reimbursement decisions*
	HTA Bodies	Health Technology Assessment	*Views on how patient engagement in research priorities affects the suitability of available evidence to assess new drugs*
	Academics, researchers	Conducting and/ or managing research	*Views on how patient engagement affects their research agenda*
	Healthcare Professionals	Healthcare providers (healthcare managers (primary care and hospital), clinicians/health professionals associations).	*Views on how patient engagement in research priorities affects the availability and adoption of new drugs*
	Patients/ Patient organizations	Participating (in the role of patient) in research priorities setting, research projects, research design, etc.	*Views on how patient engagement fits into funders' decisions and processes to set research priorities. Suitability of*

			engagement practices in place
Delphi 2 ***PE in the Design of Clinical Trials***	Clinical trials promoter (pharma companies or other)	Designing, preparing and conducting clinical trials	*Views on how patient engagement fits into their decisions and processes to conduct clinical trials*
	Academics, researchers	Designing, preparing and conducting clinical trials	*Views on how patient engagement affects their research agenda and the quality of findings*
	Healthcare professionals	Designing, preparing and conducting clinical trials	*views on how patient engagement affects new drugs availability and adoption*
	Regulators	Clinical trials regulation	*views on how patient engagement in design and analysis of clinical trials affects the quality (including ethics-wise) and usability of findings*
	Patients/ Patient organizations	Participating (in the role of patient) in designing, preparing and conducting clinical trials.	*Views on how patient engagement fits into researchers and funders' decisions and processes to design clinical trials. Suitability of engagement practices in place. How it shapes quality and usability of findings*
Delphi 3 ***PE in Early Dialogues***	HTA bodies	Participating in Early Dialogues	*Views on how patient engagement fits into early dialogues dynamics. Suitability of engagement practices in place. How it shapes results*
	Pharma companies, Industry	Participating in Early Dialogues	*Views on how patient engagement fits into early dialogues dynamics. Suitability of engagement practices in place. How it shapes results*
	Regulators	Health authority at national or regional level (reimbursement decision maker) participating	*Views on how patient engagement fits into early dialogues dynamics. Suitability of engagement*

		in early dialogues	*practices in place. How it shapes results*
	Patients/ Patient organizations	Participating (in the role of patient) in early dialogues	*Views on how patient engagement fits into early dialogues dynamics. Suitability of engagement practices in place. How it shapes results*

Annex 4. Glossary for the Delphi in PE in Medicine R&D lifecycle

GLOSSARY

Accessible

Adherence

Carer

Clinical Endpoint [Clinical Trial]

Clinical Trial Design

Culturally appropriate

Current Patient

Early Dialogue

Former Patient

HTA Assessment

HTA Body

Inclusive

Industry

Liker scale

Outcome

Patient Engagement Practice

Patient Organisations

Patient Representative/ Patient Advocate

Payer

Point of contact

Population at Risk

Practice

Regulator

Regulatory Framework

Research Priorities Setting

Sensitive

Stakeholders

Tutor

Vulnerable Populations

Work group

A

Accessible

Easily used or accessed by people with special needs.

Adherence

Taking medications (or other treatment) exactly as instructed by a health care provider (the prescriber).

C

Carer

Anyone who cares, unpaid, for a friend or family member who, due to illness, disability, a mental health problem or an addiction cannot cope without his or her support.

Clinical Endpoint [Clinical Trial]

A characteristic or variable that reflects how a patient feels, functions, or survives. Clinical endpoints are distinct measurements or analysis of disease characteristics reflecting the effect of a therapeutic intervention in a clinical trial or study.

Clinical Trial Design

Procedure by which the details of a clinical trial are defined. These aspects include the design of the protocol, the discussion the potential burden that the people who will participate in the trial may experience or the discussion the outcomes of the trial, which could be more important to patients.

Culturally appropriate

Conforming to a culture's acceptable expressions and standards of behaviour and thoughts.

Current Patient

A person that has been diagnosed of the condition studied in the practice at stake (Setting Research Priorities, Designing a Clinical Trial, Early Dialogue) and is currently following a treatment.

E

Early Dialogue

Early scientific discussions that can take place between industry, HTA bodies and regulators (and in some cases with payers) to discuss developmental plans for a medicinal product and to ensure these plans meet the requirements.

F

Former Patient

A person that has received the treatment of the condition studied in the practice at stake (Setting Research Priorities, Designing a Clinical Trial, Early Dialogue), and is not following any treatment currently, except for follow-up periodic reviews.

H

HTA Assessment

Multidisciplinary process that summarises information about the medical, social, economic, and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner. Its aim is to inform the formulation of safe and effective health policies that are patient focused and seek to achieve best value.

HTA Body

Regional and national organizations formed by multidisciplinary teams that provide recommendations on medicines and other health technologies (HTA assessment), that can be financed or reimbursed by the healthcare system in a particular Member State or region.

I

Inclusive

Not excluding any section of society or any party involved. Deliberately avoiding usages that could be seen as excluding a particular social group.

Industry

Private companies working in the development and/ or commercialization of medicines and new health technologies.

L

Liker scale

A Likert scale is a psychometric scale commonly involved in research that employs

questionnaires. It is a type of rating scale used to measure attitudes or opinions where, respondents are asked to rate items on a level of agreement.

O

Outcome

Outcomes refer to decisions made and things produced as a result of patient engagement practices (including changed research priorities and trial designs). This includes the effects on the development of medical products. Outcomes are influenced by context and mechanisms and have an influence on impact.

P

Patient Engagement Practice

The effective and active collaboration of patients, patient advocates, patient representatives and/or carers in a procedure of setting research priorities, designing clinical trials or participating in early dialogues. By effective and active collaborations of patients, we mean that their views, preferences and values are gathered during the practice and are treated in the same way as the contributions made by the other stakeholders involved.

Patient Organisations

Not-for profit organisations which are patient focused, and whereby patients and/or carers (the latter when patients are unable to represent themselves) represent a majority of members in governing bodies.

Patient Representative/ Patient Advocate

Patients, carers, parents or tutors and/or staff from patient's organization that act as a liaison between the patients and other organizations, represent their interests and advocates for their rights.

Payer

Insurer or other organization that pays for healthcare services.

Point of contact

Person or persons that can be approached for information or assistance.

Population at Risk

Population that is exposed to developing the condition studied in the practice at stake (Setting Research Priorities, Designing a Clinical Trial, Early Dialogue).

Practice

The customary, habitual or expected way, method or modality of performing an action. A

practice can be the design of the recruitment protocol of a clinical trial or the prioritization exercise of a given set of research lines, among others.

R

Regulator

Health authority at national or regional level.

Regulatory Framework

The set of rules or orders issued by an executive authority or regulatory agency of a government and having the force of law.

Research Priorities Setting

Procedure by which lines or areas of research are identified as a priority in a research-funding program.

S

Sensitive

Capable of measuring or recording very small changes

Stakeholders

Agencies, organisations, groups or individuals that have relevant knowledge and/or experience in the practice at stake (Setting Research Priorities, Designing a Clinical Trial, Early Dialogue). They make up the work group.

T

Tutor

The legal guardian of a patient.

V

Vulnerable Populations

These terms are applied to groups of people who, due to factors usually considered outside their control; do not have the same opportunities as other, more fortunate groups in society. Examples might include unemployed people, refugees and others who are socially excluded.

W

Work group

Group of stakeholder participating in the clinical trial design practice, research priority setting practice or in the early dialogue.

Sources of Information

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Annex 5. Results of the Delphi on PE in Setting Research Priorities

Results of Round 1 (Online) – Relevance assessment

Table 2: Relevant categories on PE in Setting Research Priorities (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	1	The aim and objectives of the practice on PE in research priority are agreed with all stakeholders (i.e. patients, academics, researchers, pharmaceutical companies etc.) involved.
		2	The aim and objectives of the practice on PE in research priority are related to patients' needs and interests.
2	Contextualization of the practice on PE in Research Priority	4	The practice is based on an assessment of the patients' needs and preferences who will be engaged in research priority setting processes.
3	Target participants involved in patient engagement	7	The profiles of the patients engaged in setting the research priorities reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information.
		8	Patients engaged profile in setting research priorities are selected to represent relevant patients' circumstances (e.g., former patients, patients who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organizations, level of experience in research priority setting, patient's scientific knowledge/ background).
		12	In the PE practice, the roles and responsibilities of all participants involved, including patients, are clearly defined and agreed.
4	Code of conduct	16	The practice includes a code of conduct, which clearly states the rules and mechanism of participation in setting research priority for all stakeholders involved.
		17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population involved.
		18	The practice contains mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).
5	Resources	23	The adequate infrastructures needed for patients' and other stakeholders' involvement is in place (e.g., technological support, working space, information and communication technologies) adapted to specific circumstances of participants (e.g. possible physical, mental, cognitive or any impairments etc.)
		24	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.

6	Capacity building	25	The practice identifies the competencies required by all participants involved in setting research priority (e.g. knowledge and skill such as how to perform patient engagement in setting research priority, etc.).
7	Involvement and participation	32	Patients receive timely, clear, accessible and appropriate information about their involvement (i.e. what will be addressed, what is expected from them, what their participation will entail, how the practice will be organised etc.)
		36	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into consideration potential impairments (e.g., impaired vision, blindness, deafness and cognitive problems), low literacy levels , cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).
		37	The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in setting research priority.
8	Evaluation	42	The evaluation outcomes are linked to the aim and objectives of the PE practice in setting research priority.
9	Patient Engagement Impact	45	The practice identifies relevant outcomes and impacts regarding the involvement of patients in setting research priority.
		46.1	Research topic and priorities become more appropriate, based on patients' needs
		46.2	The product profile (drug, technology) become more relevant and usable for patients.
		46.3	Research questions and outcomes/endpoints become more relevant for patients.

