share and move to face nasty bugs

WP3 ACTION PLAN DEFINITION

D3.2 ROADMAP TO OPEN AND RESPONSIBLE RESEARCH AND INNOVATION IN PANDEMICS

ASSET Project • Grant Agreement N°612236

ASSET

Action plan on SiS related issues in Epidemics And Total Pandemics

7th RTD framework programme

Theme: [SiS.2013.1.2-1 Sis.2013.1.2-1]

Responsible partner: **LYONBIOPOLE**

Contributing partners: **IPRI**

Nature: **Report**

Dissemination: **PU**

Contractual delivery date: **2015-07-31 (m18)**

Submission Date: **2016-01-20**

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 612236

DOCUMENT MANAGEMENT

PROJECT FULL TITLE	**Action plan on SiS related issues in Epidemics And Total Pandemics**
PROJECT ACRONYM	**ASSET**
	Coordination and Support Action: project funded under Theme SiS.2013.1.2 "Mobilisation and Mutual Learning (MML) Action Plans"
GRANT AGREEMENT	**612236**
STARTING DATE	**01/01/2014**
DURATION	**48 months**

D3.2 Roadmap to Open and Responsible Research and Innovation in Pandemics

Task: 3.2

Leader: LYONBIOPOLE – Other contributors: IPRI

History of changes:

Vn	Status	Date	Organisation / Person responsible	Reason for Change
V1	Draft	26/11/2015	LYONBIOPOLE – Mitra SAADATIAN ELAHI, Elodie VIDAL IPRI- Alberto d'ONOFRIO	
Vf	Final	22/01/2016	LYONBIOPOLE – Mitra SAADATIAN ELAHI, Elodie VIDAL IPRI- Alberto d'ONOFRIO	

Table of Contents

Description of the Task 3.2

As defined in the Description Of Work (DOW) of the ASSET project: *"Task 3.2 will design a roadmap towards responsible and open, citizens-driven, research and innovation on vaccines and antiviral drugs. This roadmap will complement the strategic plan developed in T3.1. Open innovation in pandemic related research requires initial investments because it demands a shift in the traditional, technology centered, approach. In T3.2 we will review existing experiences of user driven innovation in the health and pharmaceutical sector. This task will answer the question to what extent, and according to which conditions, user-driven innovation is possible in the field of research and innovation on epidemic infectious diseases prevention and response. Several "users" might be concerned by innovative products developed by industrials such as diagnostic tools, therapeutic products; clinicians and doctors are the main users, patients are the beneficiaries of the innovation products. Thanks to this task, existing initiatives and projects related to the involvement of "users" in epidemic infectious diseases prevention and response will be referenced. Projects could concern diagnostic approach, prevention actions, vaccination campaign, etc. Other type of projects in other life sciences applications such as the use of ICT in health will be analysed in order to identify potential synergies and transferability to the epidemic and pandemic issues. From these listed existing initiatives, a roadmap of recommendations targeted to industrial, academic and institutional stakeholders will be drafted. The outcomes of this task will partly feed the public consultation (WP4) and will provide the background for WP5, T5.2 Best Practice Platform and Stakeholder Portal."*

For the sake of the completeness, we also report here the DOW of the Task 3.1 ("Strategic Plan") of ASSET Project: *"T3.1 will be devoted to design the action plan that addresses the main issues enlightened in WP2. Through a series of plenary and sectorial virtual Joint Design Workshops (JADs) led by the leader, we will define vision and mission of the action plan. We will set goals, decision making processes, and will map an explicit path between the present and a vision of the future. The strategic plan will include a multi-year view of objectives and strategies for the accomplishment of goals, and criteria for assessing results. We will design the process of incorporation of Science in Society (SiS) issues in pandemic policies, discussing strategic and critical decisions, and identifying relevant stakeholders affected by these decisions. The strategic plan will chiefly address SiS issues, it will be sided by the Research and Innovation Roadmap developed in T3.2.".*

Background

The availability of information from several sources has shifted the traditional science/technology centered approach to a new one where the demands of patients and their relatives are central and they become active partners in the decision-making process with regard to their health. As a consequence, the success of new therapies and public health interventions is increasingly dependent on how the needs of users are taken into the account. The main health users are patients and their relatives and they ought to have the possibility to provide adequate information that would allow a better understanding of all medical process: understanding the etiology of the disease, formulating a prognosis, success (or failure) of treatments. Moreover, patients ought to be central in individuating the difficulties they encountered when using therapeutics, vaccines, and medical devices.

Until recently, input from patients was listened but not always taken into account. A more active participation of patients and structured interaction between main health users and health care professionals (HCPs) in charge of research and development (R&D) could certainly render R&D more efficient and effective.

The objective of task T3.2 of the ASSET project is to design a roadmap towards responsible and open, citizens-driven research and innovation on vaccines and antiviral drugs. It is supposed to answer the question to what extent, and according to which conditions, user innovation is possible in the field of research and innovation on epidemic infectious diseases prevention and response. Open innovation in pandemic related research requires initial investments because it demands a shift in the traditional technology centered approach.

The general aim of this report is to complement the Strategic Plan developed in T3.1 and contribute to the background for the Task 5.2 « Best Practice Platform and Stakeholder Portal ».

In this report, we will first review general concepts and methodological approaches that have been employed to set-up and/or improve interactions between users and HCPs. Existing experiences of user involvement in the health and pharmaceutical sector will be then revised to assess to what extent and according to which conditions, user-driven innovation is possible. Their challenges and success will be discussed to try to construct a roadmap of recommendation to open and responsible research and innovation in pandemics.

Throughout this manuscript and for ease of reference, we will use the term Patient and Public Involvement (PPI) to refer to patients, care givers, health researchers and patient organization. PPI is defined, following the lines of the INVOLVE report of UK NHS [Hayes 2012], as **a research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them.** PPI represents an ideological shift within which patients and their representatives have a formal and recognized role to effectively get involved in researches that concern their health-related issues [Mitchell 2015].

1. Research strategy and outcome

We did a comprehensive search in the MEDLINE, ISIS Web of Science and Google Scholar databases without limiting time and using the following key words: innovation, pharmaceutical, user-driven, patients organization (or association), scientist-patient partnership, public involvement in scientific or biomedical research, and many others (e.g. synonyms of the above mentioned words, and also disease-specific words). We also undertook hand-searching of reference lists of relevant studies and reviews.

In parallel, we prepared a questionnaire (See Annex 1) in order to collect examples of involving users in the process of research and development of drugs and devices. The objective was to gather concrete cases of PPI in health sector that would allow identifying and establishing best practices on when and how to involve users in health-related R&D, and in particular in the context of pandemics (diagnostic, vaccines, drugs).

The questionnaire has been sent to a list of up to 25 individuals working in pharmaceutical industry (mainly vaccine firms), academy, and more than 70 patients' organizations and federations of patients associations.

Overall, a large majority of the published literature was based on why PPI is important more than on specific and detailed practical examples of PPI that could lead to innovation in the field of biomedical research. In particular, we could not find detailed papers on PPI in vaccine development.

Participation rate to the questionnaire was very low: we received back only four filled questionnaires despite several reminders sent to each individual. In most cases, pharmaceutical industries did not accept to participate stating that their partnerships and collaborations with doctors, patient's co-researchers, collaborators, etc. are confidential and very sensitive. In one case we received an interesting *written* informal reply, which we will discuss in the conclusions of this report.

Taking into the account the above illustrated problems, this report will be more oriented in individuating methodological issues to facilitate PPI in biomedical research.

2. PPI: General concepts and methodological issues

2.1 General concepts

The role of patients in health has already been acknowledged by the epidemiologist Richard Doll (1974) who advocated that evaluation of health care services should be based on their clinical effectiveness, economical efficiency and social acceptability. While the first two points are very well recognized, social acceptability or patient-based evidence has received less attention [Staniszewska 2014]. The paradigm of resourceful patient simply implies that a respect and consideration is due to the patient's suggestions and rights the ability to provide information, but only in clinical practice. Recently, it emerged a more profound concept: the idea that patients (also named "service users" by some authors) have the full capacity and right to be directly involved in biomedical research and in all of its phases. In other words, it emerged the concept of "patients as co-researchers", as defined by van der Geest [van der Geest 2009]. Of course, when we use the term "patients", we mean also and mainly the associations of patients, as well as – at least in some cases - patients' families and care givers. It is noteworthy however to stress that "patients as co-researchers" does NOT mean that public enters in molecular biology laboratories or write together with bio-mathematicians/biophysicists/bio-informaticians equations and/or algorithms. In other words and following again van der Geest [van der Geest 2009], engagement and direct involvement of patients as co-researchers do not imply their control in all phases of the research.

The level of patient's participation can range from tokenism to joint decision making by professionals and patients [Elberse 2011]. The degree of PPI in innovation and biomedical R&D with an increasing level of patient's power can, in the ideal case, be defined as follow [Caron-Flinterman 2015]:

- Consultation: Patients are consulted for their needs. A critical issue is however that there is no guarantee that their input is taken into consideration in research agendas.
- Participation: Patients are involved in the research agenda in a more formal way but again the final decision belongs to HCPs.
- Partnership with real power-sharing between HCPs and patients-partners, and where there are genuine negotiations between patients and HCPs.
- Delegated power: Patients have a dominant position in decision-making process.
- Patient control: Decision-making in biomedical research belongs to patients.

