Innovative Medicines Initiative

Patient involvement in IMI projects from Call 1 to Call 6

20/09/2013 - Report summarizing the responses from the survey about Patient involvement in IMI projects from Call 1 to Call 6.

David Tordrup
d.p.tordrup@lse.ac.uk
+44 (0) 7570 122 770
http://www.davidtordrup.dk

DORA/INC/2013-04575

Contents

Executive Summary 3
Introduction and objectives 4
Methods 4
Results 5
Responses from organisations not currently involving patients 6
Responses from projects currently involving patients 7
General observations from respondents 9
Conclusions 12
Appendix: Project partners invited to participate 13
Appendix: Supplementary data 14
Appendix: Patient involvement by project 20

Executive Summary

This report describes the current status of patient involvement in IMI projects based on a short survey circulated among all current projects. The survey was designed to determine which projects are currently involving patients; how it is being done; and what the benefits and challenges are.

Responses were received from 39 out of 40 organisations. Approximately 2/3rds of IMI projects currently have some form of patient participation however this is most commonly in the form of clinical trials or research where patient samples are required. Less commonly, patient organisations are part of the project consortium or members of ethical boards etc. The most common reason for not involving patients is that it was not envisaged in the project scope, though small numbers of respondents note there is no clear benefit in doing so, or that there are budgetary constraints.

The benefits to involving patients generally revolve around the unique perspective patients can bring to a project; how patients can improve to more effective dissemination especially outside the scientific community; and from the patient's perspective that they can become empowered to build networks and better understand their conditions. The barriers included among other things the burden on the patient in terms of finance, time and energy; logistical, ethical and le.g.al requirements associated with involving patients, particularly across countries; language issues; and ensuring representativeness when involving a relatively small proportion of patients with a given condition.

The recommendations arising from this work include:

- Support involvement of patients in the early stages (inception phase, consortium building, scoping) to ensure patient participation is an integrated part of the project with adequate funding
- Map out for different types of projects where patient input is most appropriate and beneficial – for example, in clinical trials or biomarker validation studies with rigid protocols, patients do not have much opportunity to provide input (except as "subjects") once the study protocol has been defined.
- Provide training for researchers to understand the potential benefits of involving patients in their work and in which areas this can occur. This may be particularly valuable for projects that currently see patients only as "subjects" either as participants in trials or as providing sample material.
- Ensure the financial and accounting barriers to patient participation are limited, including understanding the limitations patient organisations face with regard to eligibility of expenses (VAT, ad hoc staff/consultants etc.)[1]
- Ensure that non-patient project partners are aware of the potential special needs of patients, including limitations in travelling (when organising meetings)
- In areas where expertise among patients is lacking, provide training and support to patients to adequately equip them to contribute meaningfully to research projects.

[1] Many of these challenges are detailed in Table 11 (Appendix), two comments marked with ***

Introduction and objectives

As part of IMI efforts to further patient involvement in research projects, this report describes the results of a brief survey aiming to identify current patient involvement in existing IMI projects. The report describes the content of survey, followed by an exposition and analysis of the results, and finally a list of conclusions drawn from the work.

Methods

A questionnaire, detailed in Table 1, was designed to capture existing patient participation in IMI projects. The questionnaire was administered online, and all project partners (n=40) were invited to participate directly. The list of invited respondents is given in the appendix. The questionnaire was semi-anonymous, as respondents were asked to identify their project in the first question, though no other details on the respondent were recorded. Several responses per project were allowed, to ensure different perspectives could be accounted for.

Table 1 Questions and response options for the questionnaire

Questionnaire
Please select your project from the list
[Drop-down list]
If your project currently involves patients, how is this implemented? (select all that apply)
N/A
Patient organisations are partners of the consortium
Patients (or patient org. representatives) are members of an advisory board
Patients (or patient org. representatives) are members of an ethical board
Patients give feedback on research protocols
Patients give input to the research itself (eg. design of patient-reported outcomes)
Patients are subjects of the research (eg. clinical trials, providing samples)
If your project does not currently involve patients, what are the reasons? (select all that apply)
N/A
Patient involvement was not envisioned within the project scope
There is no budget/personnel allocation to achieve it
No clear benefit from involving patients in the project
Project teams are not sure how to find interested patients
Project teams are not sure which processes patients should be involved in
If your project does not currently involve patients, will it do so in the future?
N/A
Not envisaged
Patient involvement under consideration
Patient involvement planned within 1 year from present
Patient involvement planned later than 1 year from present
If your project does involve patients, what are the main benefits?
[Free text]
If your project does involve patients, what are the main challenges?
[Free text]
Please share any other comments or questions you might have on the issue of patient involvement (Optional)
[Free text]

Two projects (PROactive, U-BIOPRED) provided specific feedback from patient representatives on their own initiative to questions 5-7. Due to inadvertent submissions, three responses were excluded

from the questionnaire (SUMMIT, BioVacSafe and PRO-active), all of which provided alternative submissions.

Results

The questionnaire was circulated among all active projects (n=40). In total 49 responses were received, with several projects providing more than one response as outlined in Table 2. All organisations except Pharmatrain provided at least one response.