Table 3: No consensus categories on PE in Setting Research Priorities (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	3	The aim and objectives of the practice on PE are clear and understandable for all participants.
2	Contextualization of the practice on PE in Research Priority	5	There is a clear understanding of contextual factors that could affect the outcomes of involving patients in research setting priority (e.g. funders, policy makers, industry, research promoters…etc.).
		6	Any existing policy directives, legal (governance requirements) and/or regulatory framework about how to engage patients in setting research priority have been followed.
3	Target participants involved in patient engagement	9	The practice includes methods to identify individuals who have the necessary scientific background or expertise to participate in setting research priority (e.g., patient's networks, health care professionals' networks, public advertise etc.).
		10	The practice supports patients by sharing responsibility of engaging/reaching out to vulnerable groups to involve them in

			setting research priorities, as well as to mentor other patients.
		13	There is clear guidance about how to assign roles among all participants involved in setting research priority.
		14	The practice display flexibility and open-mindedness in assigning the roles for the patients, according to the profile, interest and background of the patient (e.g. as sources of information, as consultants or as collaborating partners of the process).
		15	The practice includes specific tools (e.g., roles and responsibility charts, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), to ensure that all participants understand their own and other's roles and responsibilities.
4	Code of conduct	19	The practice contains mechanisms (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidating, and unethical behaviours resulting from their participation in the research priorities process.
5	Resources	20	All participants involved in the setting research priority practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.
		21	The practice includes an equitable financial compensation framework for all participants (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).
6	Capacity building	26	The practice includes specific training programs about setting research priority process and methods to all participants (e.g., written information, in-house training, online, personalised assistance, and webinars).
		27	The training material is adapted, comprehensible and accessible to all participants taking into consideration impairments, literacy levels, cultural background and the circumstances of vulnerable patients involved in setting research priority.
		29	The practice includes training for patients and other stakeholders involved in different areas (e.g. legal and regulatory concepts and challenges in research or deliberative processes, concepts, terminology etc.).
		30	The practice incorporates training/coaching for stakeholders, other than patients (e.g. researchers, healthcare professional, funders etc) regarding the participation of patients in research priority setting.
7	Involvement and participation	31	The type of interaction among different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.
		33	The timing requirement of the engagement in setting research priority is appropriately planned, taking into account patient's needs, and based upon the requirements of the engagement process (e.g. time of the day, duration etc.).
		34	Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc.).
		35	A regular feedback system to inform patients about the outcomes / changes is included for each phase of the involvement.

		38	Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.
8	Evaluation	40	The evaluation framework is shared and agreed among the participants to foster collaboration.
		41	Expertise in evaluation process, methods, tools and monitoring system are in place to create and populate the evaluation framework.
		43	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.
		44	The practice includes procedures by which the conclusions of the evaluation are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).
9	Patient Engagement Impact	46.4	Increased probability of success of the study during the research process (reduced failure of the project).
		46.5	Research proposals submitted to public funders are more fundable (e.g. enhanced credibility).
		46.6	Resource allocation within industry become more appropriate based on patients' needs.
		46.7	Funded studies will provide more useful information for patients and decision-making processes
10	Sustainability	47	The continuation of the practice is ensured through ownership and institutional or organisational anchoring.
		48	Human and financial resources required for the long-term continuity of the practice on PE in setting research priority are identified and secured.
		49	The practice identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity.
		50	There is a dissemination and communication plan/strategies of the results in PE in setting research priority through culturally appropriate and accessible mechanisms.

Table 4: Dropped categories on PE in Setting Research Priorities (Round 1)

Criteria ID	Criteria	Category ID	Category
3	Target participants involved in patient engagement	11	The practice includes relevant points of view other relevant stakeholders (e.g., carers, tutors, researchers, health care providers, decision-makers, policy makers, funders).
5	Resources	22	Funding is allocated to cover all the elements of the practice (e.g., human resources, material resources), and is adequate for the intended work.
6	Capacity building	28	The training program specifies time when training needs to be provided, duration and frequency of the sessions (e.g., on demand,

			once, twice a month/year).
8	Evaluation	39	An evaluation framework is included (structure, process and results) and it enables regularity evaluation (frequency, timing…).

Results of Round 2 (Online) – Prioritization

Table 5: Relevant categories on PE in Setting Research Priorities (Round 2)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	3	The aim and objectives of the practice on PE are clear and understandable for all participants.
3	Target participants involved in patient engagement	15	The practice includes specific tools (e.g., roles and responsibility charts, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), to ensure that all participants understand their own and other's roles and responsibilities.
7	Involvement and participation	33	The timing requirement of the engagement in setting research priority is appropriately planned, taking into account patient's needs, and based upon the requirements of the engagement process (e.g. time of the day, duration etc.).
		35	A regular feedback system to inform patients about the outcomes / changes is included for each phase of the involvement.
8	Evaluation	41	Expertise in evaluation process, methods, tools and monitoring system are in place to create and populate the evaluation framework.
9	PE Impact	46.6	Resource allocation within industry become more appropriate based on patients' needs.
		46.7	Funded studies will provide more useful information for patients and decision-making processes

Table 6: No consensus categories on PE in Setting Research Priorities (Round 2)

Criteria ID	Criteria	Category ID	Category
2	Contextualization of the practice on PE in Research Priority	6	Any existing policy directives, legal (governance requirements) and/or regulatory framework about how to engage patients in setting research priority have been followed.
3	Target participants involved in patient engagement	13	There is clear guidance about how to assign roles among all participants involved in setting research priority.

5	Resources	20	All participants involved in the setting research priority practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.
		21	The practice includes an equitable financial compensation framework for all participants (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).
6	Capacity building	27	The training material is adapted, comprehensible and accessible to all participants taking into consideration impairments, literacy levels, cultural background and the circumstances of vulnerable patients involved in setting research priority.
		30	The practice incorporates training/coaching for stakeholders, other than patients (e.g. researchers, healthcare professional, funders etc.) regarding the participation of patients in research priority setting.
7	Involvement and participation	34	Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc.).
8	Evaluation	40	The evaluation framework is shared and agreed among the participants to foster collaboration.
		43	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.
9	PE Impact	46.5	Research proposals submitted to public funders are more fundable (e.g. enhanced credibility).
10	Sustainability	47	The continuation of the practice is ensured through ownership and institutional or organisational anchoring.
		48	Human and financial resources required for the long-term continuity of the practice on PE in setting research priority are identified and secured.
		49	The practice identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity.
		50	There is a dissemination and communication plan/strategies of the results in PE in setting research priority through culturally appropriate and accessible mechanisms.

Table 7: Dropped categories on PE in Setting Research Priorities (Round 2)

Criteria ID	Criteria	Category ID	Category
2	Contextualization of the practice on PE in Research Priority	5	There is a clear understanding of contextual factors that could affect the outcomes of involving patients in research setting priority (e.g. funders, policy makers, industry, research promoters…etc.).
3	Target participants involved in patient	9	The practice includes methods to identify individuals who have the necessary scientific background or expertise to participate in setting

	engagement		research priority (e.g., patient's networks, health care professionals' networks, public advertise etc.).
		10	The practice supports patients by sharing responsibility of engaging/reaching out to vulnerable groups to involve them in setting research priorities, as well as to mentor other patients.
		14	The practice display flexibility and open-mindedness in assigning the roles for the patients, according to the profile, interest and background of the patient (e.g. as sources of information, as consultants or as collaborating partners of the process).
4	Code of Conduct	19	The practice contains mechanisms (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidating, and unethical behaviours resulting from their participation in the research priorities process.
6	Capacity Building	26	The practice includes specific training programs about setting research priority process and methods to all participants (e.g., written information, in-house training, online, personalised assistance, and webinars).
		29	The practice includes training for patients and other stakeholders involved in different areas (e.g. legal and regulatory concepts and challenges in research or deliberative processes, concepts, terminology etc.).
7	Involvement and participation	31	The type of interaction among different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.
		38	Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.
8	Evaluation	44	The practice includes procedures by which the conclusions of the evaluation are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).
9	PE Impact	46.4	Increased probability of success of the study during the research process (reduced failure of the project).

Table 8: Relevant categories on PE in Setting Research Priorities and their Priority (Round 2)

Criteria ID	Criteria	Category ID	Category	Priority
1	Aim and objectives	1	The aim and objectives of the practice on PE in research priority are agreed with all stakeholders (i.e. patients, academics, researchers, pharmaceutical companies etc.) involved.	**HP**
		2	The aim and objectives of the practice on PE in research priority are related to patients' needs and interests.	**HP**

3	Target participants involved in patient engagement	12	In the PE practice, the roles and responsibilities of all participants involved, including patients, are clearly defined and agreed.	**HP**
4	Code of Conduct	16	The practice includes a code of conduct, which clearly states the rules and mechanism of participation in setting research priority for all stakeholders involved.	**HP**
		17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population involved.	**HP**
		18	The practice contains mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).	**HP**
5	Resources	23	The adequate infrastructures needed for patients' and other stakeholders' involvement is in place (e.g., technological support, working space, information and communication technologies) adapted to specific circumstances of participants (e.g possible physical, mental, cognitive or any impairments etc.)	**HP**
7	Involvement and participation	32	Patients receive timely, clear, accessible and appropriate information about their involvement (i.e. what will be addressed, what is expected from them, what their participation will entail, how the practice will be organised etc.)	**HP**
		36	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into consideration potential impairments (e.g., impaired vision, blindness, deafness and cognitive problems), low literacy levels , cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).	**HP**
8	Evaluation	42	The evaluation outcomes are linked to the aim and objectives of the PE practice in setting research priority.	**HP**
9	PE Impact	45	The practice identifies relevant outcomes and impacts regarding the involvement of patients in setting research priority.	**HP**
		46.1	Research topic and priorities become more appropriate, based on patients' needs	**HP**
		46.2	The product profile (drug, technology) become more relevant and usable for patients.	**HP**
		46.3	Research questions and outcomes/endpoints become more relevant for patients.	**HP**

2	Contextualization of the practice on PE in Research Priority	4	The practice is based on an assessment of the patients' needs and preferences who will be engaged in research priority setting processes.	**MP**
3	Target participants involved in patient engagement	7	The profiles of the patients engaged in setting the research priorities reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information.	**MP**
		8	Patients engaged profile in setting research priorities are selected to represent relevant patients' circumstances (e.g., former patients, patients who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organizations, level of experience in research priority setting, patient's scientific knowledge/ background).	**MP**
5	Resources	24	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.	**MP**
7	Involvement and participation	37	The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in setting research priority.	**MP**
6	Capacity Building	25	The practice identifies the competencies required by all participants involved in setting research priority (e.g. knowledge and skill such as how to perform patient engagement in setting research priority, etc.).	**LP**

Round 3 (Meeting in person) – Discussion and Final Prioritization

Discussion and Final Prioritization process

To ease discussions at the meeting, the highly prioritised items and non-consensus categories remaining from the second round were further elaborated by the PARADIGM Delphi team. In order to avoid redundancy, a proposal was made to merge, rephrase or reallocate categories and criteria. They were presented to the expert panel and thoroughly discussed at the meeting. Comments provided by the experts in the first and second round were taken into consideration.