What does it mean PPI in biomedical research (also beyond the strict limits of research on pandemics and epidemics)? Of course, absolute patient control in biomedical research is not realistic. To our understanding, the emerging idea of PPI corresponds to point 3, i.e. real partnership between patients and HCPs. This can occur at different stages of the multistep process of innovation and biomedical R&D. The main questions are "***how"*** and "***when"*** patients should be involved and "***what"*** should be their level of involvement in different phases of R&D process i.e. 1) preparation of research topics/questions; 2) design and execution; 3) analysis; 4) communication of results/policy making decisions.

The "***how"*** side of PPI refers to the way HCPs could come into contact with the targeted population of patients and vice versa. Nowadays, this step is facilitated by existence of numerous patients' organizations, and, with some warnings (see also the report of task 2.2 of ASSET EU project), also by the use of Internet.

The "***when"*** part concerns the stage at which PPI could have the most beneficial impact on research agenda. PPI at the very beginning stage and throughout the process is the ideal condition [Caron-Flinterman 2015]. At the early phase (i.e. data collection on research topics to be investigated), it is important to include not only patients and their representatives, but also all other actors (buyers, policy makers, etc.) that could impact the research outcome. It is also key in this stage that interviews and workshops are prepared carefully in order for different stakeholders to freely express their needs.

The "***what"*** part is extremely important, of course. Thus the involvement of patients and non-research HCPs needs a careful guidance by research HCPs involved in the projects.

While high level of PPI is wished at the very beginning stage, i.e. patient's desired research questions and topics, their involvement in the extraction of key points that follow in general data collection seems to be the more sensitive point as it requests enough knowledge to separate "real" problems from biased ones that could be irrelevant to R&D. The role of PPI is also of the utmost relevance for what concerns the part of research design concerning the interplay with patients, such as: the scheduling of visits and of blood sampling, use of invasive devices, etc.
Whereas of course, patients cannot be involved in the most technical steps of a research (bimolecular experiments, statistical/mathematical/informatics analyses, etc.), they sometime might valuably contribute to the interpretation of some results, especially those that have more impact on their everyday life. Last but not least, as far as research communication is concerned, public and patients have the potentiality to add a new and extremely important dimension to scientific communication: the ability to speak to (and to be understood by) a far more large audience. This can be critical especially for clinical trials, where a clear communication of the aims and implications of a trial in the preliminary phase could help to have a larger and/or easier enrollment rate.

2.2 Development of collaborative structures

The relationship between academic researchers and patient-co-researchers can be for some so difficult that, in the field of medical anthropology, it has been used the folkloristic but very self-explanatory expression "uneasy bedfellows" [van der Geest 2009]. In particular academic researchers are not accustomed to deal with this new kind of "resourceful patients" and seem to have a scarce willingness to collaborate with patients" [Abma 2014a]. Researchers are still unsure on how to best set-up and manage patient involvement. Maybe sometimes the academic researchers erroneously feel a sensation of dispossession of the research agenda. Indeed, Abma and colleagues (2014) noticed that when academic partners perceive themselves as co-owner and lead the agenda, it has the largest chances to be implemented. However, patients and care givers have knowledge of some aspects of the disease that researchers do not have, at least directly [van der Geest 2009]. Also, they are focused on practical aspects of a research design. Thus, their inclusion as research partners in a project can bring a "unique perspective" and ensure a research of greater quality and impact [Brett 2014].

Both professionals and patients should therefore be specifically trained in order to have good and sustainable cooperative relationship.
Different models of partnership between experts and patients have been reported in the literature.

Preparing Professionals for Partnership with the Public (4Ps) is a set of educational programs that aim at helping health care professionals to involve patients and public [Pietroni 2003]. The program works at both individual (e.g. how a physician can increase patient's compliance) and group level; (e.g. reflection on user perspectives). More recently, handbooks [van der Geest, 2009, and citations therein], guidelines [Abma 2014b] and recommendations [de Wit 2011] for the inclusion of patient representative in research have been developed to foster and/or to improve the collaboration between academic researchers and patients, by developing, for example, attitude to dialogue and, for biomedical researchers, entering into the patient's perspective.

On the other hand, patients should also follow some training. The European AIDS Treatment Group (EATG), Thalassemia International Federation (TIF), The European Federation of Neurological Associations (EFNA), the European Patients' Forum (EPF) and The European patients' Academy on Therapeutic Innovation (EUPATI) are examples of patients' organizations that launched training courses with the aim of increasing the capacity of patients and their representatives to be effective partners in health-related research. In accordance with this line of thought, the French National Institute for Health and Medical Research (INSERM) developed a policy of dialogue and partnership that allowed to endeavor trusted relationships between 468 associations of patients, disabled people and their families. In 2015, two meeting entitled "Research with and for patients" gathered patients, clinicians and researchers in a context of dialogue, exchange and listening.

To facilitate the development of collaborative PPI structures with researchers, dialogue models have been constructed. These participatory approaches are based on the methodology of Responsive evaluation and the Interactive learning and Action scheme and are composed, in general, of four steps: exploration, consultation, prioritization and integration of the research agenda [Abma 2014b].

To optimize the conduct of such dialog models, the authors proposed a guideline summarized in Table 1 below.

Starting position	
Open attitude towards	
Willingness towards	
Adequate resources	
Expertise	
Collaboration between fund and patient organization with middle and long-term goals	
Funding agency	**Patient organization**
Appoint policy maker for inclusion patient perspective	Appoint patient representative to work with fund, and to provide patient perspective
Programming	
Include patient representatives in program committee	Participate in program committee
Identify priorities based on research agenda	Participate in identification of priorities based on research agenda
Write scientific article on outcomes research agenda	Co-author in scientific article on outcomes research agenda
Communicate the funding program and inclusion of patient perspective	Review and adjust program text
Implementation	
Appointment patient reviewers	Recruit patient reviewers
Set up patient assessment criteria for reviewing	Provide input and feedback on patient assessment criteria for reviewing
Involve patients in writing and disseminating call for proposals	Support patient reviewers
Pay deliberate attention to patient issues	
Request lay summary in proposals	
Inform and train researchers about working with patient research partners	Organize pool of patient research partners
Evaluate patient involvement in process of programming and implementation	Evaluate patient involvement in programming and implementation from patient perspective
Disseminate evaluation to broad public	Disseminate evaluation to patients community

Table 1: Practical guideline for patient's organizations and funding agencies (From Abma et al. 2014b)

2.3 Issues

Generally speaking, the main question concerning interactions between citizens and HCPs is how and which type of collaborative structures should be developed? Of course a systematic role of patients as co-researcher will imply a shift of the current way of performing research. First of all it is important to acknowledge and respect their role in research, which implies a new attitude toward the dialog. This will also imply to accept time delay due to a process of mutual learning, and of planning a new type of collaboration. This of course implies a cost, both economic and in term of time [Brett 2012]. An immaterial but heavy cost has also to be planned insofar as the way of thinking is concerned, since the involvement and engagement of patients and public in research will imply in many fields a total rethinking of the research process and pipeline. For example, in translational medicine Callard and coworkers advocate moving from the current pipeline-based organization to a model where the research is no more seen as an unidirectional pipeline; a model that they define as "interlocking loop" [Callard 2012] where the role of patients become potentially central (see figure 1)

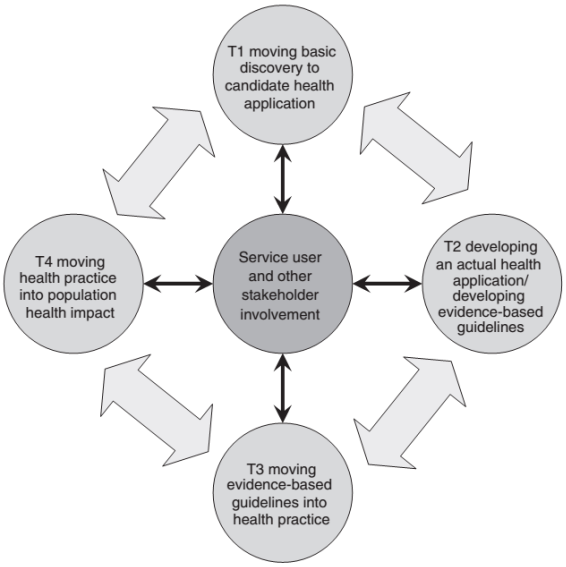


Figure 1: The "interlocked loop" of organizing the scientific research in translational medicine (from Callard et al, 2012)

Currently, in some fields there are some cases of involvement of patients in limited phases of research (final or initial depending on the research) but what is important is their sustained involvement throughout the R&D process [Abma 2014a; Callard 2012], apart, of course, the most technical ones. For example, as far as research agendas are involved, the role of patients is limited usually in early phases [Abma 2014a] and then abolished or minor, even when patients were the initiators of research agendas. On the contrary, in translational research, the contribution of patients is marginal (and barely definable as research) in the final phases of the translational medicine pipeline [Callard et al, 2012].