Table 2 Responses per project

Project	# responses	Project	# responses
ABIRISK	1	MARCAR	1
BioVacSafe	1	MIP-DILI	1
BTCure	1	NEWMEDS	1
CHEM21	2	Onco Track	1
COMBACTE	1	Open PHACTS	1
COMPACT	1	ORBITO	1
DDMoRe	2	Pharma-Cog	1
DIRECT	1	Predect	1
EHR4CR	1	PreDiCT-TB	1
ELF	1	PRO-active	1
EMIF	1	PROTECT	1
EMTRAIN	2	Quic-Concept	1
eTOX	1	RAPP-ID	1
eTRIKS	2	SafeSciMET	1
Eu2P	1	SAFE-T	1
EU-AIMS	1	STEMBANCC	1
EUPATI	4	SUMMIT	3
EUROPAIN	1	TRANSLOCATION	1
IMIDIA	1	U-BIOPRED	1
K4DD	1	Pharmatrain	0
			Sum: 48

Respondents were asked to select from a list of options how patients were already involved in their projects (if applicable). The largest proportion of respondents (21 of 49, 43%) stated patients were subjects of the research, but a significant proportion (12 of 49, 24%) also stated patient organisations were part of the project consortium (Table 3). In a smaller proportion of cases, patients were members of an advisory or ethical board, or gave feedback on research protocols (all 6 of 49, 12%), and least commonly patients gave input to the research itself eg. in the form of designing patient-reported outcomes (5 of 49, 10%). Six respondents provided answers under the "other" response option (Table 4), two of which related to training of researchers and patients, and a further two highlighting involvement in dissemination activities. One project reported the use of patient involvement in the clinical trial setting, but with no direct involvement in the project.

Table 3 Current modes of patient involvement

If your project currently involves patients, how is this implemented?

Patients are subjects of the research (eg. clinical trials, providing samples)	21
Patient organisations are partners of the consortium	12
Patients (or patient org. representatives) are members of an advisory board	6
Patients (or patient org. representatives) are members of an ethical board	6
Patients give feedback on research protocols	6
Patients give input to the research itself (eg. design of patient-reported outcomes)	5

Table 4 Responses to how patients are involved in projects

Other responses to how patients are currently involved in projects
EMTRAIN aims at creating an Education and Training environment in Europe to develop and maintain the skills and competencies researchers and professionals need - to develop and make accessible new health care solutions which ultimately benefit patients.
Patient organisations are members of the steering committee and are active disseminators of the findings.
The collaboration between the education and training projects includes EUPATI.
No direct involvement. Integration of clinical data may occur, processes to fully define this are underway.
The patient organisation JDRF (Juvenile Diabetes Research Foundations) and IMIDIA have implemented common projects funded by JDRF.
Patients or their representatives provide input on communication and dissemination activities (flyers, symposia, website, feedback to participants), and are involved in valorisation strategies.

Responses from organisations not currently involving patients

For projects which did not have existing patient involvement, the following question sought to identify reasons for this. Table 5 shows that in most cases (12 of 49, 24%) patient involvement was not envisioned in the project scope. Three respondents (6%) also reported that there were no clear benefits of involving patients in the project or that there was no budget/personnel to achieve it. One respondent indicated it was difficult to locate patients interested in participating. Seven respondents provided responses under the "other" response option Table 6), most of which indicated that patients would be involved at a later stage of the project, though two respondents noted that patient involvement was not relevant for the type of project, eg. pre-clinical stage research.

Table 5 Reasons for lack of patient involvement

If your project does *not* currently involve patients, what are the reasons?	
Patient involvement was not envisioned within the project scope	12
No clear benefit from involving patients in the project	3
There is no budget/personnel allocation to achieve it	3
Project teams are not sure how to find interested patients	1
Project teams are not sure which processes patients should be involved in	0

Table 6 Other reasons for not currently involving patients in research projects

Other reasons for not currently involving patients
Project focused on pre-clinical research knowledge management of drug and target interactions. Anticipated use cases are early research focussed.

We will approach patient organisations later in the project for recruitment of assays and follow-up of successful screens.
We are in the process of considering patient engagement in future stages of the project
Clinical trials (2 phase II and 2 Phase III) have not started yet.
Originally we planned to include patient data from old clinical trials. There is no plan to directly involve patients in the project.
Not directly related to research.
Planned to take place in a later phase. A community meeting is planned for January and patients will be invited to that.

Respondents who indicated no present involvement of patients were then asked to indicate whether this was planned for the future. The majority of responses that were not "N/A" suggested involvement was not envisaged (12 of 21, 57%). Only three (14%) stated patient involvement was planned within the next year, and a further three stated it was under consideration. One respondent indicated involvement was planned later than one year from present (Table 7). Two "other" responses were given, describing a future IMI initiative to form a joint platform for patient involvement education and training (Table 8).

Table 7 Project plans for patient involvement

Planned patient involvement in the future	
Not envisaged	12
Patient involvement under consideration	3
Patient involvement planned within 1 year from present	3
Patient involvement planned later than 1 year from present	1

Table 8 Other responses to future patient involvement

Other responses to future patient involvement
All IMI Education & Training Project work together to form a joint platform in future, including EUPATI as the initiative representing patients and patient advocates.
The single platform for education and training will include EUPATI

Responses from projects currently involving patients

Those projects already implementing patient involvement were asked to report what the main benefits were. The full list of responses is given in the Appendix Table 10, and summarised in bullet points below. Apart from the reasons given below, many projects responded with the technical implications of their work – e.g. how using fresh tumour samples provide improved data, or how the information gathered from patients will help patients in the future due to new knowledge on biomarkers etc. These responses suggest that in some cases the perception of "patient involvement" still leans towards a model where patients are mainly seen to benefit from the results of the work, rather than as contributors to the work and how it is defined.