From the initial 10 thematic criteria, the experts agreed on 8 criteria that consisted of 29 categories, and 6 subcategories. The experts rephrased categories in order to avoid redundancy and overlapping.

Some parts of the discussions are captured below to provide more clarity on the key discussions during the meeting.

Overall, experts hold that the disclaimers agreed at the meeting should be captured in the document in a clear and accessible way. Besides, it was highlighted that it is necessary to take

into consideration any stakeholder and participant involved along the practice (e.g. patient representatives, researchers, industry partners, etc.). Furthermore, they agreed on removing brackets along the document to be read with ease, and because they were already included in the glossary and /or footnotes (Annex 4).

Experts agreed on merging **criterion 1, "Aim and objectives", criterion 2, "Contextualization of the practice on patient engagement in research priority"** and **criterion 3, "Target participants involved in patient engagement"**. The new criterion was named "Key elements of the practice design". All the categories included in this criterion were considered basic and relevant for the practice.

Experts pointed out that features approached in categories 1, 2 and 3 overlapped, so they were combined in a new one.

Category 4 was considered relevant but it was rephrased with regard to every stakeholder: researchers, industry and patients.

Categories 7 and 8 were merged and experts considered that two new definitions should be included in the glossary: "target population" and "patient's circumstances". Additionally, category 15 was rephrased, making it easy to read, and with clarifications about some words: "specific tools" and "mechanisms".

Criterion 4, "Code of conduct", did not experience many changes. The three categories included in this criterion were rephrased.

The expert panel refused the idea of merged criteria 5, 6, and 7. All of them were barely changed.

Regarding the categories within the **criterion 5, "Resources"**, some categories were merged and rephrased for the criterion to be clearer and more concise. The panel identified overlapping of categories 20 and 21, which were merged to avoid redundancy. Experts made clear that "it is necessary an equal framework and compensation to support all the participants during the process". Concerning categories 23 and 24, they were rephrased.

Criterion 6, "Capacity building", was barely changed. Experts discussed category 30 and they considered that the training is really relevant. They put into context that well-selected patients must be trained before their participation.

Again, categories within **criterion 7, "Involvement and participation",** experienced rephrasing and merging to avoid repetition. Experts highlighted the need to clarify that this criterion reviews the expectations of the involvement in the practice, not patient expectations.

Regarding former **criterion 8, "Evaluation of the practice in setting research priorities",** categories 41 and 42 did not suffer any change. Categories 40 and 43 were rephrased. In regard to category 43, the expert panel underlined that feedback is essential after the completion of the process.

Experts discussed about the location of category 45, previously part of criterion 9, and finally reallocated in criterion 8. They considered that this category is an introductory step to the

following criterion "Patient engagement impact". The experts added the term SMART to the category, to define relevance with specific and achievable outcomes. Each letter in SMART refers to a different criterion for judging objectives: Specific, Measurable, Assignable, Realistic and Time bound.

In relation to **criterion 9, "Patient engagement impact"** category 45 was removed from "Patient Engagement Impact" as mentioned before. The rest of the categories were barely changed, with the exception of subcategories 46.4 and 46.6. They focused the category 46.4 in enhancing patients. In regard to category 46.4, the panel considered that "individual patients, who are not members of any organisation, should be involved as well".

Respecting former subcategory 46.6, it was rephrased to enforce its message.

Finally, categories 48 and 50 from criterion 10, "Sustainability", were rephrased to clarify some terms. Categories 47 and 49 were merged; as it was considered that its combination gives more contexts and enhances the message. This criterion was extensively discussed, because some experts held that the public entities or patients organisations seek partnerships in order to participate in long-term sustainable practices, being not so important for the private sector.

Once the work on new specification was completed, the resulting categories in each criterion were weighted. Later, experts weighed the final 8 criteria by distributing 100 points among them. The highest weight was assigned to current criterion 1: "Key elements of Practice design" (19.5/100), while the criteria with the lowest score were "Sustainability" (8/100), followed by "Resources" (10/100).

Current criteria and category and their corresponding weights are detailed in Table 9.

Table 9: Final set of criteria and categories, and their weights, recommended for evaluating PE in setting research priorities

New criteria names	Criteria weight	Categories	Category weight
1. Key elements of Practice design	19.5	The aim and objectives of the practice in setting research priorities are agreed and understandable by all stakeholders (e.g. patients, academics, researchers, pharmaceutical companies, etc) involved and related to patient's needs and interest.	26.0
		The practice is based on an assessment of the patients' needs and preferences.	22.5
		Any relevant policy directives, legal, ethics, governance requirement and/or regulatory framework about how to engage patients in setting research priorities have been considered.	11.5

		The patients engaged in setting research priorities reflect diversity of the target population *, patients' circumstances** and vulnerability. * Refers to cultural background, social-economic status, gender, age, ethnicity, educational level, disease, disability and vulnerability. ** Former patients, patients who are at risk for a disease but do not yet have the disease, severity of the disease, patient's advocate, carers, patient's representatives, patient organizations, level of experiences, patient's scientific knowledge/background).	14.5
		The roles and responsibilities are clearly defined, agreed and assigned among all participants	12.0
		The practice includes specific tools* and mechanisms**, to ensure that all participants understand their own and other's roles and responsibilities. * (e.g., roles and responsibility charts, procedural guidance documents, protocols) ** (e.g., meetings, workshops, training sessions)	13.5
			Total must be 100
2. Code of conduct	11.5	The practice includes a code of conduct, which clearly states the rules and procedures, including ethical principles, of participation in setting priorities for all stakeholders.	44.0
		The terms and conditions of confidentiality agreements are in place, presented in a clear and accessible way to the target population involved.	30.0
		The practice contains clear and accessible mechanisms to manage potential conflicts of interest.	26.0
			Total must be 100
3. Resources	10.00	All participants are informed of the available resources, including equitable financial compensation framework to support them during the process (e.g., travel and subsistence expenses, time missed from work, child/elderly care etc.).	27.5
		The infrastructures needed for participants are in place * and adapted to specific circumstances of participants** * (e.g., technological support, working space, communication technologies) ** (e.g. possible physical, mental, cognitive or any impairment, etc)	41.0
		The practice includes guidance, ready-to-use tools and templates material to facilitate effective patient engagement implementation.	31.5
			Total must be 100
4. Capacity building	11.0	The practice identifies the competencies that are required to perform patient engagement in setting research priorities by all participants.	34.0
		The training material is adapted, comprehensible and accessible to all participants taking into consideration impairments, literacy levels, cultural background and the circumstances of vulnerable patients involved in setting research priorities.	35.5
		The practice ensures that all stakeholders (other than patients) are adequately trained for their role.	30.5
			Total must be 100

5. Involvement and participation	12.0	Patients receive timely, clear, accessible and appropriate information about their involvement and what is expected of them.	26.0
		The patient's participation will be properly planned, taking into account timing requirements, accessibility, and vulnerability.	18.5
		Whenever appropriate, and as agreed by participants, regular feedback about the outcome is communicated in a clear and adapted way.	20.0
		All participants are given the opportunity to give regular feedback about the process.	19.0
		The practice ensures there is a named key contact that patients can reach out throughout the process.	16.5
			Total must be 100
6. Evaluation of the PE practice in setting research priority	12.0	The evaluation framework is included and shared among the participants.	15.5
		Methods, tools and monitoring system are in place to evaluate the PE practice.	22.0
		The evaluation outcomes are linked to the aim and objectives of the PE practice in setting research priority.	24.5
		The evaluation outcomes are shared with all the participants and feedback is enabled after the completion of the process.	14.5
		The practice identifies SMART* relevant outcomes regarding the involvement of patients in setting research priority. *SMART: Specific Measurable Assignable Realistic Time bound	23.5
			Total must be 100
7. Patient engagement impact	16.0	Impacts:	
		Research topic and priorities become more appropriate, based on patients' needs.	22.0
		The product profile (drug, technology) become more relevant and usable for patients.	19.0
		Research questions and outcomes/endpoints become more relevant for patients.	19.5
		Credibility of submitted research proposals are enhanced when involving patients and patients' organisations.	10.5
		Resource allocations when engaging patients within industry become more appropriate and are based on patients' needs.	12.5
		Completed studies will provide more useful information for patients and decision-making process when involving patients and patient organisations.	16.5
			Total must be 100
8. Sustainability	8.00	The practice is embedded in the institution or organisation and, when relevant, the alliances with private and/or public institution are fostered.	46.0
		Human and financial resources are allocated for the long-term continuity of the practice on PE in setting research priorities.	31.0

		There is a dissemination and communication plan demonstrating the process and outcome of PE.	23.0
			Total must be 100
Total must equal 100			

Annex 6. Results of the Delphi on PE in Designing Clinical Trials

Results of Round 1 (Online) – Relevance assessment

Table 10: Relevant categories on PE in Designing Clinical Trials (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	3	The aim and objectives of the practice on PE are clear and understandable for all participants
3	Target participants involved in patient engagement	7	The patient profiles engaged in the design of clinical trials reflect the relevant diversity of the population targeted (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information.
		11	The role and responsibilities of all participants involved in the design of clinical trials, including patients, are clearly defined and agreed.
4	Code of Conduct	15	The practice includes a code of conduct, which clearly states the rules and mechanism of participation in design of clinical trials for all stakeholders involved.
		16	Efforts are made to ensure that all individuals involved know the rules of participation in clinical trials design (e.g., workshops, meetings).
		17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population involved.
		18	Potential conflicts of interest are addressed and managed (e.g., policies that require full disclosure, transparency, and accountability).
		19	The practices contains mechanisms (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidation, and unethical behaviours resulting from their participation during the design of the clinical trials process.
		20	Funding resources for the practice on PE in design of clinical trials are clearly explained to all stakeholders involved prior to involvement, and any changes that occur during the practice are communicated up-front.
5	Resources	21	All participants involved in design of clinical trials practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.
		22	An appropriate and equitable financial compensation framework is in place for all participants (e.g. professionals, patients etc.) invited to participate in the PE practice in design of clinical trials (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care).
6	Capacity building	26	Comprehensive and accessible training or induction material and programs to respond to the need of the people involved in design of clinical trials.
7	Involvement and participation	30	The type of interaction among the different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.