In the past, ZonMw, a leading health charity in Netherlands has elaborated a list of 21 recommendations to foster and implement projects including patients as co-researchers [Geest 2009]. More recently, The European League Against Rheumatism has elaborated a shorter list of recommendations [de Wit 2011] that are the following:

1. Participation of patients should be considered in the overall process of research to provide experiential knowledge that can improve the quality, relevance and validity of the research process
2. A minimum of two patient research partners should be involved
3. Identification of potential patient co-researchers should be supported by obvious definition of the expected contribution
4. The selection of patients should take into account communication skills and motivation and in a team setting
5. The principal investigator must facilitate and encourage the participation of patient partners and consider their specific needs
6. The principal investigator must insure that partner patients receive appropriate information and training
7. The contribution of patients should be officially recognized.

While PPI is increasingly appreciated in other fields of biomedical research, its role in clinical trials-based research is limited. To increase the ability of researchers to involve patients in clinical trials' development and implementation, the West Wales Organization for Rigorous Clinical Trial in Health developed Standard Operating Procedure (SOP).
The key principals of the SOP define the process to achieve effective patient involvement (how, who), management and the level of involvement in each stage [Evans 2013].

3. Examples of PPI in health related research

The role of users can be critical especially in health-related technical innovation because users are among the main drivers of general innovation, together with price, and technology [Røtnes 2009]. Note that in some cases, users might constitute a bigger "mass" that would have more power in orienting the decision-making process.

According to [Røtnes 2009], there are two main models of user-driven innovation in health sector: lead-users and people-generated design. In the former model, users are only a source of information while the first refers to a model where users are responsible to express their need, to create new ideas and solutions.

Rresearch elaborations on PPI are not only theoretical speculations, but they have been implemented in practice in Europe and other developed countries. Public involvement in international health technology assessment activities is also growing.

By establishing user-driven innovation as national policy, Denmark has the leading position in this field. The Danish Ministry of Economic and Business affairs suggested three types of initiatives areas including 1) education and research that support user-driven innovation; 2) the spread of user-driven innovation and 3) establishing networks. Several projects in different sectors of health (e.g. diabetes, patients in ICU, etc.) are conducted.

In the UK, PPI has become a central part of clinical research, so that many funding agencies request information on the extent of PPI involvement in the planned research study [Evans 2013]. Furthermore, as reported by Mr. Stephenson in his answer to our questionnaire, especially in the UK there is a very long standing experience in PPI thanks, among others, to the propensity of Cancer Research UK towards PPI. As Mr. Stephenson stated "every single cancer study now launched in the NHS in the UK has had user-involvement at some point, and many have had user involvement at several stages, with some having continuous involvement as more consumers now sit on Trial Management Groups".

The United States has also a pioneering position in the field of user-driven innovation via the Centre for Information Technology Research in the Interest of Society (CITRIS) in Berkeley. Research carried out by this center is rather technology and product based and include a large variety of subjects such as telemedicine, using game to screen for fragile X syndrome, and bloody small microscope on a cell phone to monitor patient's blood from home.

In recent years, a number of online communities have been also developed by patient organizations, providers, and nonprofit organizations. These virtual forums, where patients and sometimes caregivers can discuss health concerns and exchange information, could be potential drivers of innovation in the field of health despite their inherent quality concerns.

The following paragraphs will describe disease-specific examples of PPI that led to improve participation of the civil society, associations of consumers and patients in health-related research

3.1. Breast Cancer

As far as one of most common cancer is concerned, breast cancer, a very large number of associations exists and also a general coordinating forum "Europa Donna" (http://www.europadonna.org/), which presents itself as "the first European woman's movement against breast cancer" [Mosconi 1999]. Europa Donna, which is active in more than 20 European nations, has among its main objectives the promotion and direct involvement of women in Cancer Research, and in particular in the research for the development of best treatment practices, cancer prevention and education.

For example: Europa Donna has directly been involved in the definition of recent ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2) [Cardoso 2014] (see also Cardoso, 2012).

Europa Donna advocates for breast cancer screening and it has contributed to conceptual research for the improvement of best practice in this field [Knox 2011]. In addition, Europa Donna has developed Training Modules for Advocates who serve on Clinical Trial Committees (http://www.europadonna.org/research).

In particular, Europa Donna is member of the Scientific Committee of the "Breast cancer International Group" (BIG), which is one of largest non-profit organisations for academic breast cancer research groups from around the world (http://www.bigagainstbreastcancer.org/). In the framework of this collaboration, Europa Donna entered in the steering group of the AURORA international study, aimed the molecular investigation of metastatic breast cancer and of its responsiveness/unresponsiveness to chemotherapies (http://www.europadonna.org/research). Europa Donna is thus very active also in the field of translational research, and it is part of the TRANSBIG research consortium.

3.2. Rare diseases

The field of rare diseases suffers from a deficit of medical and scientific knowledge and, as such, it is potentially a medical topic where users could have a significant impact on issues related to diagnosis, treatment, etc. Indeed, due to their low prevalence, physicians are seldom faced by these diseases. As a consequence, they could be recognized and diagnosed at a late stage of development. In other words, these diseases have a reduced chance for early adequate treatments and good prognosis. This complexity is mirrored in the various classifications provided by Orphanet which is the reference portal for information on rare diseases and orphan drugs, for all audiences (http://www.orpha.net/consor4.01/www/cgi-bin/?lng=EN).

A very good example of the implication of users in diagnosis of rare disease is Lyme disease, recognized initially in 1975. It was first brought to medical attention through the concern of two mothers that contacted HCPs about the unusual illness spreading through their community; a small town approximately 15 km north of Long Island Sound, near the mouth of the Connecticut River [Elbaum-Garfinkle 2011]. Their inquiries sparked an intensive clinical and epidemiologic investigation that allowed the discovery of the Lyme disease.

In the era of the centrality of internet, also in the everyday life, the use of the Net is a powerful tool to build a repository of self-reported signs, symptoms and other biological parameters for these diseases. This could be subsequently used by health professionals as a clinical decision support program and for drawing algorithms for best practices in diagnostic and treatment of such diseases. On the other hand, patients and/or their relatives can also find relevant information that may be unknown to their physicians, in line with the emerging concept of "resourceful patients". The utility of publicly available information in diagnosing rare diseases has been reported by a study where concerned parents identified the lysosomal storage disorder in their child by searching the internet [Bouwman 2010]. A survey conducted by the Italian federation of rare diseases (FIMR) among parents of children with such pathologies provided evidence that the use of internet improved the management of the child's disease and initiated further discussions with their physicians [Tozzi 2013]. The survey showed also that a relatively large percentage of parents run a blog where they report information on their child's disease.
However, the heterogeneous quality of health information available on internet limits its use by both patients and physicians. A questionnaire-based cross sectional study carried out among patients attending a genitourinary medicine clinic showed that out of 101 patients who diagnosed their own symptoms, only 14 (13.9%) made the correct diagnosis [Schembri 2009]. The use of internet to diagnose rare and difficult cases could be more efficient if handled by professionals. Indeed, an internet-based study carried out by researchers blind to the diagnosis, allowed the correct diagnosis of 58% (95%CI: 38%-77%) of case series published in the case records of the New England Journal of Medicine [Tang 2006]. In a similar study, the average success was 22.1% (95% CI: 4.5%-39.7%) when non-physicians tried to determine a diagnosis by using internet resources [Siempos 2008].

Currently, several PPI initiatives for rare diseases are in place. The European Organization for rare Diseases (EURORIDS) is the most notable of those initiatives (http://www.eurordis.org/).

This is a patient-driven alliance of patient's organization that has been involved in several aspects of rare diseases ranging from regulatory issues to communication [Mavris 2012]. A successful example of this organization is that of the AKU Society for alkaptonuria who has teamed up with academics and pharmaceutical industry and has been funded by the European Framework program 7 (FP7) to investigate for a medicinal product for this disease.
ERA-Net (http://www.cordis.europa.eu/coordination/era-net.htm) is another European project that has been established to coordinate research on rare diseases at national and regional level [Marvis 2012]. Patients' organizations have participated in this project as observers. International Rare Disease Research Consortium (IRDiRC; http://www.irdirc.org/) is another example of initiative that includes patients' organizations at different level of research and development [Marvis 2012]. RareConnect (https://www.rareconnect.org/fr) is an additional initiative that has been created by EURORIDS and its American partner, the National Organization for rare Disease (NORD; http://rarediseases.org/) to build awareness about these diseases. The Life Raft Group (LRG; https://liferaftgroup.org/) started in 2000, is one more example of community patients composed of individuals with a rare cancer: gastrointestinal stromal tumor. Members of this group are actively involved in research programs and in monitoring new treatments. By confronting data collected from their patient's registry system and ongoing clinical trials, the group attempts to examine questions that are not looked at in clinical trials.

3.3. HIV/AIDS

The example of HIV/AIDS infection is perhaps among the most relevant areas where civil society organizations are involved in nearly all aspects of prevention, control efforts and drug development.

The European AIDS Treatment Group (EATG; http://www.eatg.org/) is a voluntary membership-based patient organization that has been at the forefront of the development of the civil society response to the HIV/AIDS epidemic in Europe since its foundation in 1991. EATG, together with the European Community Advisory Board (ECAB), address critical scientific questions around HIV drug-development and related co-infections such as tuberculosis or hepatitis B and C infection, and access to treatment in the European region. The majority of ECAB members are living with HIV. As mentioned earlier, EATG holds also several trainings per year to help developing up-to-date treatment knowledge for people living with HIV/AIDS and their care providers. The HIV in Europe is another initiative that includes an independent group of experts, representatives from civil society, policy makers, health professionals and European public health institutions. The main objective is to insure early diagnosis and access to HIV care through Europe [http://newsite.hiveurope.eu/]. The initiative has achieved considerable work on the definition of late presentation and on the burden of infected, not yet diagnosed patients. Several other projects (HIV testing, access to treatment, co-infections, etc.) are ongoing.