Benefits from involving patients were reported as follows:

- Validation of scientific objectives (e.g. of biomarkers) and being able to stratify benefit of research according to patient subgroups.
- Knowing what patients really want in terms of the next generation of therapies

- Gaining visibility outside the scientific community and ensuring appropriate and relevant communication with patients and society
- Providing samples and/or trial participants
- Input into what requirements patient organisations have for training and education
- Giving marginalised patient populations a voice
- Patient perspectives on benefit-risk evaluations and on the value of a project for public health
- Input on ethical considerations
- Feedback in the design of clinical trials
- Benefits to patients in terms of improving understanding of the R&D process, regulatory mechanisms etc. (in the context of EUPATI)
- Helping to adjust information (e.g. leaflets to patients) and procedures (eg. medical diagnostics that are particularly burdensome) to better suit patients
- Enabling patients to build networks in the field and add to their personal development
- Enabling patients to learn more about their own condition

Respondents from projects currently involving patients were then asked to indicate what the most significant challenges were. The full list of responses is given in the Appendix Table 11, while the general themes are summarised in bullet points below:

- Recruiting patients if there are no direct benefits, presence of risks (such as radiation) or the project places a large burden on patients in terms of examinations/diagnostics required
- Time requirements for often already busy patients or their representatives
- Ensuring representativeness over all patients when involving a patient group
- Language barriers, culture barriers and access to internet can be an issue
- Uncoupling involvement from personal experience
- Data confidentiality, ethical and legal considerations required when handling patient material across partners, or sharing sample material for research outside consortium.
- Diverging rules or other problems associated with involvement across countries or companies
- Trust between patients and others stakeholders (pharmaceutical industry)
- Involvement of vulnerable, marginalised, poor or uneducated patient groups
- Recruiting patients in a timely manner for clinical trials
- Logistical issues related to timely distribution of patient samples (eg. living tissue)
- Lack of resources for patient organisations to participate (unfunded) in grant application phase
- Few patient representatives available with the required skills and knowledge – those who are available are often already very busy and difficult to engage
- Patient organisations are unable to reclaim VAT on expenses according to IMI project and local tax authority rules, leading to a funding gap
- IMI funding rules may be incompatible with patient organisation structures which often rely on ad-hoc staffing, which can be ineligible for IMI funding
- Accounting issues when patient organisations receive funding from pharmaceutical companies, particularly if the organisation has a limit for their proportion of industry funding but do not know prospectively how large their grant from industry will be (eg. if they are part of the consortium)
- Perceived significant extent of private industry involvement in IMI, due to presence of industry partner logo's in brochures (though IMI is legally an EC/EFPIA construct). Could dissuade patients to participate due to perceived excessive industry influence.

- Identifying project partners who really support patient involvement as more than a superficial exercise
- Patient's facing difficulties balancing work, family and having an illness, on top of contributing to a project and meeting deadlines.

General observations from respondents

As the final question, respondents were asked to share any additional comments they might have on the issue patient involvement (Table 9). Some of the main points made are listed below:

- It is difficult to ensure representativeness of the whole patient population when only a few patients are involved in the project. This is particularly an issue when patients are involved in defining the research questions.
- Some activities would be of great benefit to patients, for example education about medicines usage and outcomes, but there is no budget support for this.
- It is not always easy to involve external stakeholders within the same area – for example, PREDECT was not successful in enlisting the support of EORTC.
- Awareness should be raised among researchers that patients and study participants are more than merely patients, carers or diseases sufferers. Education activities for researchers could help spread understanding of how patients can contribute to research.

Taking into account the information given by respondents, it was concluded that 24 projects already implemented some form of patient involvement, while 15 projects did not (Figure 1). A breakdown of which projects currently involve patients and the ways in which they do so are given in the Appendix Table 12.