		31	Consideration has been given to specific participants' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).
		32	The timing requirement of the engagement in design of clinical trials is appropriately planned, taking into account patient's needs, and based upon the requirements of the engagement process (e.g. time of the day, duration etc.).
		35	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language and using accessible, clear and understandable formats, taking into account potential impairments (e.g., impaired vision, blindness, and deafness and cognitive problems), low literacy levels, cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).
		36	A single point of contact for or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in design of clinical trials.
8	Evaluation	41	The evaluation outcomes are linked to the aim and objectives of the PE practice in design of clinical trials.
		42	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.
		43	The practice includes procedures by which the conclusions of the evaluation are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).
9	PE Impact	45.1	Improved recruitment of study participants
		45.2	Increased retention (i.e. lower drop out) of study participants
		45.4	Better adherence to the research protocol, less amendments
		45.6	Faster study completion as a result of improved recruitment and adherence to the protocol
		45.8	More appropriate, inclusive, sensitive and ethical trial design
10	Sustainability	46	The continuation of the practice is ensured through ownership and institutional or organisational anchoring.

Table 11: No consensus categories on PE in Designing Clinical Trials (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	1	The aim and objectives of the practice on PE in design of clinical trials are agreed with all the stakeholders (i.e. patients, academics, researchers, pharmaceutical companies etc.) involved.
		2	The aim and objectives of the practice on PE respond to patient's needs and interests.
2	Contextualization of the practice on PE in the	4	The practice on PE in design of clinical trials is based on a pre-assessment of patients' wants and needs when participating in design

	Design of Clinical Trials		of clinical trials.
		5	A clear understanding of contextual factors that would affect the outcomes of involving patients in design of clinical trials is demonstrated (e.g. funding, health system and coverage, characteristics of the population, socioeconomic environment).
		6	Any existing policy directives, legal (governance requirements) and/or regulatory framework (e.g. EMA) about how to engage patients in clinical trials' design have been followed.
3	Target participants involved in patient engagement	8	The target participant's profile who participate in the design of the clinical trial represent the target population that will be recruited to the clinical trials (e.g., former patients, people who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organizations, level of experience in design of clinical trials).
		9	The practice includes methods to identify individuals with the perspectives (or points of view) needed to engage in clinical trials design (e.g., patient's networks, health care professionals' networks, public ads).
		14	The practice includes specific tools (e.g., roles and responsibility charts, procedures, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), are used to ensure that all participants understand their own and other's roles and responsibilities.
5	Resources	23	Funding is allocated to cover all elements of the practice (e.g., human resources, material), and is adequate for the intended work.
		24	The adequate infrastructures needed for patients' and other stakeholders' involvement in design of clinical trials practice is in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g. possible physical, mental, cognitive or any impairments etc.)
		25	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.
6	Capacity building	29	Practices on PE in design of clinical trials incorporate training/coaching for stakeholders, other than patients, regarding how to incorporate patients in the design of clinical trials.
7	Involvement and participation	33	Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc).
		34	A regular feedback system to inform patients about the outcomes/changes is included for each phase of the involvement.
8	Evaluation	38	An evaluation framework is included (structure, process and results) and it enables regularity of the evaluation (frequency, timing…).
		40	Methods, tools and monitoring system are in place to evaluate the PE practice.
9	PE Impact	44	The practice identifies relevant outcomes and impacts regarding the involvement of patients in the design of clinical trials.

		45.5	Improved study participants' trial experience.
		45.9	More appropriate wording and timing of research instruments (e.g. questionnaires and interventions).
		45.10	Improved patient information accessibility (e.g. lay summaries, information sheets, consent form, recruitment material).
10	Sustainability	47	Human and financial resources required for the long-term continuity of the practice on PE in design of clinical trials are identified and secured.
		48	The practice on PE in design of clinical trials identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity, as long as confidentiality is respected.

Table 12: Dropped categories on PE in Designing Clinical Trials (Round 1)

Criteria ID	Criteria	Category ID	Category
3	Target participants involved in patient engagement	10	Practices on PE in in clinical trials design consider the inclusion of other relevant points of view separate to that of the patients (e.g. carers, tutors, research and academia, healthcare professional, pharmaceutical/biotechnology/medical technology industry, policymaker, regulator, health technology assessment (HTA) agency, funder, payer…).
		12	There is clear guidance about how to assign roles among all participants involved in in the design of clinical trials.
		13	The practice displays flexibility and open-mindedness in assigning the roles for the patients, according to the profile and background of the patient (e.g. as sources of information, as consultants or as collaborating partners of the process).
6	Capacity building	27	The training program specifies time when training needs to be provided, duration and frequency of the sessions (e.g. on demand, once, twice a month/year).
		28	Training for patients includes areas, such as legal and regulatory concepts and challenges in research or deliberative process, concepts (e.g. basic statistics etc.), terminology etc.
7	Involvement and participation	37	Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.
8	Evaluation	39	The evaluation framework is shared and agreed among the participants to foster collaboration.
9	PE Impact	45.3	Increased diversity of study participants
		45.7	Decrease costs as a result of improved recruitment, retention and positive trial experience
10	Sustainability	49	There is a dissemination and communication plan/strategies of the results in PE in design of clinical trials through culturally appropriate and accessible mechanisms.

Results of Round 2 (Online) – Prioritization

Table 13: Relevant categories on PE in designing clinical trials (Round 2)

(New categories in orange)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	2	The aim and objectives of the practice on PE respond to patient's needs and interests.
2	Contextualization of the practice on PE in the Design of Clinical Trials	6	Any existing policy directives, legal (governance requirements) and/or regulatory framework (e.g. EMA) about how to engage patients in clinical trials' design have been followed.
3	Target participants involved in patient engagement	9	The practice includes methods to identify individuals with the perspectives (or points of view) needed to engage in clinical trials design (e.g., patient's networks, health care professionals' networks, public ads).
		14	The practice includes specific tools (e.g., roles and responsibility charts, procedures, procedural guidance documents, protocols) and mechanisms (e.g., meetings, workshops, training sessions), are used to ensure that all participants understand their own and other's roles and responsibilities.
5	Resources	23	Funding is allocated to cover all elements of the practice (e.g., human resources, material), and is adequate for the intended work.
		24	The adequate infrastructures needed for patients' and other stakeholders' involvement in design of clinical trials practice is in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g. possible physical, mental, cognitive or any impairments etc.)
		25	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.
7	Involvement and Participation	33	Mechanisms to ensure the meaningful participation and contribution of all participants involved in the PE activity are in place taking in consideration characteristics and circumstances of vulnerable population (e.g., meetings, interviews, focus group, workshops etc.).
		34	A regular feedback system to inform patients about the outcomes/changes is included for each phase of the involvement.
		38	An evaluation framework is included (structure, process and results) and it enables regularity of the evaluation (frequency, timing…)
8	Evaluation	40	Methods, tools and monitoring system are in place to evaluate PE practice.
		44	The practice identifies relevant outcomes and impacts regarding the involvement of patients in the design of clinical trials.

9	PE Impact	45.5	Improved study participants' trial experience
		45.9	More appropriate wording and timing of research instruments (e.g. questionnaires and interventions)
		45.10	Improved patient information accessibility (e.g. lay summaries, information sheets, consent form, recruitment material)
		New category	Identification clinical trial endpoints that better reflect functional outcomes/benefits for patients from using a given therapy compared to traditional/standard regulatory endpoints
10	Sustainability	47	Human and financial resources required for the long-term continuity of the practice on PE in design of clinical trials are identified and secured.

Table 14: No consensus categories on PE in designing clinical trials (Round 2)

(New categories in orange)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	1	The aim and objectives of the practice on PE in design of clinical trials are agreed with all the stakeholders (i.e. patients, academics, researchers, pharmaceutical companies etc.) involved.
6	Capacity Building	29	Practices on PE in design of clinical trials incorporate training/coaching for stakeholders, other than patients, regarding how to incorporate patients in the design of clinical trials.
7	Involvement and Participation	New category	When engaging patients in the design of clinical trials, patient-oriented outcomes are obtained through valid instruments

Table 15: Dropped categories on PE in designing clinical trials (Round 2)

Criteria ID	Criteria	Category ID	Category
2	Contextualization of the practice on PE in the Design of Clinical Trials	4	The practice on PE in design of clinical trials is based on a pre-assessment of patients' wants and needs when participating in design of clinical trials.
		5	A clear understanding of contextual factors that would affect the outcomes of involving patients in design of clinical trials is demonstrated (e.g. funding, health system and coverage, characteristics of the population, socioeconomic environment).

3	Target participants involved in patient engagement	8	The target participant's profile who participate in the design of the clinical trial represent the target population that will be recruited to the clinical trials (e.g., former patients, people who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organisations, level of experience in design of clinical trials).
10	Sustainability	48	The practice on PE in design of clinical trials identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure its continuity, as long as confidentiality is respected.