In France, HIV infected patients were actively involved for the preparation of the National campaign on **"Positive Prevention" (**http://www.aidsmap.com/Positive-prevention-and-its-implications-for-responsibility/page/1442643/**).**

In China, PPI allowed to tackle unregistered men who have sex with men (MSM) in order to provide them with prevention, treatment and care services. Similarly, PPI-led implementation models had a positive impact on antiviral treatment adherence and HIV testing among MSM. Civil Society Organizations in China initiated also programs on HIV behavioral changes interventions [Hui Li 2010]. As reported in details in our previous report (Task 2.2), this point is of major importance in the case of epidemics and pandemics.

3.4. Other chronic diseases

Patients with chronic diseases suffer from life-lasting medical condition, and as such are among the most motivated to collaborate in biomedical research projects. The nursing staff is the central link between physicians and patients and can monitor the disease and collect crucial information directly by the patients during the therapeutic process.

This can lead to contribute improving the quality of life of patients [Golik 2014]. The impact of nursing staff on the quality of life could be further accentuated if standardized guidelines and procedures are used. Nurses-European Crohn's & Colitis Organization (N-ECCO; https://www.ecco-ibd.eu/) is an international network of nurses specialized in the care of patients with inflammatory bowel disease (IBD). By developing user-driven guidelines for the management of patients with IBD, members of the nurses' network reported to be able to positively impact on the process of treatment.

In a similar way, the impact of web-guided therapy and disease self-management in ulcerative colitis patients was assessed in a cohort of Danish patients. The study showed that the web guided approach was feasible, safe, and cost effective, increased patient's adherence to acute treatment, improved Quality of Life, increased patients' ability to sufficient self-initiated treatment and reduce out-patient visits [Elkjaer 2012].

3.5. Therapeutic products

Off-label use of therapeutic products already in the market is common and represents almost 21% of prescriptions [Radley 2006], but it is often done in the absence of medical evidence [Stafford 2008; Radely 2006]. Though, it has the potential to be the source of innovation in medicine because prescribers can ascertain novel areas of their use while monitoring tolerability, effectiveness and safety [Frost 2011]. The main obstacle to reach a meaningful conclusion on the potential off-label use of a given drug in a specific health condition is the limited number of patient that each prescriber will monitor. Social media can be an effective and economical mean to collect data by creation of patient-centered research platforms. Data reported by patients could enrich the traditional trials for a better understanding of potential additional benefits of medications after they have reached the market. PatientsLikeMe (https://www.patientslikeme.com/) is an example of such initiatives where patient members share details about their treatments, and symptoms, and learn from aggregated data how to improve their outcomes. The goal of the website is to help patients answer the question: "Given my status, what is the best outcome I can hope to achieve, and how do I get there?"[Wicks 2010]. Post hoc analysis of the off-label use of amitriptyline using the website suggested that the drug was more efficacious for off-label uses than for the FDA-approved uses [Frost 2011].

3.6. Parkinson Disease

Associations of patients suffering Parkinson are very active in the domain of triggering healthcare research, as evidenced by a number of research projects, kindly provided by the *UK Parkinson association*, together with some useful considerations we report in the following:

Given the complexity of Parkinson Disease, a direct role of patients as well as of non-scientific HCPs in research is held of the maximal relevance, because it is a priority that researchers may get a "thorough understanding of Parkinson and that studies are designed to accommodate people with Parkinson is essential right from the beginning".
In the UK especially, many examples where a good level of PPI has been reached are available. One of the most interesting due to its specificity is "devices for dignity" (http://www.devicesfordignity.org.uk/), a joint initiative of INVOLVE and of the National Institute of Health Research of UK.

The UK association of Parkinson patients has recently been involved in a project on the off-label use of drugs that were initially intended in therapies of other diseases.
In our opinion this is a highly promising field of research, which could be extended in other fields, and where the direct collaboration of users is of the utmost relevance. Moreover, even the methodology of this research is innovative because patients involved in the research are allowed to recruit other patients. Quite interesting, it has been stressed that the involved patients have interest in the potentiality of scientific research.

3.7. Bio-banking

The use of Bio-banks, i.e. collection and storage of human biological materials (DNA, blood, tissues, etc.) and their related clinical data, is now common for the purpose of scientific research and medical treatment. Patients have been used to play the 'passive" role of donors, but are now acting as partners with different degrees of involvement. Some bio-banks (PATH bio-bank in Germany http://www.path-biobank.org/index.php/en/, Chordoma foundation bio-bank in the USA http://www.chordomafoundation.org/, Italian bio-bank for alternating hemiplegia of childhood) have been initiated by patients themselves, and some (Wales cancer bank http://www.walescancerbank.com/, the Mayo clinic biobank in the USA http://www.mayo.edu/research/centers-programs/mayo-clinic-biobank/overview, Nottingham health science bio-bank http://nuhrise.org/nottingham-health-science-biobank/) involve patients in their governance.

To facilitate PPI in bio-banking activities, appropriate training is key. The European Patients' Academy (EUPATI) funded by the European Innovative Medicine Initiative (IMI) is an example of such training program that provides educational materials in all aspects of research and development for health-interested general public and patient advocates in seven languages [Parsons 2015]. The Vision on Information, Confidence and Engagement (VOICE; http://independentcancerpatientsvoice.org.uk/voice-science-for-patient-advocates/) is another training program for patients in the UK that delivers courses on basic cancer biology, research terminology, set-up and evaluation. Similarly, the Genetic Alliance Bio-bank (http://www.biobank.org/) assists patients in creating or maintaining bio-banks.

4. Research Networks of GPs

One of most interesting examples of user-involvement in research is the case of research networks of General Practitioners (GPs). Indeed GPs can provide both very valuable real time (and retrospective) data and they may also represent needs of potential patients with an appropriate scientific filter represented by their medical background and experience in the field.

As stressed by Lam [Lam 2004]: "Family medicine has matured as an academic and scientific discipline with its own core concepts, knowledge, skills, and research domains. It has acquired much expertise in studying common illnesses; the integration of medical, psychological, social, and behavioral sciences; patient-centered care; and health services delivery. Stakeholders, such as the World Health Organization, governments, and funding agencies, are becoming more supportive to family medicine research because they recognize its key importance in bridging the gap between biomedical research and clinical practice."
Note that there also exist two research journals in this field: "BMC Family Practice" and "Annals of Family Medicine".

The role of GPs in research for pandemics might be crucial, also taking into the account that the possible research networks might be huge. Indeed, the DRIM study in France revealed that 30% of the interviewed French GPs was in favor of their direct involvement in medical research [Supper 2010; 2012]. This is not surprisingly because "research in general practice has an undisputed legitimacy in France" [Cadwaller 2014], an example that should be studied and expanded in all EU.

5. Mapping the impact of PPI in health research agendas

Despite the increased number of research programs involving patients, robust evidence on the outcome of PPI is yet desirable. PPI could impact a research study at different levels, ranging from shaping research question to the choice of control arm, ethical issues and communication of the results. A systematic review of published literature (1995-2009) provided evidence that at early phase of research, users' involvement had a positive effect on identifying user-relevant topics and priorities [Brett 2012].

During the development and implementation of research protocol, users' participation was valuable in identifying cultural issues to be taken into consideration, patients' outcome measures, scientific vulgarization of patient's informed materials (information letter, consent form), finding the study sample and consulting about the adequateness of research design form the diseased people standpoint, in order to avoid trials difficult to be implemented or of difficult compliance. Most importantly, dissemination and implementation of the study results could be done more efficiently due to the influence of users in the community. The review found also challenging impact of PPI such as power struggle between academics and "co-researchers"; increased time and cost to organize user's involvement; over-emphasis of some problems and threatened academic publication. In a more recent systematic review, the authors investigated the impact of PPI on users and researchers [Brett 2014]. The results showed gain of confidence in patients involved in the research programs and improved understanding of HCPs with regard to the added value of such collaborative research with non-HCPs. The challenging points reported by users were lack of training and preparation and huge amount of work.

As mentioned earlier, PPI is very well established in the UK. The economic cost and impact of PPI on the UK-NHS health care services was the subject of a systematic review that provided evidence that PPI can take various concepts and terminology [Mockford 2012]. Although the impact of PPI on different health services (service planning and development, information development and dissemination, attitudes of service-users, etc.) was evidenced, the study could not determine the extent of impact and its cost due to the absence of valid measurement tools.

It has been reported that the impact of PPI is highly context-oriented [Brett 2012; Staley 2014]. A review has addressed this issue to better understand the contextual factors (how, when) that make PPI to have the greatest effect on health research [Staley 2014].

6. Conclusions and Roadmap

The public collaboration in research until now has been accidental [de Wit 2015] whereas it should be systematic. However, as we illustrated in the previous sections, there is a significant increase in PPI in health research. Patients and their relatives/representatives are not seen any more as "subjects/participants" but as "collaborators".