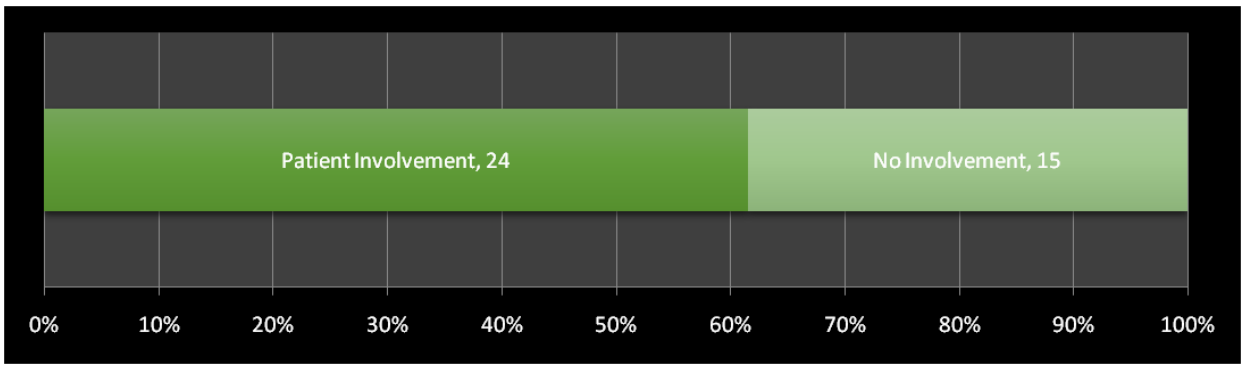

Figure 1 Proportion of IMI projects with existing patient involvement

Table 9 Free text comments from respondents

Comments from respondents
Projects can partner with patients, but I'm not convinced patients should drive research questions, UNLESS one is sure the whole spectrum of patients is represented (seldomly the case when including patients, or even patient associations). I think the PROactive project has found a healthy balance here with respect for all stakeholders in research (including patients).
EUPATI is a critical stepping stone in collaboration between patient groups and the pharma industry. We can then build on this as we expand into other areas of patient involvement in IMI-2.
Patient involvement helps to keep the research in focus.
In hindsight, it might have made sense to involve patient organisations in the project to improve visibility and ease recruitment, e.g. of patients at risk of developing serious drug side effects.
Within the ENSO extension of eTox, some pre-existing clinical data will be gathered and associated with animal toxicology data; however, there will be no new data generated, hence no involvement of patients.
Education of patients about medicines usage and outcome would be of great benefit but we do not have the budget to develop this.
PREDECT needs to have patient support groups informed of our work. Support for cancer is disparate. We tried, without success, to have EORTC help us.
Patient involvement in IMI projects is very important. We would like to congratulate IMI for having patient involvement in research on IMI's agenda, and for making a project like EUPATI as a public private partnership within the neutral platform of IMI possible! Given the public scrutiny that a PPP between industry and patient organisations will have, IMI is a great framework to strengthen patient involvement in R&D as well as building PPPs.
1) Patients should also be involved in defining the research question rather than only commenting on it. *2) PROactive is a good example for active and real patient involvement in research, impacting on the project and other projects. Also the major impact patients made on the results (development of a patient reported outcome instrument) as being "subject" in the study should be mentioned.* *3) Patients or their representatives can help in valorisation of research results, in connecting results with patients' lives.* *4) It is really important that there is a good spread of patient representatives – both from the various participating countries and in terms of age and ethnicity. Language differences should be elaborated on. And the burden of the disease for travel should be taken into account when organising meetings.* *5) The questions and issues patients advise on, can be highly theoretical and complex. Therefore, it is often difficult for regular patient members in the boards to discuss with or get more information on that topic from their own patient organisation. A specific group of patient advisors within an internal advisory board may work even better;* *6) Awareness should be raised among researchers that patients and study participants are more than a patient, parent or their disease.* *7) Participation or active involvement is a challenge in different ways for participants. This should be taken into account by host organisations.* *8) Apart from emphasis on patient partnership as a structural element of research and healthcare, sufficient budget and coordinating support needs to be provided as well.* *9) A crash course for researchers (and other partners in projects) on what patient involvement is, seems to be needed. Patient involvement not only applies to clinical research but can also be worthwhile in other types of research and its procedures (incl. ethics). This should be implemented as a structural learning activity in all IMI projects.*
1) Patients should also be involved in defining the research question rather than only commenting on it. *2) U-BIOPRED is a good example for active and real patient involvement in research, impacting on the project and other projects.* *3) Patients or their representatives can help in valorisation of research results, in connecting results with patients' lives.*

4) It is really important that there is a good spread of patient representatives – both from the various participating countries and in terms of age and ethnicity. Language differences should be elaborated on.
5) Awareness should be raised among researchers that patients and study participants are more than a patient, parent or their disease.
6) Participation or active involvement is a challenge in different ways for participants. This should be taken into account by host organisations.
7) Apart from emphasis on patient partnership as a structural element of research and healthcare, sufficient budget and coordinating support needs to be provided as well.
8) A crash course for researchers (and other partners in projects) on what patient involvement is, seems to be needed. Patient involvement not only applies to clinical research but can also be worthwhile in other types of research and its procedures (incl. ethics). This should be implemented as a structural learning activity in all IMI projects.

*Statements which are **in italic** are reported to be from patient project participants.*

Conclusions

According to this brief survey, approximately 2/3^{rds} of current IMI projects already include some form of patient participation, while most of the remaining projects do not envisage involving patients in the future. The majority of patient involvement is in the form of clinical trials or other forms or research where patients provide samples as a direct input. The second most common form of involvement is to involve patient organisations in the project consortium.

The most common reason for not involving patients in research was that this was not envisaged in the project scope, while only a few respondents indicated there was no clear benefit to involving patients. The majority of projects not currently involving patients also did not plan to do so in the future.

Diverse reasons were given in response to the benefits of involving patients, mostly relating to the perspectives patients can provide on which research objectives are important to patients; how to disseminate results outside the scientific community; how patients perceive particular risks and benefits; and empowering patients to build networks and learn more about their condition. The challenges reported are too numerous to accurately reproduce here, but among other things included the burden (financial, time, energy) on patients; handling logistical and ethical requirements associated with data confidentiality, ethical approval and legal considerations especially in an international contexts; overcoming barriers of language and technical terms; and ensuring representativeness when including a relatively small sample of patients to represent the views of all others.

From the concerns raised among participants in this survey, a number of recommendations can be made to facilitate future patient involvement:

- Support involvement of patients in the early stages (inception phase, consortium building, scoping) to ensure patient participation is an integrated part of the project with adequate funding
- Map out for different types of projects where patient input is most appropriate and beneficial – for example, in clinical trials or biomarker validation studies with rigid protocols, patients do not have much opportunity to provide input (except as “subjects”) once the study protocol has been defined.
- Provide training for researchers to understand the potential benefits of involving patients in their work and in which areas this can occur. This may be particularly valuable for projects that currently see patients only as “subjects” either as participants in trials or as providing sample material.
- Ensure the financial and accounting barriers to patient participation are limited, including understanding the limitations patient organisations face with regard to eligibility of expenses (VAT, ad hoc staff/consultants etc.)[2]
- Ensure that non-patient project partners are aware of the potential special needs of patients, including limitations in travelling (when organising meetings)
- In areas where expertise among patients is lacking, provide training and support to patients to adequately equip them to contribute meaningfully to research projects.