Table 16: Relevant categories on PE in designing clinical trials and their Priority (Round 2)

Criteria ID	Criteria	Category ID	Category	Priority
1	Aim and objectives	3	The aim and objectives of the practice on PE are clear and understandable for all participants	**HP**
4	Code of Conduct	16	Efforts are made to ensure that all individuals involved know the rules of participation in clinical trials design (e.g., workshops, meetings).	**HP**
		17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population involved.	**HP**
		18	Potential conflicts of interest are addressed and managed (e.g., policies that require full disclosure, transparency, and accountability).	**HP**
5	Resources	21	All participants involved in design of clinical trials practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.	**HP**
		22	An appropriate and equitable financial compensation framework is in place for all participants (e.g. professionals, patients etc.) invited to participate in the PE practice in design of clinical trials (e.g., reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care).	**HP**
7	Involvement and participation	31	Consideration has been given to specific participants' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).	**HP**
		35	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language and using accessible, clear and understandable formats, taking into account potential impairments (e.g., impaired vision, blindness, and deafness and cognitive problems), low literacy levels, cultural backgrounds and other	**HP**

			relevant factors (e.g. age, disease / condition, etc.).	
8	Evaluation	41	The evaluation outcomes are linked to the aim and objectives of the PE practice in design of clinical trials.	**HP**
		42	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to the participant's characteristics and needs.	**HP**
9	PE Impact	45.8	More appropriate, inclusive, sensitive and ethical trial design	**HP**
10	Sustainability	46	The continuation of the practice is ensured through ownership and institutional or organisational anchoring.	**HP**
3	Target participants involved in patient engagement	7	The patient profiles engaged in the design of clinical trials reflect the relevant diversity of the population targeted (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information.	**MP**
4	Code of Conduct	15	The practice includes a code of conduct, which clearly states the rules and mechanism of participation in design of clinical trials for all stakeholders involved.	**MP**
		20	Funding resources for the practice on PE in design of clinical trials are clearly explained to all stakeholders involved prior to involvement, and any changes that occur during the practice are communicated up-front.	**MP**
6	Capacity Building	26	The practice includes comprehensive and accessible training or induction material and programs to respond to the need of the people involved in design of clinical trials.	**MP**
7	Involvement and participation	30	The type of interaction among the different stakeholders (e.g., cooperation, co-creation, information, advice…) is clearly defined.	**MP**
		36	A single point of contact for or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in design of clinical trials.	**MP**
8	Evaluation	43	The practice includes procedures by which the conclusions of the evaluation are used (e.g., mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).	**MP**
9	PE Impact	45.1	Improved recruitment of study participants	**MP**
		45.2	Increased retention (i.e. lower drop out) of study participants	**MP**
		45.4	Better adherence to the research protocol, less amendments	**MP**
		45.6	Faster study completion as a result of improved recruitment and adherence to the protocol	**MP**

3	Target participants involved in patient engagement	11	The role and responsibilities of all participants involved in the design of clinical trials, including patients, are clearly defined and agreed.	**LP**
4	Code of Conduct	19	The practices contains mechanisms (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidation, and unethical behaviours resulting from their participation during the design of the clinical trials process.	**LP**
7	Involvement and participation	32	The timing requirement of the engagement in design of clinical trials is appropriately planned, taking into account patient's needs, and based upon the requirements of the engagement process (e.g. time of the day, duration etc.).	**LP**

Round 3 (Meeting in person) – Discussion and Final Prioritization

Discussion and Prioritisation

To ease discussions at the meeting, the highly prioritised items and non-consensus categories remaining from the second round were further elaborated by the PARADIGM Delphi team. In order to avoid redundancy, a proposal was made to merge, rephrase or reallocate categories and criteria. They were presented to the expert panel and thoroughly discussed at the meeting. Comments provided by the experts in the first and second round were taken into consideration.

From the initial 10 criteria the experts agreed on 9 criteria comprised of 32 categories, and 11 subcategories (Table 17).

The experts rephrased categories in order to avoid redundancy and overlapping.

The following paragraphs provide more information about the key discussion followed during the meeting of the categories, which created more controversy and debate

Mainly, it was considered that the categories related to patients' needs and types of stakeholders should be clarified across the document. Furthermore, experts preferred the term "patient representatives" to "patients", as this term includes not only patients but carers, parents/tutors and/or staff from patient organisations too. It was replaced across the questionnaire. Some terms have been included as footnotes.

Criterion 1, "Aim and objectives" experimented several changes. On one hand, categories 1 and 3 were merged, because of overlapping, and category 2 was rephrased using synonyms.

On the other hand, category 32 was reallocated from "Involvement and participation" as experts considered this category should be at the beginning of the questionnaire.

Criterion 3, "Target participants involved in PE" contained four categories at the end of the second round, all of them were rephrased at the meeting.

Criterion 2, "Contextualisation of the practice on PE in the Design of Clinical Trials") and 4, "Code of conduct" were merged into a new criteria named "Legal and ethical consideration". These criteria triggered a deep debate, as there were different points of view.

All the categories were rephrased with the consensus of the panel. Besides, experts reordered categories to facilitate the assessment. Language, aims of the categories, recipient of the assessment, etc. were exhaustively discussed. The merges proposed by the PARADIGM team were not accepted, as experts considered that the concepts covered across the criterion would be really difficult to understand.

It is noteworthy that within this new criterion, category 16 was rephrased with the aim of making clear that the description of the efforts made in the process must be contemplated.

Likewise, category 18 generated an extensive debate about the management and communication of potential conflicts of interest, especially those referred to patients and healthcare professionals. Some experts held that a patient or a patient representative does not necessarily represent all the relevant points of view, which could cause a conflict. Moreover, it should be clarified, in every practice, what a conflict of interest for a patient/patient representative is.

It was also pointed out that "…conflicts of interest must be avoided, not managed" in a PE practice. However, it was discussed that this is not always possible. For example, if the involvement of some healthcare professionals is avoided because of their conflicts of interest, experts with strong knowledge in the field would be excluded; therefore, a valuable contribution could be missed

Likewise, in the discussion of category 20, related to the funding resources for participants, discussion about payments and funding recipients were debated. There was diversity of points of views. On one side, some of the experts considered, neither patients nor professionals should collect payments for their participation because of the potential conflicts of interest. Other views considered that any activity should be remunerated to any stakeholder, healthcare professionals and patients involved because they are contributing with their knowledge, expertise, time and effort.

Criterion 5, "Resources", was minimally changed. Three of the categories were rephrased.

After the analysis of the results in second-round, it was not clear that category 29 within **criterion 6, "Capacity building"**, was relevant. Finally, it was rephrased.

Categories 29 and 30 assessed the same activity but in different population, so they were maintained separated.

Criterion 7, "Involvement and participation", suffered several changes. The panel of experts accepted the suggestion of merging the categories 21 and 33. Likewise, they accepted to merge categories 34 and 36 into a more comprehensive category, considering that to give regular feedback closes the loop of patient representatives' involvement in the implementation of the practice.

As mentioned before, category 32 was removed from this criterion and reallocated in criterion 1.

The new category proposed by an expert in the previous Delphi rounds (Criterion 7: Involvement and participation: *When engaging patients in the Design of clinical trials, patient-oriented outcomes are obtained through valid instruments*, when presented to the panel of experts, it was discarded because they considered that "valid instruments" were too difficult to have in this context so they discarded the category.

Criterion 8, "Evaluation of the PE practice in the design of clinical trials" was kept as originally presented.

The panel detected overlapping among categories 38 and 40, all identifying different features for which the PE practice should be evaluated (methods, tools and monitoring systems).

Categories 41 and 43 were rephrased. In the case of category 42, experts rephrased to "close the feedback loop". The aim was to "make sure the information is shared and patient representatives receive it".

Category 44 was dropped since it was considered to be confusing. However, it was thought to better fit as a new subcategory within the category "Impact".

Criterion 9, "Patient engagement impact", triggered a deep debate about how to measure some categories, how to make the rephrasing ethical and inclusive, etc. Finally, categories in this criterion were organised as subcategories within category 45: "Impacts".

Category 44 was rephrased and reallocated as a new subcategory and a new subcategory was added by the panel.

Criterion 10, "Sustainability", has two categories. Category 46 was rephrased; it was said that it's not always necessary to ensure the continuation of the practice because it is systematically embedded.

Finally, category 47 was kept as originally presented to the panel.

Once this work was completed, the resulting categories in each criterion were weighted as well as the final 8 criteria, by distributing 100 points among them.

The highest weight was assigned to current criterion 1: "Patient engagement impact" and "Aims and objectives" (both of them with a weight of 14/100), while the criteria with the lowest score were "Sustainability" (8/100), followed by "Resources" (10/100) and "Evaluation of the PE practice in setting clinical trials" (10/100).

Current criteria and category and their corresponding weights are detailed in Table 17.

Table 17: Final set of criteria and categories, and their weights, recommended for assessing PE practices in the design of clinical trials (following the assessment practice process).

New criteria names	Criteria weight	Categories	Category weight

1. Aims and objectives	**14**	There is general agreement on the aims and objectives of the practice on PE and these are understandable by all relevant stakeholders involved in the design of CT.	**40.6**
		The aims and objectives of the practice on PE focus on patient's needs and interests.	**34.7**
		The timeline for the engagement in the design of clinical trials is appropriately planned and allows for incorporation throughout the process.	**24.7**
Total must equal 100			
2. Target participants involved	**12**	The patient representatives* engaged in the design of clinical trials reflect the relevant diversity** of the target population. * Patients, carers, parents or tutors and/or staff from patient's organization that act as a liaison between the patients and other organisations, represent their interests and advocates for their rights. ** Including but not limited to cultural background, socio-economic status, gender, age, ethnicity, educational level, disease, disability, vulnerability, etc.	**32.9**
		The practice of PE includes a clear description of the process and criteria followed to identify patient representatives to participate in the design of clinical trials.	**19.0**
		The role and responsibilities of all target participants involved in the design of clinical trials, including patient representatives, are clearly defined and agreed.	**23.7**
		The practice includes a clear description of the process followed* to make sure that all participants understand their own and other's roles and responsibilities. *Including documents, charts, guidance, training, meetings, workshops.	**24.4**
Total must equal 100			
3. Legal and ethical consideration	**11**	The practice includes a code of conduct, which clearly states the principles of participation in design of clinical trials for all stakeholders involved.	**18.9**
		The practice contains procedures to identify and address unethical behaviours, towards all stakeholders, during their participation in the design of the clinical trials process.	**10.9**
		There is a clear description of efforts made to ensure that all stakeholders involved know the principles of participation in clinical trials design (e.g., workshops, meetings).	**11.0**
		The terms and conditions of all legal agreements are written and communicated in a clear and accessible way and adapted to the target population involved.	**14.2**
		Potential conflicts of interest are addressed and managed (up to avoidance). For this, policies that require full disclosure, transparency and accountability are developed.	**15.7**
		Funding resources for the practice on PE in the design of clinical trials are clearly documented and explained to all stakeholders involved prior to involvement, and any changes that occur during the practice are communicated up-front.	**14.0**