As stated by Jenner et al, lay members of biomedical research projects bring new views on practical aspects of the research that could help researcher to setup studies with realistic timescales and understand how the research can affect both patient and caregivers [Jenner 2015]. Furthermore, according to Elberse et al, experiential knowledge of patients is an added value that can complement scientific knowledge and also lead to better acceptance of research by patients [Elberse 2011]. The impact of PPI has been investigated in a literature review that concluded that overall, public involvement has a positive impact on design, conduct and inclusion rate of clinical trials and is of particular value in qualitative research [INVOLVE 2009].
PPI has positive effects not only on the interactions between researchers and patients/civil society but also on a larger spectrum. For example, as we stressed in the Report of the task 2.2 of ASSET project, one of the key problem in increasing the awareness on pandemics and epidemics is that the trust towards national and international public health authorities is extremely low. This is essentially due to the fact that we are living in post-trust society [Loefsted, 2005]. As de Wit et al recently stressed [de Wit 2015]: "collaborative research" between biomedical researchers and patients "may improve healthcare by building increased trust between the research and patient communities and enhancing communication between patients and health professionals". Thus PPI can be an important tool to overcome the current lack of trust towards public health authorities and towards biomedical scientists.
The relationship between scientists and health users is often described as asymmetrical due to difference in education level; and has been postulated as a barrier to setup genuine partnership between the two groups [Elberse 2011]. For this reason it is fundamental to train both biomedical scientists and public/patients in a way so that their communication skill and ability of mutual interaction may be substantially enhanced.
To avoid confusions, Platform for public participation should be constructed in a way that is reliable and understandable for the general population and effective for optimizing patient outcome [Hesse 2010].
To allow patients to design their own agenda without being influenced by professionals, several authors propose a first step that consists of a consultation of each group separately to develop their own agenda before interaction with other group to finalize the research program [Baart 2011; Elberse 2011]. Furthermore, whenever patients and civil society representatives are involved as co-researchers, greatest care should be taken to respect their emotional problems.

Indeed, a key point is that users involved in the research projects should not feel themselves as guests in the project but as intellectual co-owners. As Nierse and coworkers stressed [Nierse 2011] the feeling of intellectual co-ownership is fundamental to improve the dynamics of research collaboration as this feeling result in a positive outcome and in mutual learning.
Another key issue is that the users involved in a project have to be as heterogeneous as possible, both in their personal health experience and in their socio-cultural background, in order to avoid biases in the results of the research [Nierse 2011; Parveen 2013]. Indeed, if patients are too much homogenous in their disease experience, the research might insufficiently investigate other aspects of the disease that were not experienced by the patients co-researchers; if the socio-cultural status of patients representative is too low, researchers could too easily dominate.

We want also to honestly stress that the current literature on the PPI in biomedical research is until now excessively biased on benefits. In our bibliographic research we found only one paper stressing drawbacks and risks [van Staa 2009]. Thus, in our opinion there is not enough body of research on how to avoid negative effects caused by real PPI in biomedical research, where with "real" we mean that researches are jointly in control by scientists and public. In particular, an effort ought to be done in avoiding limitations in the freedom of research of scientists.

Moreover, an excess of stress of the relevance of user-focused research objective might distract founds from researches that are of less immediate benefit for users, but that might have huge positive benefit to users in a non-immediate future.
To be provocative, are we really sure that vaccinations would be really understood by hypothetical general public research-agenda setting partners in the 18th century UK? Indeed, the ideas of Jenner were very innovative, and had a lot of difficulties in being accepted by the general public worldwide. Thus it is not unreasonable to hypothesize that at the Jenner's times a hypothetical Research Agenda Committee, with an excessively influential role of representatives of civil society, would probably not have given a priority the newly introduced (and, at that age, highly controversial) concept of "vaccine".

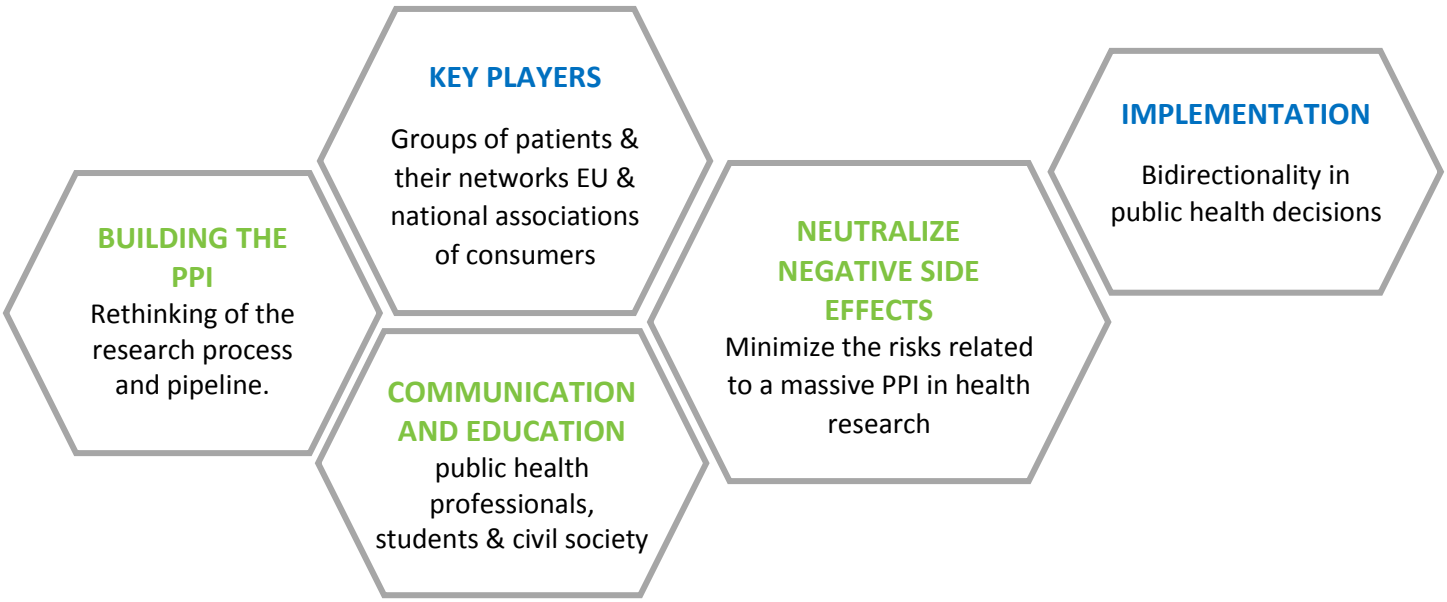
On the other hand the public involvement has huge potentialities, among which one of the most important is to make scientists aware of a wide range of problems to be investigated and that are "orphans" until now. This will avoid the existence of issues of primary relevance for users that are unexplored in the scientific literature. This problem is not simply hypothetical, but it is real. Existence of such orphan problems has, for example, been evidenced in [Teunissen 2011] that stressed the existence of a "gap between the scientific research community and patient networks". As another example, the "James Lind alliance" (http://www.lindalliance.org/index.asp) has been created in the UK in order to identify major mismatches between "topics that patients nominate for clinical research, those that clinicians and clinical researchers find important for further research, and current research practice" [Nierse 2011].

As far as internet and internet-based social networks are concerned, often health-related internet information are subject to reporting bias (incomplete information or lack of report from a subset of patients), and lack source citation. Nevertheless, improved user interface designs, along with appropriate patient education will increase the value of online patient platforms to study the off-label effect of marketed products. Evidence raised from these online platforms can be further evaluated by peer-reviewed literature and other online communities. Thus, a major joint researchers-public effort should focus on to increase the involvement of health professionals in dedicated sites, which would result in enhancement of validated information. This would lead to the set-up of specific, validated and official sites some already exist such as CDC or NIH website, but we need to educate citizens to refer preferentially to these sites.

However, what has not been fully perceived by biomedical researchers (and by researchers in many other scientific and humanistic fields) is that the internet age does not only provide easy access to previous body of research to researchers. Indeed, it has at least three features that are likely to deeply change the attitudes of the general public towards scientific research. First, public has nowadays increasingly *direct* access to all body of research. Second and most important, the result of research ought to be disseminated to a much more vast audience. This is slowly also perceived by publisher of scientific online journal which increasingly require authors to include layman summary of each published paper. Third, Internet nowadays allows the general public to directly interact with whatever citizen in the world wanting to ask a question and/or propose a problem and sometimes a solution. It is now not uncommon that biomedical researchers receive an email or a Facebook message by a patient. Thus, internet and its social networks can be both the first stage of the PPI and a tool to develop it. Of course, this requires specific training.
Biomedical researcher must be conscious of these facts. In our opinion, these huge challenges require an equally huge educational effort. Some training does exist, but larger effort is needed. It is our opinion that since MSc students (thus well before PhD) in biomedical sciences should follow courses to enhance their communication skills towards general public. We are well aware of the difficulties of this, because currently it often exist a problem of lack of specific education in the field of communicating science even to other scientists. Without this training, an effective collaboration with the public in scientific research will be difficult, if not impossible. Symmetrically, it is important to integrate in the school the development of skills in understanding science. Moreover, for interested university students in humanities, it could be important to acquire skills in interacting with scientists.