[2] Many of these challenges are detailed in Table 11 (Appendix), two comments marked with ***

Appendix: Project partners invited to participate

ABIRISK
BioVacSafe
BTCure
CHEM21
COMBACTE
COMPACT
DDMoRe
DIRECT
EHR4CR
ELF
EMIF
EMTRAIN
eTOX
eTRIKS
EU-AIMS
Eu2P
EUPATI
EUROPAIN
IMIDIA
K4DD
MARCAR
MIP-DILI
NEWMEDS
Onco Track
Open PHACTS
ORBITO
Pharma-Cog
Pharmatrain
Predect
PreDiCT-TB
PRO-active
PROTECT
Quic-Concept
RAPP-ID
SAFE-T
SafeSciMET
STEMBANCC
SUMMIT
TRANSLOCATION
U-BIOPRED
Total: 40

Appendix: Supplementary data

Table 10 Main benefits of involving patients

If your project does involve patients, what are the main benefits?
Patients are accrued in the clinical trials to qualify imaging biomarkers (the main objective of the project)
Patient insight into next generation therapies. "What do patients really want"
Inclusion of a relevant and crucial stakeholder in the design of Patient Reported Outcomes (PROs). Dissemination of findings directly to patients. Translation to lay public. Visibility outside the scientific community. Pre-screening of protocols prior to local EC submission.
Reusing de-identified patient information as part of the partner Hospitals Electronic Health Records (EHRs) is the core of the project.
Ensuring our research and communication about this research is relevant for patients and society at large
EU-AIMS involves two large-scale studies: the infants at risk study (including about 300 babies at risk for autism and 100 low-risk "control" babies) and the accelerated longitudinal study, including approximately 420 participants with autism spectrum disorder from 6-30 years and 300 control volunteers. Participants (and parents, caregivers) are made aware in the study information sheet and consent form that the research does not have any direct benefits for themselves and that it is not intended to replace a clinical assessment. However, the overall study goals are to identify biological risk markers to a) aid in more reliable and earlier clinical diagnosis, and b) develop effective treatments for core symptoms of ASD.
Assessment of anti-drug antibodies using standardised assay methods. Opportunity to gather information regarding kinetics of anti-drug antibodies and model approaches to reduce adverse events. Opportunity to identify key biomarkers to predict adverse events and to stratify patients for maximal drug benefit.
The basis of our (educational) project is Translational Drug Safety Sciences, i.e. drug safety from molecule to patient.
Provision of patient samples that are essential for various aspects of the scientific programme of work for the MIP-DILI project
Input from patient organisations into the education and training needs of patient ambassadors and patients
Current drug discovery programmes are based on biological models that do not reflect patient populations. Promising chemicals can be identified in animal models or current cell culture systems, but they frequently fail in clinical settings, through poor efficacy or unexpected toxicity. Drug discovery based on human models representative of the patient population would represent a great improvement. However it is generally not possible to have access to sufficient relevant tissue for high throughput experimentation. Stem cell based disease modelling is a solution whereby patient tissue is reprogrammed to pluripotency and differentiated into a cell type closely resembling the tissue bearing the brunt of disease. This allows findings to be related directly to actual genetics and clinical histories of those suffering from diseases studied.
Having a voice of a marginalised, hard to reach population helps define that we are on the right way to getting them what they need but cannot ask for.
Getting patients' perspectives on: added value of some aspects of the project for public health; how to best communicate about the project; patients' perspectives in benefit-risk evaluations; recruitment of patients through representatives of patients' association.
Visibility of the project and the research. Ongoing possible interactions during the yearly conference.
We are generating data on new safety biomarkers across a range of different patient populations. These new markers are expected to significantly improve safety of new and established medicines for patients.