		All relevant policy directives, legal and/or regulatory framework have been followed when engaging patients in the design of clinical trials.	**15.3**
Total must equal 100			
4. Resources	**10**	All participants involved in the design of clinical trials practice are informed, in clear and accessible way, of the resources available to support their tasks during the process.	**19.3**
		A clear, transparent and equitable financial compensation framework is in place for patient representatives who participate in the PE practice in the design of clinical trials (e.g., reimbursement of expenses for travel, time missed from work, subsistence, child/elderly care, stipends).	**24.1**
		Funding is allocated to cover governance, administration and operations of the practice in PE on design of clinical trials, is adequate for the intended work.	**18.6**
		Infrastructure is in place to support the practice in PE on design of clinical trials and is adapted to specific circumstances of patient representatives (e.g. technological support, working space, information and communication technologies).	**21.4**
		The resources include guidelines, and ready-to-use tools and templates, material that facilitates effective patient engagement implementation in a clear and accessible way.	**16.6**
Total must equal 100			
5. Capacity building	**10**	Comprehensive and accessible trainings or induction materials and programs are available to respond to the needs of the patient representatives involved in the design of clinical trials.	**54.8**
		Practices on PE in design of clinical trials incorporate training/coaching for stakeholders, other than patient representatives, regarding how to incorporate patients in the design of clinical trials.	**45.2**
Total must equal 100			
6. Involvement and participation	**11**	The type of interaction among the different stakeholders is defined at each stage (e.g. co-creation, advice, consultation...).	**18.4**
		There are mechanisms (e.g. language, format of meetings, the venue, time of the day, etc.) in place to ensure participation of patient representatives, taking into consideration participant's characteristics, and circumstances of vulnerable population.	**29.4**
		Patient representatives receive timely and regular feedback about the outcomes/changes for each phase of the involvement, in a clear and understandable format and adapted to patients' circumstances.	**31.7**
		A clear point of contact is available to whom patient representatives can reach out to when needed for information and/or support, throughout their involvement in the design of clinical trials.	**20.6**
Total must equal 100			
7. Evaluation of the PE practice in setting clinical trials	**10**	There are methods, tools and monitoring systems in place to evaluate the PE practice.	**24.2**
		The evaluation criteria are linked to the aims and objectives of the PE practice.	**23.3**

		The evaluation outcomes are shared with all the stakeholders involved in the practice using appropriate channels and formats suited to patient perspectives' circumstances and needs.	**25.6**
		The evaluation outcomes are used to improve future PE practices for design of clinical trials.	**26.9**
Total must equal 100			
8. Patient engagement impact	**14**	Impacts:	
		Improved recruitment.	**7.2**
		Improved retention (i.e. fewer drop outs) of study participants.	**6.8**
		Better adherence to the research protocol.	**7.1**
		Fewer amendments to the research protocol.	**7.3**
		Improved trial experience for study participant.	**11.1**
		More timely study completion.	**7.3**
		More inclusive, sensitive and ethical trial design, which are appropriate for specific needs and circumstances of the target population.	**12.4**
		The wording and timing of research instruments (e.g. questionnaires and interventions) are appropriate for specific needs and circumstances of the target population.	**9.8**
		Patient information and education materials (e.g. lay summaries, information and education sheets, consent form, recruitment material) are appropriate to the specific needs and circumstances of the target population.	**10.9**
		Additional study-specific relevant measure are included to complement the described ones.	**5.6**
		Identification of meaningful endpoints for patients.	**14.5**
Total must equal 100			
9. Sustainability	**8**	The continuation of the practice is ensured through ownership and it is systematically embedded in the institution or organisation for all stakeholders.	**47.8**
		Human and financial resources required for the long-term continuity of the practice on PE in the design of clinical trials are identified and secured.	**52.2**
		Total must equal 100	
Total must equal 100			

Annex 7. Results of the Delphi on PE in Early Dialogues

Results of Round 1 (Online) – Relevance assessment

Table 18: Relevant categories on PE in Early Dialogues with HTA & Regulators (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	3	The aim and objectives of the practice on PE in early dialogues are clear and understandable for all participants.
2	Contextualization of the practice on PE in Early Dialogues	6	Any existing policy, legal (governance requirements) and regulatory framework (e.g. EMA) about how to engage patients in early dialogues with HTA and regulators have been followed.
4	Code of Conduct	17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population.
		18	The practice on PE in early dialogues incorporates mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).
		19	The practice contains procedures (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidating, and unethical behaviours resulting from the participation during the early dialogue process.
5	Resources	21	All participants involved in early dialogues with HTA and regulators are informed in clear and accessible way, of the resources available to support their tasks during the process.
		22	The practice includes an equitable financial compensation framework for all participants (e.g. professionals, patients etc.) invited to participate in the early dialogues with HTA and regulators (i.e reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).
		23	Funding is allocated to cover all the elements of the practice (e.g., human resources, material resources), and is adequate to the intended work.
		24	Adequate infrastructures needed for PE in early dialogues are in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g. possible physical mental, cognitive or any impairments etc.).
		25	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.
6	Capacity building	26	The practice on PE in early dialogues identifies the competencies required by all stakeholders involved in early dialogues with HTA bodies and regulators (e.g. knowledge and skill such as how to

			perform patient engagement in early dialogues, etc.).
		28	The practice includes comprehensive and accessible training or induction material and programs to respond to the need of the participants involved in early dialogues with HTA and regulators.
7	Involvement and participation	31	The mechanism of interaction among the stakeholder is adapted to their needs. (e.g. meetings, online, skype.. etc.).
		32	Patients receive timely, clear, accessible and appropriate information about their involvement (i.e. what will be addressed, what is expected from them, what their participation will entail, how the practice will be organized etc.)
		33	The practice considers specific patients' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).
		34	The timing of the engagement in early dialogues with HTA and regulators is appropriately planned, based upon the requirements of the review process.
		35	The practice on PE in early dialogues sets mechanisms to ensure a proper deliberative process (e.g. meetings, interviews, focus group, workshops…).
		36	A regular feedback system to inform patients about the outcomes/changes is included in each phase of the involvement.
		37	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into account potential impairments (e.g., impaired vision, blindness, and deafness), low literacy levels , cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).
		38	The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in early dialogues.
8	Evaluation	41	An evaluation framework is included (structure, process and results) and it enables regularity evaluation (frequency, timing…).
		44	The evaluation outcomes are linked to the aim and objectives of the PE practice in early dialogues.
		45	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to participants' characteristics and needs.
9	PE Impact	48.1	Better understanding of technologies' impact in real life context and the quality of life aspects
		48.2	More practical and better designed development plan for medicines.
		48.3	Higher accuracy in measuring needs and preferences of patients.
		48.4	Better quality of the evidence assessed during the later HTA assessment.
		48.5	More useful advice given to aid company decisions.

		48.6	Higher relevance of the advice given to the local context of application
		48.10	Inclusion of patients' relevant outcomes and end-points in clinical trials data collection and analysis.

Table 19: No consensus categories on PE in Early Dialogues with HTA & Regulators (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	1	The aim and objectives of PE in Early Dialogues reflects patients' needs, experiences and expectations in the early dialogues process.
2	Contextualization of the practice on PE in Early Dialogues	4	In the practice on PE in early dialogues, the process is based on the assessment of the patient's preferences and needs.
		5	A clear understanding of contextual factors that inform the process of patient engagement is demonstrated so that the quality of dialogue when involving patients in early dialogues with HTAs and regulators is improved.
3	Target participants involved in patient engagement	7	The profiles of patients engaged in early dialogues with HTA and regulators reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information
		9	The practice of PE in early dialogues includes methods to identify patients who match the clinical criteria needed for a particular dialogue (e.g., patient's networks, health care professionals' networks, public advertise etc.).
		10	The practice supports patients to engage and/or reach out to vulnerable groups to involve them in early dialogues with HTA and regulators, as well as to other patients.
		11	Relevant points of view other than patients (e.g. carers, parents etc.) are considered.
		12	In the practice, the role and responsibilities of all participants involved, including patients are clearly defined and agreed.
		14	Guidance, training adequate is provided to ensure that all participants understand their own role and responsibilities, as well as the responsibilities and roles of others.
4	Code of Conduct	15	The practice includes a code of conduct, which clearly states the rules of participation in early dialogues with HTA and regulators for all participants involved.
		20	Funding resources for the practice on PE in early dialogues are clearly explained to all stakeholders involved, prior to involvement, and any changes that occur during the practice of PE in early dialogues are communicated up-front.
6	Capacity building	27	The practice on PE in early dialogues includes training programs on HTA/Regulatory processes/clinical trial design and methods to patients (e.g., written information, in-house training, online, personalized assistance, and webinars).

		30	The practice on PE in early dialogues incorporates training/coaching for all stakeholders, other than patients, regarding how to incorporate patients in early dialogues with HTA and regulators.
8	Evaluation	42	The evaluation framework is shared and agreed among the participants to foster collaboration.
		43	Methods, tools and monitoring system are in place to evaluate the PE practice.
		46	The practice includes procedures by which the conclusions of the evaluation are used (e.g. mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).
9	PE Impact	47	The practice identifies relevant outcomes and impacts regarding the involvement of patients in early dialogues with HTA and regulators.
		48.8	Transparency of HTA/regulation processes.
		48.11	Mutual understanding between all involved stakeholders including the patient community about the regulatory and HTA process.
10	Sustainability	50	Human and financial resources required for the long-term continuity of the practice on PE in early dialogues are identified and secured.