The key problem for defining best practices for public involvement in research on pandemics is that the vast majority of the research body developed in the field of public involvement in medical research focuses on the involvement of patients. For self-evident reasons, this is impossible when we are dealing with pandemics of diseases that do not become chronic, and, namely, for influenza. Thus, the first requirement to define best practices without wasting the accumulated knowledge is to shift from the concept of patient to the concept of "potential patient" as far as influenza and other non-chronic infectious disease are concerned.
This will require a huge effort since it has recently been noticed [de Wit 2015] that the level of involvement of patients with chronic diseases in the research process concerning their disease largely depends on their personal history, and especially on the severity, duration and symptoms of their disease, including their response to therapeutic agents. These factors do not apply to prevention of future pandemics, and form an important barrier to public involvement in pandemic research (and in transferring in our domain the previous body of research in patient involvement).

Summarizing the various and inter-related topics we illustrated in this report, we may sketch a tentative roadmap towards best practices for the PPI in biomedical research concerning pandemics.



BUILDING THE PPI: Rethinking of the research process and pipeline.	The public collaboration in research until now has been accidental whereas it should be systematic and it should start in the very beginning of the research process. It should also be promoted a sustained involvement throughout all the research process, although, of course, with variable degree of involvement. Thus appropriate actions have to be implemented, by sensitizing stakeholders of public and private sectors. Users involved in a research project should not feel themselves as guests in the project but as intellectual co-owners. Their participation must be effective: one must allow patients/representative of civil society to contribute to design their own agenda without being influenced by professionals. Note that the involvement of patients/civil society representative in research projects has to be well "designed". Indeed, users involved in a project have to be as heterogeneous as possible, both in their personal health experience and in their socio-cultural background. In particular, it is important to involve patients and public in those parts of research design concerning the interplay with patients, such as: the scheduling of visits and of blood sampling, use of invasive devices etc.… Concerning design, we also think that the role of PPI in clinical trials-based research should be expanded. During this phase, users and patients are crucial to identify cultural issues to be taken into consideration. This point might be of the utmost relevance in researchers aimed at increasing the awareness of the relevance of vaccination with the aim of increasing the vaccination rates. In the implementation phase of projects, civil society representatives ought to be involved in the extraction of key points, as well as in the interpretation of research results, especially those that have more impact on their everyday life. These are two very sensitive points as they request enough knowledge to separate "real" problems from biased ones that could be irrelevant. Of course, civil society representatives and associations of consumers should not be involved in the most technical steps of a research (biomolecular experiments, statistical/mathematical/informatics analyses etc.). However, preliminary to the above-mentioned actions it is important to establish a universal terminology that clearly defines the level and the extent of patient's participation in a health-related research. Indeed, PPI or other terms that design patients participation in research is not yet very well defined. The creation of a consensus terminology will also be very helpful for the evaluation of the impact of patient's involvement in health-related research.
KEY PLAYERS	In order to implement a real PPI, it is of utmost importance to involve a range of associations. First, GPs can provide a unique expertise in some domain and can also act as an interface between professional researchers and civil society representatives. Thus networks of GPs (and especially research networks of GPs) ought to be involved in all PPI research and innovation projects. We highly suggest as first step that leaders of possible research & innovation projects contact the EU association of GPs. Indeed this association, in principle, may allow contacting all EU GPs. However, contacting pre-existing associations and/or networks of GPs might be insufficient. Especially in the field of pandemic prevention, it is highly appropriate to encourage/form new research network of GPs as integral part of projects in this area. Other important key players are EU and national associations of consumers. However, at this stage their role in PPI is minor. It is mandatory to sensitize them concerning the risks of

	possible future influenza pandemics and the relevance of their direct involvement in the related scientific and technological health research.
COMMUNICATION AND EDUCATION	The mutual understanding between research and public health professionals and civil society representatives is fundamental for PPI. As a consequence, both previously-trained biomedical scientists and public/patients ought to be in a way so that their communication skill and ability of mutual interaction may be substantially enhanced. As far as professionals are concerned, a new and extremely important dimension to scientific communication has to be learned: the ability to speak to (and to be understood by) a far more large audience. Thus, MSc students in biomedical sciences should follow courses to enhance communication skills towards general public with the prospective of PPI. Symmetrically, as far as civil society is concerned, it is important to integrate in school the development of skills in understanding science. Of course, the above-mentioned steps are not reachable in the short term. Preliminary to all PPI projects, it is crucial that all participants follow a training course in this field. Note that a number of such courses are already enacted. As far as the main communication tool is concerned, the Internet, one should encourage the set-up of specific, validated and official internet sites similar to some already existing such as CDC or NIH website. We need to educate citizens to refer preferentially to these sites. Indeed, current heterogeneous quality of health information available on internet limits its use as a diagnostic tool by patients. A hard task should thus be to stimulate the ability to discriminate between a good quality website with scientifically serious content from websites that contain false contents (often written in a Para-scientific style). Actions should be enacted to foster the internet-based dialogue between biomedical scientists and patients as well as general public, thus making internet and its social networks both the first stage of the PPI and a tool to develop it.
NEUTRALIZE NEGATIVE SIDE EFFECTS	Real PPI in biomedical research is similar to a drug: its main effects are positive but, as in all human actions, negative side effects are possible and one must be prepared to face them. With “real” we mean that the researches are jointly in control by scientists and public. As a consequence, a serious and consistent body of research on how to prevent and minimize the risks related to a massive PPI in health research has to be started. In particular, an effort ought to be done in avoiding limitations in the freedom of research of scientists. Moreover, the relevance of user-focused research objective ought not to be outweighed because it might distract founds from researches that are of less immediate benefit for users, but that might have huge positive benefit to users in a non-immediate future. Beside research on PPI-related potential risks, an important practical issue is that one has to accept time delays and costs due to a process of mutual learning, and of planning a new type of collaboration.
IMPLEMENTATION	Development of collaborative structures should start with a research effort (of course in collaboration with civil society) on how to implement bidirectionality in public health decisions. To do this, one can advantage from similar researches areas in political sciences (see report of task 2.1 of ASSET project). Concerning these points, an essential issue is avoiding dissipating the precious heritage of comments and criticisms that civil society has elaborated during and after the 2009 H1N1 pandemics. In particular, in collaboration of civil society periodic « surveys » have to be designed in order to measure the public opinions fear and expectance concerning pandemics. Of course,

	these surveys must be more frequent and more specialized when small epidemics appear and the related information is widely communicated by media. Another pillar of implementation of PPI is that civil society has the burden of making aware scientists of a wide range of problems to be investigated and that are "orphans" until now. Until now, we focused on design and implementation issues of PPI. However, in the research process it is equally important the phase of evaluation. As a consequence, it has to be supported the introduction of patients-reviewers for project design, scientific articles, grant applications. Moreover, PPI projects should be evaluated in order to assess the value and impact of such partnerships. This implies that specific measurement tools that could evaluate what work, and in which circumstances, have to be developed and validated. Finally, in our experience confidentiality in PPI industrial projects was a serious obstacle in investigating the nature of PPI. On the contrary information on this kind of projects would be essential to enrich methodological research on PPI.

7. Implementation of the roadmap

7.1. Implementation of the roadmap within the ASSET project lifetime

We are going to delineate a possible implementation in the framework of the ASSET project and its strategic plan, by proceeding in a systematic order, rather than by numerical order of the work-packages or a merely temporal order, although there is temporal interrelation among some of the topics we are going to illustrate.

7.1.1. ALL ASSET EVENTS

Since **communication and education** (which are at the center of the action line tree of the strategic plan) are two crucial and difficult issues of the roadmap, ideally in all ASSET-related events we should include special sessions/discussions/events related to both topics. Facing in a priority way the issue of education and communication, it is of paramount importance to create what is required in the Strategic Plan: real conditions of co-operation between stakeholders, decision makers, health professionals, scientists and the citizens.

Organize events discussing on **what we have learnt from civil society during the H1N1 pandemic.** Indeed, the 2009/10 pandemics has to be considered a turning point in the history of communication and of public participation in Public Health. Moreover, the arising discussion will constitute a useful update with respect to our current knowledge.

7.1.2. WP6: High Level Policy Forum

This task is central for the implementation of the roadmap in the framework of the lifetime of ASSET, because in it there is the most substantial interplay between ASSET and high level deciders. Of course, to this aim is would be highly appropriate to **invite** to the **next** events representatives of civil society. Among them, and in line with the roadmap, it will be essential to invite high level representative of **networks of GPs (in particular the EU association of GPs)** and of **associations of consumers**.

Primarily, the real presence of civil society representatives will be fundamental to discuss on the one hand the key topic of pandemics preparedness: the **implementation of bidirectionality** in the public health decisions; on the other hand

they can **start the process of rethinking of the research pipeline in order to build an effective PPI**, along the line indicated in the first point of our roadmap.
A forum with persons committed at high level in public health and in civil society is the natural arena where the delicate point of **possible negative side effects of PPI** (as well as its intrinsic increase of costs and time with respect to traditional research pipeline) can be discussed.
The interplay between high level public health officers and GPs and consumers is a unique occasion in order to **assess whether these heterogeneous categories have the same perception** concerning which are **orphan problems** in the field of pandemics.
Finally of course, continuing the experience of the first HLPF, it is important to focus on **H1N1** experience, in particular exploring **what we have not yet learnt from civil society** concerning that pandemic.
As far as Internet is concerned, as stressed during the discussions in the first HLPF, a key topic to discuss in these events should be **how to help citizens to identify trustable sources of information**. Conversely, the presence of representatives of civil society in our forums should allow us to learn from them which are their deepest information needs. This might result **in guidelines** to build pandemic-related websites that are both informative and trustable but also of immediate comprehension by their users.