Not applicable yet, although we envisage that it will help provide feedback on some of the ethical issues that arise within the project, and could be useful for designing clinical studies in the later stages of the project.
Patients are subjects in clinical baseline and follow-up investigations on cardiovascular and retinopathy diabetic complications. The collected information will form a database on an extremely well-characterised case-control cohort, which connects the genetics, biomarker and imaging work packages in the project.
Molecular analysis is being conducted on fresh tumour samples from patients with colon cancer. The use of fresh tissue is essential to ensure high quality sequencing data and is also necessary for the generation of xenograft tumour models. The data collected in this project do not benefit the tissue donors directly.
Human tumour material (all with Ethical Approval) for preparation of tissue slices and engraftment to mice.
Sample collection: optimisation of protocols on real samples, developed tests would otherwise be far less useful in clinical practice. Use of diagnostics: tests under development expected in future clinical trials.
Patients have a unique and complementary insight and expertise that should be included in any project addressing patients directly or indirectly, which is the case for most projects connected to medicines R&D. For many years, pan-European patient organisations like European Patients' Forum, EURORDIS, EGAN and EATG have built key expertise in engaging with all stakeholders on medicines R&D, and there are many more pan-European networks of patient organisations in specific disease areas. Their knowledge is crucial for an educational project like EUPATI. The core of EUPATI is about empowering patients on medicines R&D. The development of medicines is a highly regulated, costly, long and complex process that is largely unknown to the general public. In an era of growing demand and emphasis on both quality and sustainability of healthcare, better-informed patients and carers have a key role to play in the implementation of patient-centred clinical research strategies and approval processes, access to treatments and treatment optimisation approaches. Patients are becoming more actively engaged in the many processes involved in the development of new treatments - from advising on protocols and informed consent and ethical review to participation in clinical trials - the overall medicines development process, marketing authorizations and healthcare policies. The EUPATI consortium project was initiated and is led by major patient umbrella organisations, making sure that the material that EUPATI will develop is patient-centric and meets the real needs of patients.
Including the perspective of the patients facilitates the dialogue with other stakeholders and serves to identify real needs that have to be addressed in treatment developments.
Training patients can obviously only be done if patients are involved in the definition and preparation of the training programme and content. Participation of patients is a success factor for this specific project.
Patients are involved through their participation in clinical studies and providing samples for analysis. Through this support key research objectives of the project are enabled.
The concept that an integrated set of clinical data will provide more predictive power (eg. for clinical trial design) than smaller sets.
JDRF is very interest in this PPP.
Participation of patients or their representatives in PROactive meant: *1) no tokenism but true participation;* *2) giving meaning to patient involvement in research;* *3) providing a way to patients to have a say in the project (from the beginning to the end of the project);* *4) ability to provide advice from patient's perspective and getting feedback at an equal level as scientists and other professionals in the boards;* *5) For the patient organisations it meant a means to be involved as a partner in the project from the*

beginning to the end, to contribute to the changes from the patient's perspective in the presubmission stage of the project proposal, to collaborate with academics, health care organisations, pharmaceutical organisations and peer patient organisations in an equal, rather open and non-excluding way, and contribute to the project throughout including offering ways to improve the substudies. Also for patient organisations it is a challenge to get the project at the level of a "model project" regarding participatory research.
Participation of patients or their representatives in U-BIOPRED meant: *1) no tokenism but true participation;* *2) giving meaning to patient involvement in research;* *3) providing a way to patients to have a say in the project (from the beginning to the end of the project);* *4) ability to provide advice from patient's perspective and getting feedback;* *5) feeling empowered using own experience while rights of pts was monitored and taken, and hence participation made a difference to the project and participants (e.g. leaflets in lay language, adjustment of burdening bronchoscopy protocol);* *6) meeting and sharing knowledge and experiences with other patient representatives from all over Europe was stimulating and contributed to personal development for pts wishing to go on to similar roles representing patients;* *7) a way to contribute to research and giving back to society;* *8) a means to learn about one's own condition;* *9) For the patient organisations it meant a means to be involved as a partner in the project from the beginning to the end, to contribute to the changes from the patient's perspective in the pre-submission stage of the project proposal, to collaborate with academics, health care organisations, pharmaceutical organisations and peer patient organisations in an equal, rather open and non-excluding way, and contribute to the project throughout including offering ways to improve the substudies. Also for patient organisations it is a challenge to get the project at the level of a "model project" regarding 4P medicine.*
Ensuring direct interaction, formalise engagement and dialogue with patients through their representative organisations

*Statements that are **in italic** are reported to be feedback from patient project participants.*

Table 11 Challenges of involving patients

If your project does involve patients, what are the main challenges?
The willingness of patients to join the study. Patients will not have a direct benefit from the trials, because the results will only be used in future research. To qualify imaging biomarkers, patients need to spend their time, and be exposed to radiation. Furthermore, they will receive additional biopsy to evaluate the response, but this is not the routine practice.
Collecting views of many patients. Usually a few patient representatives contribute.
Individual patient: language barrier, jargon, uncoupling from personal experience is difficult but necessary for the project.
Creating trust and understanding across the organisation in partner hospitals.
The study protocol is complex and involves a number of logistic and ethical considerations: This includes length of the study protocol and burden for participants including comprehensive phenotypic characterisation, cognitive testing, eye-tracking, EEG, structural and functional MRI and biological samples (blood, urine, saliva, hair). Data protection/management: We have devised a secure system to acquire, transfer and analyse data to protect participant confidentiality. Our project involves about 100 volunteers with moderate learning difficulties. Challenges include assessment of these vulnerable volunteers (including MRI scan, blood sample) building on previous expertise with a similar volunteer group.