Table 20: Dropped categories on PE in Early Dialogues with HTA & Regulators (Round 1)

Criteria ID	Criteria	Category ID	Category
1	Aim and objectives	2	The aim and objectives of the practice on PE in early dialogues were co-designed and agreed with all the stakeholders involved.
3	Target participants involved in patient engagement	8	Patients engaged in early dialogues with HTA and regulators are selected to represent relevant patients' circumstances (e.g., former patients, patients who are at risk for a disease, but do not yet have the disease, patients' advocates, patients' representatives, patient organizations, level of experience in early dialogues with HTA and regulators, patient's scientific knowledge/ background).
		13	There is clear guidance about how to assign roles among all participants involved in early dialogues.
4	Code of conduct	16	The practice on PE in early dialogues includes mechanisms, adequate and adapted to the target population to ensure that all individuals involved know the rules of participation in early dialogues with HTA and regulators (e.g., workshops, meetings).
6	Capacity building	29	The training program specifies time when training needs to be provided, duration and frequency of the sessions (e.g., on demand, once, twice a month/year).
7	Involvement and participation	39	Mechanisms are in place to guarantee all members have the same status within the work group, regardless of their experience and knowledge.
		40	The practice on PE in early dialogues fosters discussion and agreement with patients about identifying and selecting preferences about the ED process with HTA bodies and regulators.
9	PE Impact	48.7	Increased public knowledge and awareness of HTA and regulatory

			processes.
		48.9	Acceptability of regulatory decisions/HTA reports for stakeholders.
10	Sustainability	49	The continuation of the practice is ensured through ownership and institutional or practice organization anchoring.
		51	The practice on PE in early dialogues identifies and establishes alliances with other private and/or public institutions, citizens and others, to ensure the continuity of the PE in ED as long as confidentiality is respected.
		52	There is a dissemination and communication plan/strategies of the results of the process of PE in early dialogues through culturally appropriate and accessible mechanisms.

Results of Round 2 (Online) – Prioritization

Table 21: Relevant categories on PE in Early Dialogues with HTA & Regulators (Round 2)

Criteria ID	Criteria	Category ID	Category
3	Target participants involved in patient engagement	11	Relevant points of view other than patients (e.g. carers, parents etc.) are considered.
		12	In the practice, the role and responsibilities of all participants involved, including patients are clearly defined and agreed.
		14	Guidance, training adequate is provided to ensure that all participants understand their own role and responsibilities, as well as the responsibilities and roles of others.
4	Code of Conduct	15	The practice includes a code of conduct, which clearly states the rules of participation in early dialogues with HTA and regulators for all participants involved.
		20	Funding resources for the practice on PE in early dialogues are clearly explained to all stakeholders involved prior to involvement, and any changes that occur during the practice of PE in early dialogues are communicated up-front.
9	PE Impact	47	The practice identifies relevant outcomes and impacts regarding the involvement of patients in early dialogues with HTA and regulators.
		48.8	Transparency of HTA/regulation processes.

Table 22: No consensus categories on PE in Early Dialogues with HTA & Regulators (Round 2)

Criteria ID	Criteria	Category ID	Category

1	Aim and objectives	1	The aim and objectives of the practice respond to patient's needs when participating in the early dialogues process.
3	Target participants involved in patient engagement	9	The practice on PE in early dialogues includes methods to identify individuals eligible to participate in early dialogues with HTA and regulators (e.g., agency databases, those involved in other parts of HTA or regulatory processes, patients' networks, health care professionals' networks, public advertise etc.).
		10	The practice supports patients to engage and/or reach out to vulnerable groups to involve them in early dialogues with HTA and regulators, as well as to other patients.
8	Evaluation	43	Methods, tools and monitoring system are in place to evaluate PE practice
		46	The practice includes procedures by which the conclusions of the evaluation are used (e.g. mechanisms to integrate the results of the evaluation in the design of the next practice or in the current one with a continuous improvement process).
9	PE Impact	48.11	Mutual understanding between all involved stakeholders including the patient community about the regulatory and HTA process.
10	Sustainability	50	Human and financial resources required for the long-term continuity of the practice on PE in early dialogues are identified and secured.

Table 23: Dropped categories on PE in Early Dialogues with HTA & Regulators (Round 2)

Criteria ID	Criteria	Category ID	Category
2	Contextualization of the practice in PE in Early Dialogues	4	In the practice on PE in early dialogues, the process is based on the assessment of patients' preferences and needs.
		5	A clear understanding of contextual factors that inform the process of patient engagement is demonstrated so that the quality of dialogue when involving patients in early dialogues with HTAs and regulators is improved.
3	Target participants involved in patient engagement	7	The profiles of patients engaged in early dialogues with HTA and regulators reflect the relevant diversity of the population targeted. (e.g., gender, socioeconomic status, ethnicity, cultural background, geographical location etc.) and includes gender sensitive information
6	Capacity building	27	The practice on PE in early dialogues includes training programs on HTA/Regulatory processes/clinical trial design and methods to patients (e.g., written information, in-house training, online, personalized assistance, and webinars).
		30	The practice on PE in early dialogues incorporates training/coaching for all stakeholders, other than patients, regarding how to incorporate patients in early dialogues with HTA and regulators.
9	Evaluation	42	The evaluation framework is shared and agreed among the participants to foster collaboration.

Table 24: Relevant categories on PE in Early Dialogues with HTA & Regulators and their Priority (Round 2)

Criteria ID	Criteria	Category ID	Category	Priority
1	Aim and objectives	3	The aim and objectives of the practice on PE in early dialogues are clear and understandable for all participants.	**HP**
4	Code of conduct	17	The terms and conditions of confidentiality agreements are adequate, written in a clear and accessible way and adapted to the target population.	**HP**
		18	The practice on PE in early dialogues incorporates mechanisms (explained to all stakeholders in a clear and accessible way) to manage potential conflicts of interest when patients engage with different stakeholders (e.g., policies that require full disclosure, transparency, and accountability).	**HP**
7	Involvement and participation	36	A regular feedback system to inform patients about the outcomes/changes is included in each phase of the involvement.	**HP**
		37	The information about the outcomes included for each phase of the involvement is communicated in plain and respectful language, using accessible, clear and understandable formats, and taking into account potential impairments (e.g., impaired vision, blindness, and deafness), low literacy levels , cultural backgrounds and other relevant factors (e.g. age, disease / condition, etc.).	**HP**
9	PE Impact	48.1	Better understanding of technologies' impact in real life context and the quality of life aspects	**HP**
		48.2	More practical and better designed development plan for medicines	**HP**
		48.3	Higher accuracy in measuring needs and preferences of patients	**HP**
		48.10	Inclusion of patients' relevant outcomes and end-points in clinical trials data collection and analysis.	**HP**
2	Contextualization of the practice in PE in Early Dialogues	6	Any existing policy, legal (governance requirements) and regulatory framework (e.g EMA) about how to engage patients in early dialogues with HTA and regulators have been followed.	**MP**
4	Code of conduct	19	The practice contains procedures (e.g., personalized meetings, ways of anonymous uncovering) to identify and address discriminatory, coercive, intimidating, and unethical behaviours resulting from the participation	**MP**

			during the early dialogue process.	
5	Resources	21	All participants involved in early dialogues with HTA and regulators are informed in clear and accessible way, of the resources available to support their tasks during the process.	**MP**
		22	The practice includes an equitable financial compensation framework for all participants (e.g. professionals, patients etc.) invited to participate in the early dialogues with HTA and regulators (i.e reimbursement of expenses for travel, subsistence, time missed from work, child/elderly care etc.).	**MP**
		23	Funding is allocated to cover all the elements of the practice (e.g., human resources, material resources), and is adequate to the intended work.	**MP**
		24	Adequate infrastructures needed for PE in early dialogues are in place (e.g., technological support, working space, information and communication technologies) and adapted to specific circumstances of participants (e.g. possible physical mental, cognitive or any impairments etc.).	**MP**
		25	The practice includes guidance, and ready-to-use tools and templates material that facilitates effective patient engagement implementation in a clear and accessible way.	**MP**
6	Capacity building	26	The practice on PE in early dialogues identifies the competencies required by all stakeholders involved in early dialogues with HTA bodies and regulators (e.g knowledge and skill such as how to perform patient engagement in early dialogues, etc).	**MP**
7	Involvement and participation	31	The mechanism of interaction among the stakeholder is adapted to their needs. (e.g. meetings, online, skype.. etc).	**MP**
		32	Patients receive timely, clear, accessible and appropriate information about their involvement (i.e what will be addressed, what is expected from them, what their participation will entail, how the practice will be organized etc)	**MP**
		33	The practice considers specific patients' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., use of language, format of meetings, the venue, information provided).	**MP**
		34	The timing of the engagement in early dialogues with HTA and regulators is appropriately planned, based upon the requirements of the review process.	**MP**

		38	The practice includes a single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in early dialogues.	**MP**
9	PE Impact	48.4	Better quality of the evidence assessed during the later HTA assessment.	**MP**
		48.5	More useful advice given to aid company decisions	**MP**
		48.6	Higher relevance of the advice given to the local context of application.	**MP**
6	Capacity building	28	The practice includes comprehensive and accessible training or induction material and programs to respond to the need of the participants involved in early dialogues with HTA and regulators.	**LP**
7	Involvement and participation	35	The practice on PE in early dialogues sets mechanisms to ensure a proper deliberative process (e.g. meetings, interviews, focus group, workshops…).	**LP**
8	Evaluation	41	An evaluation framework is included (structure, process and results) and it enables regularity evaluation (frequency, timing…).	**LP**
		44	The evaluation outcomes are linked to the aim and objectives of the PE practice in early dialogues.	**LP**
		45	The evaluation outcomes are shared with all the participants involved in the practice using appropriate channels and formats suited to participants' characteristics and needs.	**LP**

Round 3 (Meeting in person) – Discussion and Final Prioritization

Discussion and Final Prioritisation

To ease discussions at the meeting, the highly prioritised items and non-consensus categories remaining from the second round were further elaborated by the PARADIGM Delphi team. In order to avoid redundancy, a proposal was made to merge, rephrase or reallocate categories and criteria. They were presented to the expert panel and thoroughly discussed at the meeting. Comments provided by the experts in the first and second round were taken into consideration.

From the initial 10 thematic criteria, the experts agreed on 8 criteria made up of 29 categories and 7 subcategories (see table 25).

For each criterion and category, consensus was reached on whether to retain, rephrase, merge with another category, or discard it.

The following paragraphs provide more information about the key discussion followed during

the meeting of the categories which created more controversy and debate

In general, it was agreed by the expert panel to use the term "PE practice" throughout the discussion. Furthermore, the term "patient" was also replaced with "patient representative", in order to reflect that this is a role that represents the whole target population. Experts agreed on removing brackets along the document to be read with ease.