7.1.3. WP1: ASSET Website

The ASSET portal is central in the strategic plan, because it is a communication medium addressed to large layer of population. As a consequence, ideally the ASSET portal should become the **field of common contact** and discussion between associations of consumers, networks of GPs, HCPs and common readers. As outlined in the strategic plan, the web portal will host and update the ongoing debate on ethical issues, engaging the different sections (and members) into the debate.

For example, the ASSET portal should devote some dedicated sections to **discuss with the users on how to discriminate** between a good quality websites on pandemics, epidemics or vaccinations from non-scientific websites. Particularly, it could be of interest to help citizens to **recognize para-scientific statements** form scientific ones. This section of our portal could be an integral part, together with the HLPF, of the development of the above mentioned guidelines for building trustable websites.
Of course, the above two topics are innovative and quite sensitive, thus this will require a non-trivial **effort for the designing of the website**.

7.1.4. WP4: Civil Society consultation

As stressed in the strategic plan, the citizen consultation is a key tool that will allow to obtain a realistic picture on the perception of citizen regarding their own role in pandemic planning and response and whether and to what extent they claim a more important part in the decision making process.

For this reason, it will be fundamental to design the consultation questionnaire by taking into account the literature on the pandemics as described in task 2.2. In particular, what we have learnt and what we have not yet learnt concerning the H1N1 pandemic. In particular, **treasuring the experience of the 2009 pandemic**, it would be essential to **catch what citizens want** and what they do not want form political and public health deciders, as well as their real **willingness in being involved in innovation and research**, between and during pandemic crises.

The civil society consultations might also be an opportunity to **understand which problems** are actually considered **"orphans"** by citizens. Of course, only a limited number of questions might concern their experience during (and memory of) the H1N1 pandemic.
Finally **representation of gender and of social-economic and cultural heterogeneity** must be guaranteed for raising awareness within special groups belonging to different societal sectors. This is a key factor for the optimum implementation of the strategic plan.

7.1.5. WP5: Local Initiatives

As stressed in the strategic plan, local initiatives are expected to be an effective approach to convey inputs coming from citizens' consultations and the stakeholders' platforms aiming to promote mobilization and mutual learning at local level and to enhance the transferability of the most effective policies and practices. A relationship with the outcomes of the High level Policy Forums is also a fundamental point to design these initiatives.

Local Initiatives must be **designed i**n order to **exploit the natural heterogeneity** across EU countries and, in some cases, also within countries. Thus, a challenge is how to include in each single local initiative a representation of many local cultures internal to the host country. For this, it is useful to **involve local associations of consumers and of GPs in the organization** of these events. The **cultural differences emerged** during these events **should be reported** and taken into the utmost considerations in the other WPs. As specified in the Strategic Plan, at each local initiative selected stakeholders will be present. It will be thus a key opportunity to sensitize them concerning the involvement of Civil Society in the process of scientific research.
Discuss with citizens on their perception of the pandemic-related material on internet; their **experience during H1N1** pandemics, and about **"orphan" problems** and organize initiatives for increasing the awareness of the **relevance of vaccinations**.
Start Initiatives aimed at **popularizing what really is a good internet website, and to learn from the citizens what type of communication they like the most**. Initiative on the **unperceived influence** that **media** have on citizens, including - if possible – questionnaire are also needed.
Finally, last but not least, in the local initiative **gender representation** must be very carefully guaranteed.

7.1.6. WP3: the toolbox

As we stressed, **PPI terminology** is essential, thus it should be discussed among ASSET partners whether include a section on terminology in the toolbox.

7.1.7. WP6 ASSET Bulletins

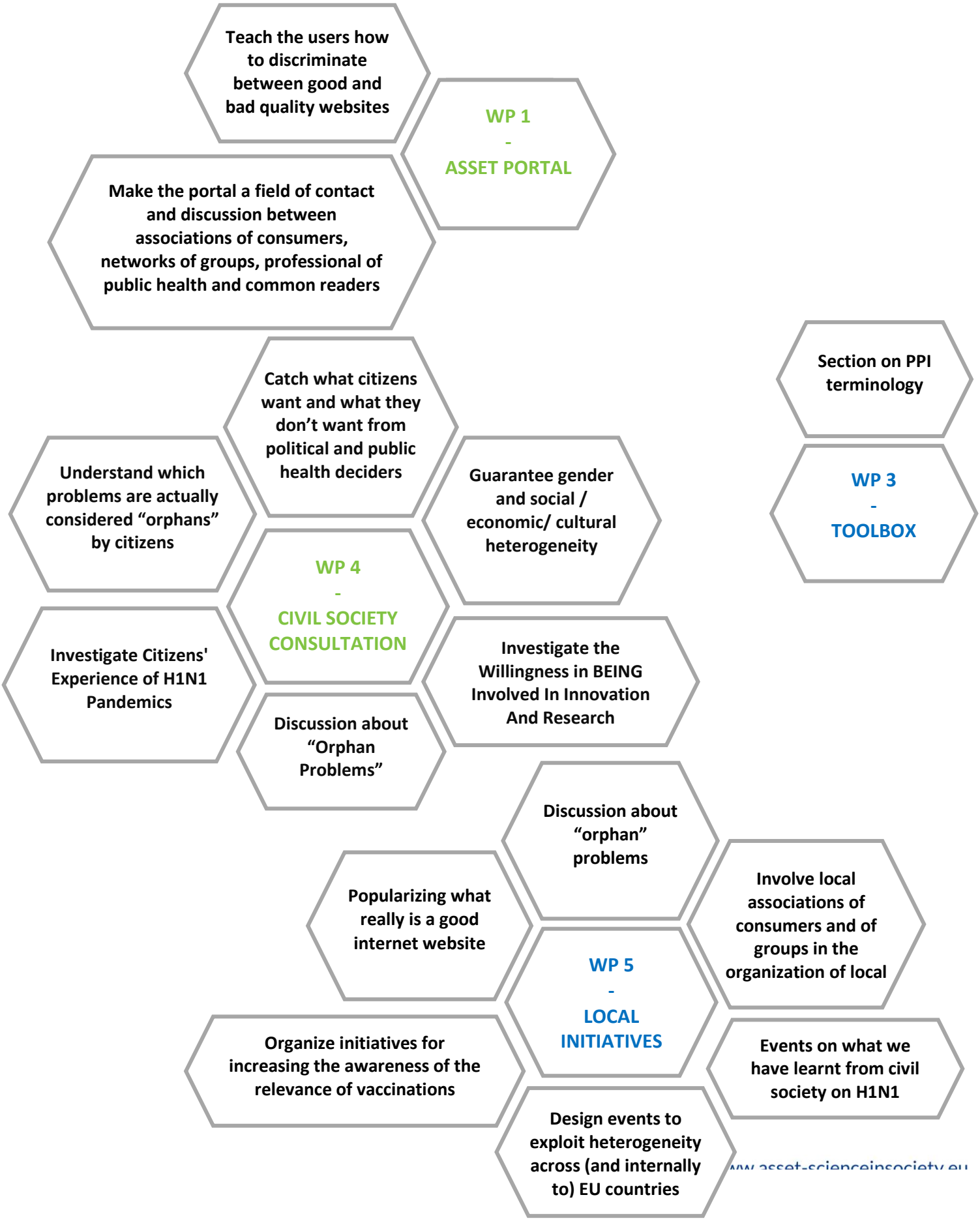
Publish articles discussing on **what we have learnt from civil society on H1N1 pandemic.**
Enhance the **diffusion of the bulletin among the organizations of consumers and** among the networks/associations of **GPs**.
Prepare **special issues of the bulletin devoted to the key points of the roadmap by taking into the account what emerged in other tasks of the project during the implementation phase of the roadmaps itself**. In particular, more than one special issue ought to be devoted to the rethinking of the research pipeline for implementing PPI.

7.1.8. WP5 Best Practices Portal

The results of the civil citizen's consultations and of HLPFs, as well as the feedback in the ASSET platform, should nurture the task concerning the best practices. The best practice portal must be meant in a wide sense because the best practices treated in an extensive way in the portal must synergically be synthetized in scientific papers published in high level international journals which in turn must contain references to the portal. In this way, we may potentially attract the attention of stakeholders (in science, in public health and in policy making) towards the portal and the main objectives of the ASSET project.