Multi-country consortium, many different rules across countries and companies
Translation from *in vitro* - *in vivo* and animal - human. Crucial to understand mechanisms underlying inter-individual differences.
Ensuring appropriate ethical and legal frameworks are in place for storage, use and sharing of the samples between partners in such a large multi-partner consortium, which can be extremely time-consuming.
Building trust between the pharma industry and patient groups.
Consent and involvement of vulnerable populations and patient withdrawal.
Marginalised, poor, and uneducated patients are difficult to reach and concepts hard to get across.
Patients' representatives are often involved in a large number of activities and may not have enough time to perform field work. There is a need to explain the project in lay terms and clearly convey the project's objectives.
Recruitment - Alzheimer's Disease (AD) is a very competitive field; early onset AD is not easily diagnosed, some of the basic research may not easily be linked to the patient's everyday challenges.
Recruiting a sufficient number of patients across different populations. More flexible use of samples (e.g. use of samples after end of the project, sharing samples with collaborators outside the consortium, need to re-consent patients having donated samples in the past).
Not applicable yet, but one of the major challenges we are facing in designing how they will be involved stems from coordinating engagement across the different countries involved in the project.
Patients have been asked to participate in the investigations, which involved more samples and longer interviews than a regular clinical investigation would have taken. The extensive data collection was in order to be able to study the question from different perspectives. Recruitment has not always moved forward as fast as we had hoped.
Major logistical challenge to ensure rapid distribution of living tissues to all involved participants.
No particular challenges. Requires close collaboration with clinicians. So far, so good.
Sample collection: logistics, but well set up and once ongoing, very few problems. Clinical trials: alignment with trial's timelines
*** The main challenges are usually resources. Even though IMI projects are fully funded, only a relatively small number of patient advocates have the right knowledge, skills and organisational resources to engage (in an unfunded way) during the grant application phase as well as (on a funded basis) during the project. These patient advocates with the right knowledge and skillset are usually utilised to the limit already, so it is quite challenging to have their time commitment which is required to engage in a quite demanding consortium project, independent of the availability of funding. Additionally, there are financial challenges which are connected to the IMI funding rules. First of all, patient organisations are usually exempt from VAT, so they cannot reclaim VAT. VAT is an ineligible cost for third party invoices according to the IMI rules, while VAT-exempt NGOs cannot reclaim VAT from their tax authorities. Patient organisations usually do not have the financial reserves to cross-subsidize this ~20% VAT funding gap, which might be an inhibitor for patient organisations to engage in IMI projects. In addition, many patient organisations operate without permanent staff but with volunteers or project-based contractors (which may or may not be patients themselves), in order to reduce financial exposure and commitments. Their "virtual organisations" usually do not have brick and mortar offices, but a virtual team of strong, well-educated individuals distributed all over Europe. The IMI funding rules are very restrictive on subcontracting and using in-house contractors, which may make those "permanent contractors" of patient organisations ineligible to work on IMI projects. Many strong and powerful patient organisations, especially internationally operating networks, have only very little permanent staff, but large virtual teams that could provide valuable contributions to IMI projects, if their costs were eligible.

Patient participation often depends on their knowledge of R&D processes. Patients have different knowledge levels and capacity which needs to be improved.
*** The IMI rules, in particular the financial rules, are not adapted to patient organisations' accounting rules and, to some extent, put patient organisations at risk. For example, when there is a cash pot from industry partners, as there is no budget planning when this cash pot will be paid, and which amount will be transferred, the patient organisation (in particular for a patient organisation which is leading the consortium) cannot forecast revenues. Patient organisations need to have clear rules on the % of their revenues that can consist of pharmaceutical funding, and without clear insight on how much will be paid and when (sometimes very near the end of the year-account end), this % cannot be properly respected. Another difficulty lies in the communication with industry partners in the project. Legally, IMI is a construct between the European Commission and EFPIA. Yet, in project brochures the logo of each industry partner appears, not just the EC and EFPIA logos. Even though this is a public-private partnership, a large number of industry logo can be detrimental for the project success, when for example patients who would be interested in participating in training become hesitant when they see the number of industry logos and question the training content independence.
Ensuring conformity with regulatory, ethical and data protection provisions at the European level and beyond. Implementing database protection protocols and a reliable data and sample exchange framework.
To ensure that the potential benefits are important enough to deal with the large hurdles involved in integrating patient level data.
1) identifying project partners who really believe and support patient partnership in all aspects of research (saying yes to patient involvement is not enough); *2) as the questions and issues the boards advise on are highly theoretical and complex, it is often difficult for regular patient members in the boards to discuss with or get more information on that topic from their own patient organisation. A specific group of patient advisors within an Ethics Board may work even better;* *3) from the work package leader's point of view: dealing with often tight timelines during review or advice procedures versus the voluntary work by and battling disease of patient (representatives). It really needs commitment and devotion of the work package partners to keep everyone on board and focussed on the project knowing that the patients' work is voluntary;* *4) communication: people need lay and clear language. This is what patients can advise on and do in PROactive* *5) the patient's perspective should be integrated into research and patients should be seen as partners automatically by researchers. Hence, researchers should not need to be reminded of this each and every time. The participatory models (e.g. Involve UK; Lung Foundation Netherlands; Value+ by EPF; P. Kirby et al, Handbook building a culture of participation, 2003) should be integrated whether it is patients or citizens for their engagement;* *6) in general: the commitment as the duration of a project can be burdening and tasks need to be fitted around other things (e.g. doing teleconferences amidst busy life). Keeping patients involved is challenging and may also affect consistency of the work;* *7) visibility of patient involvement: organising regular meetings with patients or their representatives adds to their visibility and relationship with key players in the project;* *8) getting a good patient representation over Europe - language, internet access and cultural habits and disease-related travel issues (e.g. oxygen) are main barriers;* *9) for patient organisations it also meant a challenge to continue being involved amongst the many other workflows. Not each and every employee is convinced that a national patient organisation should be involved and working at the European level, despite all communication. The latter is something that is of less importance as the project progresses and shows relevant results.*