Criterion 1, *"Aim and objectives*" consisted of two categories. Category 1 was barely modified.

Criterion 2, *"Contextualization of the practice on PE in Early Dialogues"* was dropped, moving Category 6 to Criterion 4.

Criterion 3, *"Target participants involved in patient engagement"* consisted of five categories, two of which were merged. This criterion generated discussion on concepts related to representativeness and diversity of the participants involved in ED. They flagged the difficulty to find a patient with the right profile or specific experience for a particular ED, and with the capacity to participate. They also acknowledged that the problem of targeting individual patients led to end up contacting the same patients due to the difficulty it encounters to find the right patient.

Category 9 was slightly modified and experts decided to add the concept of "vulnerable population" to the glossary (see Annex 4). Category 10 was rephrased to reflect that, when assessing the practice, evaluators should take into account whether the practice tries to capture diversity (regardless of whether it ultimately succeeds). Likewise, Category 11 was modified to show the relevance of representing other points of view, different from those of their specific patients. Finally, Category 12 and 14 were merged; the expert panel agreed that all participants in a PE practice should be clear about their role. To achieve this, information and guidance should be provided.

Criterion 4, *"Code of conduct"* contained four categories. All of them were rephrased and Category 6 was included, moved from Criterion 2 "Contextualization of the practice on PE in Early Dialogues". Categories 15, 17 and 19 were rewritten to simplify and avoid overlapping concepts and Category 18 was rephrased to reflect every kind of conflicts of interest. For its part, Category 6 was modified by including concepts about the regulatory framework determined by bodies such as the EMA (European, national, etc.).

Criterion 5, *"Resources"* included 6 categories, one of them was discarded and the rest were rephrased. Firstly, Category 20 was rephrased to include that financial arrangement represents the framework established by the different parties in the ED. On the other hand, Category 21 was dropped due to its contents were also considered within Category 20. Category 22 was rewritten in order to clarify the definition of financial framework. Thus, explicit mention was made to the idea that PE practices are subject to a context/rules. Besides, Categories 23 and 24 were rephrased due to overlaps and to clarify concepts. Then Category 25 was rewritten to indicate that tools used should be based on existing methodology.

Criterion 6, *"Capacity building"* was renamed "Capability building". The two existing

categories in this criterion were maintained, one of them was rephrased. Category 26 was modified in order to differentiate patients' experience from the knowledge requirements.

Criterion 7, *"Involvement and participation"* initially consisted of six categories, one of which was discarded and two were merged, the remaining categories were rephrased. Hence Category 31 was merged with Category 33 and Category 32 was discarded since the role of the patient representative was already described. Category 34 was adapted to explain that the process plan should take into account PE preparation time, with a view to involve the patient from the beginning and Category 35 was rewritten to determine that an equal deliberative process is required. Likewise, Category 36 was rephrased. Experts placed emphasis on having an iterative process when including patients in ED. It was considered important to provide feedback about their contribution during the ED process. However, in the discussion it was pointed out the difficulty of giving feedback without breaking confidentiality, due to the nature of this information. It was also highlighted that patients should be able to provide feedback on the information received related to results, documents, final output, etc. For its part, Category 37 was amended to highlighted the importance of considering possible "disabilities and impairments" rather than limitations due to cultural background or low literacy. Category 38 was adapted to take into account that contact information should be updated, because of changes that may occur within the institutions.

Criterion 8, *"Evaluation of the PE practice in early dialogues with HTA bodies and regulators"* was composed of five categories. An additional category was included from the "Patient Engagement Impact" criterion, three categories were merged and the rest were rephrased. Category 47 was added as an analogous category to that existing within the "Patient Engagement Impact" domain; in this case the word "impact" was removed to avoid overlapping. Likewise, Categories 41, 43 and 44 were merged based on the proposal made by the PARADIGM Delphi Team. Furthermore, Categories 45 and 46 were rephrased to avoid redundancies.

Criterion 9, *"Patient Engagement Impact"* consisted of two main categories, Categories 47 and 48, which experts decided to merge and rephrased. The panel discussed about the practical difficulties for observation and measurement them when the PE practice is assessed. Therefore subcategories were interpreted just as a list of examples of potential impacts of a PE practice on ED, accordingly the panel agreed not assigning weights to each subcategory.

Individually, the subcategories were discussed by the panel: Subcategories 48.1 and 48.2 were rephrased. Besides Subcategory 48.3 and Subcategory 48.4 were rephrased; and Subcategory 48.5 was discarded because overlaps with Category 48. Subcategory 48.8 was adapted to describe the concept of transparency and Subcategory 48.10 remains unchanged, but its order was modified to improve the coherence of the list of examples of potential impacts. Eventually, Subcategory 48.11 is discarded because of its overlap with Subcategory 48.8.

Criterion 10, *"Sustainability"* it was proposed to merge with Criterion "Resources", given that issues related to sustainability had been covered. Finally, it was established by the panel that this criterion and its contents could be included somewhere else in the PARADIGM project, but

it should not be an element to be evaluated in each PE practice.

Once the work on specification was completed, the resulting categories in each criterion were weighted. Later, experts weighed the final 8 criteria by distributing 100 points among them. The highest weight was assigned to current Criterion 1, "Aim and objectives" (17.9/100), while the criteria with the lowest score were "Evaluation" (8/100), followed by "Patient Engagement Impact" (10/100).

Current criteria and category and their corresponding weights are detailed in table 25.

Table 25: Final set of criteria and categories, and their weights, recommended for assessing PE practices in early dialogues

Criteria	Criteria weight	N	Categories	Weight
1. Aim and objectives	17.9	1	The practice aims to meet patients' expectations when participating in the early dialogue process.	46.5
		2	The aim and objectives of PE in Early Dialogues are clear and understandable for all stakeholders involved.	53.5
				Total must be 100
2.Target participants involved in patient engagement	15.3	3	The practice of PE in early dialogues includes rigorous methods to identify patients or patient representatives* from the relevant target population needed for a particular dialogue. *Patients, vulnerable population, carers, parents or tutors and/or staff from patient's organization that act as a liaison between the patients and other organizations, represent their interests and advocates for their rights.	30.5
		4	The process captures the diversity of the target population and their range of perspectives.	25
		5	Relevant points of view other than those patients (e.g. carers, parents etc.) are also considered.	16.5
		6	Guidance and adequate training are provided to ensure that the role and responsibilities of all stakeholders involved are clearly defined and understood by all.	28
				Total must be 100
3. Code of conduct	11.3	7	Any applicable policies, legislative and regulatory frameworks (e.g. EMA) about when and how to engage patients in early dialogues with HTA and regulators have been followed	26.5
		8	The practice includes a code of conduct, which clearly states the rules of participation in early dialogues for all stakeholders involved.	25
		9	The terms and conditions of all policies and confidentiality	16.5

			agreements are adequate, clear and accessible.	
		10	The PE practice incorporates mechanisms to disclose and manage all potential conflicts of interest of all stakeholders.	18
		11	The PE practice contains procedures to identify and address potential discriminatory, coercive, intimidating, and unethical behaviours before, during and after the participation.	14
				Total must be 100
4. Resources	10.9	12	The practice uses relevant PE methodologies, guidance and tools.	20.2
		13	The practice includes a fair financial framework* for participating patient representatives. * Mechanism for payment/reimbursement	19.7
		14	Sufficient funding is in place to ensure that all the elements of the practice are covered in its entirely.	19.7
		15	Financial arrangements for the practice of PE in early dialogues are clearly explained to all stakeholders involved, prior to involvement, and any changes that occur during the practice are communicated up-front.	17.2
		16	An adequate infrastructure is in place (e.g., technological support, working space, information and communication technologies) and adapted to specific requirements of participants (e.g. possible physical mental, cognitive or any impairments etc.).	23.2
				Total must be 100
5. Capacity building	11.1	17	The practice on PE describes the relevant competencies, expertise and experience required by all stakeholders to effectively engage in this process.	42.9
		18	The practice includes comprehensive and accessible training or induction material and programs to respond to the needs of the participants involved in early dialogues with HTA and regulators.	57.1
				Total must be 100
6. Involvement and participation	14.7	19	The process respects the need for appropriate planning and preparation time, to allow patient representatives to effectively engage from the beginning.	19
		20	The mechanism of interaction with patients' representatives is adapted to their needs to ensure effective PE. More specifically, it considers specific patients' circumstances and characteristics linked to but not limited to possible physical or mental impairments, cultural background, age and other relevant features (e.g., recordings, virtual communication,	28.5

			use of language, format of meetings, the venue, and information provided).	
		21	The practice on PE in early dialogues sets mechanisms to ensure a fair deliberative process* that allows equal opportunity for participants' contribution.	16.2
		22	A regular feedback system is in place to inform patient representatives about the outcomes/changes, as appropriate, including the option for patients' representatives to comment on the final output.	10.8
		23	The information about the outcomes included for each phase of the involvement is communicated in clear and plain language, using accessible formats, and taking into account potential disabilities and impairments, as appropriate.	10
		24	The practice includes an up-to-date single point of contact or a named person to whom patients can reach out to when needed, for information and/or support, throughout their involvement in early dialogues.	15.5
				Total must be 100
7. Evaluation	8.8	25	The practice includes an evaluation framework linked to the aim and objectives, including methods, tools and monitoring system, which enables systematic evaluation at appropriate phases of the process.	29.8
		26	The practice identifies relevant outcomes regarding the involvement of patients in early dialogues with HTA and regulators.	31.8
		27	The evaluation outcomes are shared with all the participants involved.	16.6
		28	The practice includes procedures by which the conclusions of the evaluation are used to support a continuous improvement process.	21.8
				Total must be 100
8. Patient Engagement Impact	10	29	The practice identifies potential impact from the practice, for example: ● Better understanding of the impact of health technologies and treatments in real life context and the quality of life aspects. ● More practical and better designed development plan for health technologies and treatments. ● Better reflection of the needs and preferences of patients in development plans for new technologies. ● Inclusion of patients' relevant outcomes and end-points	

			in clinical trials data collection and analysis. ● Better quality of the evidence assessed during the later regulatory and HTA assessment. ● Higher relevance of the advice given to the local context of application. ● Transparency of regulatory and HTA processes leads to better understanding and trust of the scientific procedures.	