The main challenges for patient involvement in research are: *1) identifying project partners who really believe and support patient partnership in all aspects of research (saying yes to patient involvement is not enough);* *2) the actual participation. This deals with integration with normal life (job, family) on top of battling disease. But also feeling guilty when deadlines could not be met or questions could not be answered due to time or disease constraints.* *3) from the work package leader's point of view: dealing with often tight timelines during review or advice procedures versus the voluntary work by and battling disease of patient (representatives). It really needs commitment and devotion of the work package partners to keep everyone on board and focussed on the project knowing that the patients' work is voluntary;* *4) in general: unwillingness to assist or know about disease can be challenging to involve patients in research as a study participant ("subject" which is the lowest level of involvement);* *5) communication: people need lay and clear language. This is what patients can advise on and constantly do in this U-BIOPRED;* *6) tokenism is avoidable. Patients want to make a difference, to be taken seriously, to impact via contribution. Therefore this needs (structurally) a strong project manager on this which we have in U-BIOPRED. However, patients or their representatives can still feel unequal and inadequate to their task even in U-BIOPRED. In addition, the patient's perspective should be integrated into research and patients should be seen as partners automatically by researchers. Hence, researchers should not need to be reminded of this each and every time. The participatory models (e.g. Involve UK; Lung Foundation Netherlands; Value+ by EPF; P. Kirby et al, Handbook building a culture of participation, 2003) should be integrated whether it is patients or citizens for their engagement;* *7) patient involvement can also be achieved in local institutions, not only at the project level. However, there are large differences in getting this done.* *8) in general: the commitment as the duration of a project can be burdening and tasks need to be fitted around other things (e.g. doing teleconferences amidst busy life). Keeping patients involved is challenging and may also affect consistency of the work;* *9) some test are not so enjoyable as they can affect the condition of the disease;* *10) visibility of patient involvement: organising regular meetings with patients or their representatives adds to their visibility and relationship with key players in the project;* *11) getting a good patient representation over Europe - language, internet access and cultural habits are main barriers;* *12) for patient organisations (most of them are rather small) it also meant a challenge to continue being involved amongst the many other workflows. Not each and every employee is convinced that a national patient organisation should be involved and working at the European level, despite all communication. The latter is something that is of less importance as the project progresses and shows relevant results.*
To provide continuous input on the personal data protection principles and their applicability (transposition).To create a permanent forum for dialogue on the issues that affect patients the most.

*Statements which are **in italic** represent input reported to be from patient project participants.*

Appendix: Patient involvement by project

Table 12 Responses from individual projects on patient involvement

Responses from individual projects on patient involvement		
Project	**PI**	**Type of involvement**
ABIRISK	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples)
BioVacSafe	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples)
BTCure	Yes	Patient organisations are partners of the consortium
CHEM21	No	N/A
COMBACTE	No	N/A
COMPACT	No	N/A
DDMoRe	No	N/A
DIRECT	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
EHR4CR	Yes	Patients (or patient org. representatives) are members of an ethical board, Patient organisations are partners of the consortium
ELF	No	N/A
EMIF	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples),Patient organisations are partners of the consortium
EMTRAIN	No	EMTRAIN aims at creating an Education and Training environment in Europe to develop and maintain the skills and competencies researchers and professionals need
eTOX	No	N/A
eTRIKS	Yes	Patients (or patient org. representatives) are members of an advisory board
Eu2P	No	N/A
EU-AIMS	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples),Patients give feedback on research protocols, Patients (or patient org. representatives) are members of an ethical board, Patient organisations are partners of the consortium
EUPATI	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples),Patients give input to the research itself (e.g. design of patient-reported outcomes),Patients give feedback on research protocols, Patients (or patient org. representatives) are members of an ethical board, Patients (or patient org. representatives) are members of an advisory board, Patient organisations are partners of the consortium
EUROPAIN	No	N/A
IMIDIA	Yes	The patient organization JDRF (Juvenile Diabetes Research Foundations) and IMIDIA have implemented common projects funded by JDRF.
K4DD	No	N/A
MARCAR	No	N/A
MIP-DILI	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples)
NEWMEDS	No	N/A
Onco Track	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples)
Open PHACTS	No	N/A
ORBITO	No	N/A
Pharma-Cog	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples),Patient organisations are partners of the consortium
Predect	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples)

PreDiCT-TB	Yes	Patients (or patient org. representatives) are members of an advisory board
PRO-active	Yes	Patient organizations member of steering committee. Active disseminators of the findings, Patients are subjects of the research (e.g. clinical trials, providing samples),Patients give input to the research itself (e.g. design of patient-reported outcomes),Patients give feedback on research protocols, Patients (or patient org. representatives) are members of an ethical board, Patient organisations are partners of the consortium
PROTECT	Yes	Patients are subjects of the research (e.g. clinical trials, providing samples),Patients give input to the research itself (e.g. design of patient-reported outcomes),Patients give feedback on research protocols, Patients (or patient org. representatives) are members of an advisory board,Patient organisations are partners of the consortium
Quic-Concept	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
RAPP-ID	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
SafeSciMET	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
SAFE-T	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
STEMBANCC	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
SUMMIT	Yes	Patients are subjects of the research (eg. clinical trials, providing samples)
TRANSLOCATION	No	No direct involvement. Integration of clinical data may occur, processes to fully define this are underway/A
U-BIOPRED	Yes	patients or their representatives provide input on communication and dissemination activities (flyers, symposia, website, feedback to participants), and are involved in valorisation strategies. Patients are subjects of the research (e.g. clinical trials, providing samples). Patients give input to the research itself (e.g. design of patient-reported outcomes). Patients give feedback on research protocols. Patients (or patient org. representatives) are members of an ethical board. Patients (or patient org. representatives) are members of an advisory board. Patient organisations are partners of the consortium

PI: Patient Involvement