This must be an important component of the wider strategy to attract the attention to the Best Practices portal. Another key component of this attention strategy will be of course the high level policy forum.
All the above actions are synthetized in Figure 2:

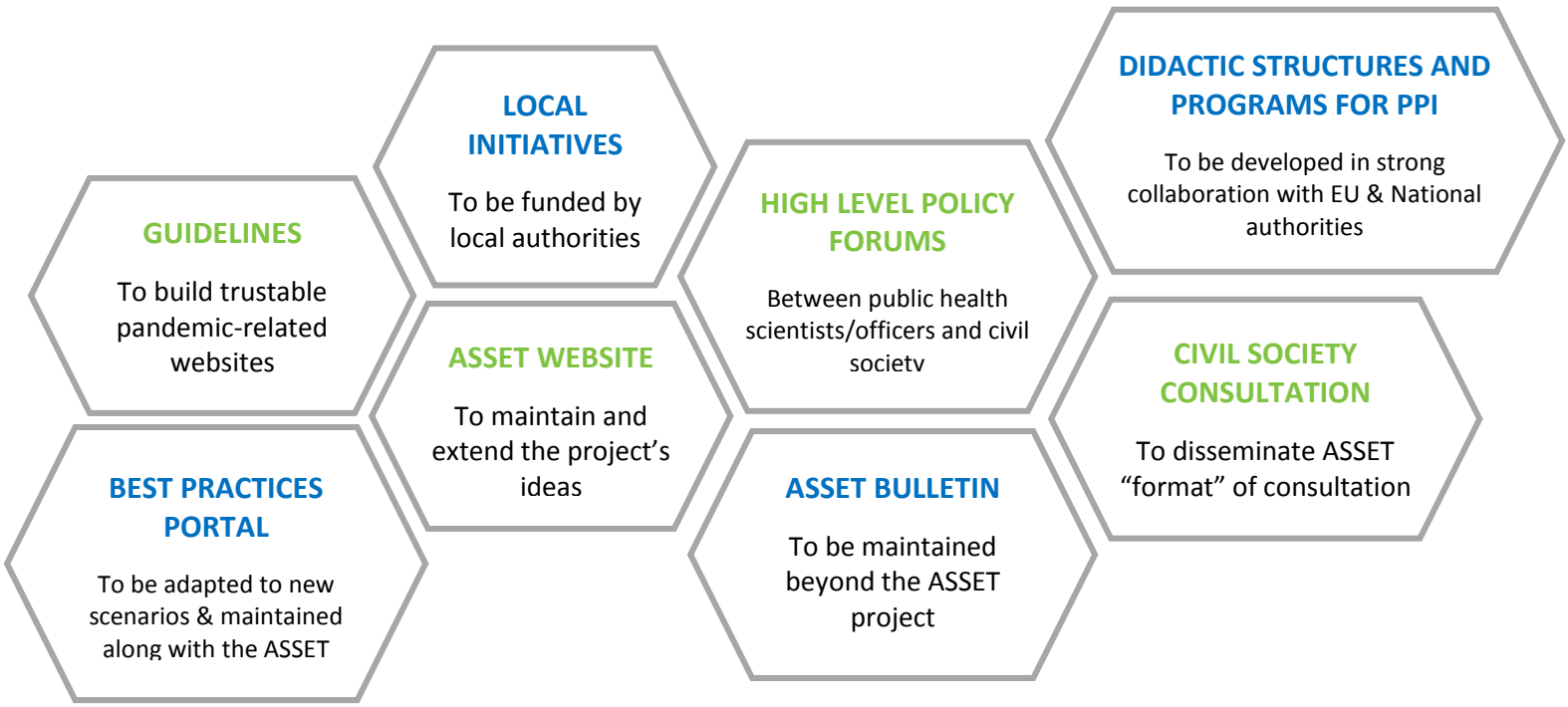
Figure 2: Graphical representation of the implementation of the roadmap within the ASSET project lifetime




WP 5
-
BEST PRACTICES AND PORTAL
To be nurtured with the key points of the roadmap on the light of the related results of the civil citizens' consultation, the HLPFs, the feedback in the ASSET platform, the feedbacks to the Bulletin
GPs, consumers, PH officers have all the same perception concerning which problems are orphan?
Start the process of rethinking of the research pipeline in order to build an effective PPI
Invite networks of GPs and associations of consumers
Elaborate guidelines to build pandemic-related websites informative and trustable but also easily readable
Discuss on the implementation of bidirectionality in the public health decisions
WP 6
-
HLPF
How to help citizens to identify trustable sources of information?
Discuss possible negative side effects of PPI
H1N1 experience: what we have not yet learnt from civil society?
Papers on what we have learnt from civil society on H1N1 pandemics
Diffusion of the bulletin among the organizations of consumers and among the network associations of GPs
WP 6
-
BULLETIN
Multiple issues to be devoted to the rethinking of the research pipeline for implementing PPI
Special issues devoted to the key points of the roadmap. Take into account of what emerged in the other tasks

7.2. Implementation of the roadmap: suggestion for the period after ASSET

Due to the paucity of the time from now to the end of the ASSET project, it is more than obvious that, within the ASSET lifetime, only the basic part of the Roadmap can be effectively implemented with real actions aimed to change a long-established paradigm in research and innovation.
However, by means of the above detailed internal ASSET actions we hope that we will have accumulated a sufficient quantity of scientific material that might remarkably influence the current research debate on PPI and, which is more important, it might start making enhance the concept of PPI in the agenda of national, inter-national and regional stakeholders of public health.
Of course, our initial work of rethinking and disseminating of PPI to be durable should be sustained after ASSET lifetime by other projects and dedicated organisms.
In particular, among the roadmaps key points some of them will need a particularly longer action (indeed, none of them are of short duration). We are going to re-examine some of them:



a) The action started in the **High Level Policy Forums**, which are in the ASSET project the main events where public health scientists/officers and civil society representatives can meet, should continue in a consolidated series of similar events. In order that this can happen it will be vital to interface ASSET with similar future EU projects and EU-level initiatives and research institutes in public health. It will be equally important to sensitize national health authorities to start series of such events at regional, national and poly-national levels. For this, the dissemination actions within the ASSET project will be fundamental. Ideally a project that might partially continue and extend the key ideas of ASSET would be highly appropriate. Another potential way of making HLPFs durable is to highly commit the invited associations of consumers and the networks of GPs in the organization of the forums, i.e. gradually shifting their role from "invited" to "co-organizers". The general aim will be that they can be among the key actors that could organize such events after the end of ASSET, within or not other EU projects.

b) As far as the envisaged **guidelines** for building trustable pandemic-related websites, they must be designed in a way that they can live and be continuously updated also after the end of ASSET. In order to do this, it is important that ASSET design them in collaboration with institutions and associations that are willing to update them in the future. As a consequence, these organisms will have to have a parity role in the design process of these guidelines.

c) As far as the **ASSET website** is concerned, we recommend that this website ought to survive to ASSET in order to maintain and extend – at dissemination level – the key ideas of the ASSET project. To do this, it will be important to render the site autonomous in the last part of ASSET project by searching appropriate funds and/or by linking it to future projects. Again here involving associations of GPs and of consumers might be useful

d) As far as the **Civil Society consultation** is concerned, we might envisage integrating, in the dissemination of ASSET, some actions aimed to convince other future projects to include similar consultations. In other words, we think that our consultation has to be designed also as a "format" of consultation, which may be of interest also for future similar projects in the same or related areas

e) As far as **local initiatives** as such those envisaged for WP5 are concerned, we should design these initiatives in a way that they can be autonomous, and durable in time. In order to do this, it will be highly appropriate to devise a strategy allowing funding them by local authorities.

f) As far as the **ASSET bulletin**, again they must be designed to be as autonomous as possible from ASSET so that they can survive to ASSET.
Thus, it is fundamental that the report of ASSET work is not the backbone of the bulletin itself.

g) PPI requests, as already mentioned, a long term educational effort by all parts, both HCPs and civil society. As a consequence, during ASSET and its events a major effort has to be devoted to start a process that ought to lead to the creation of **didactic structures and programs for PPI**. It is highly probable that these structures will be put in practice after the end of ASSET. For this reason this part of our project has to be enacted in strong collaboration with national and EU authorities.

h) As far as the **best practices portal** is concerned, these best practices will be deigned in order to be durable thus by definition adaptable to new scenarios. It will remain the problem of durability of the portal, which is intimately related to the problem of durability of the ASSET website, of which the best practice portal will be a part.

To conclude, one must be well aware that it might be extremely difficult to implement the above roadmap, although it contains apparently common-sense recommendations. There are a number of evidences concerning the potential difficulties one might face. We give here an example. As briefly mentioned in the methodology section, we received an informal but written reply to our questionnaire by the chairman of a very influential national association of patients of a serious and very diffuse disease in a large EU nation, who wrote us that 1) in his/her country there are no significant examples of collaboration between his/her association and research bodies (both public and in the industry) 2) he/she thinks that this kind of collaboration is not wanted at all by research bodies. This answer clearly illustrates how much it must be done to enter in a new paradigm where PPI in biomedical research is a common way to design research projects and agendas.

Finally, one of the most important point to be stressed is that it is needed a strong effort of joined research between professionals and civil society in order to find the best ways to make general public understand that anyone might be a "potential patient" of a pandemic. How to do this is, at this stage, a matter of speculation. However, we may say this: the concept of "potential patient" has not to be introduced by increasing societal alarmism and anxiety, since on the long run it might worsen the phenomenon of "post trust society". For this reason the collaboration with civil society is fundamental in order to find the correct cultural, anthropological and communication strategy, as well as to precisely define, by means of the above-mentioned research effort, this concept.

8. References

Abma TA, Baur VE. User involvement in long-term care. Towards a relational care-ethics approach. Health Expect. 2014a. doi: 10.1111/hex.12202.

Abma TA, Pittens CA, Visse M, Elberse JE, Broerse JE. Patient involvement in research programming and implementation: A responsive evaluation of the Dialogue Model for research agenda setting. Health Expect. 2014b. doi: 10.1111/hex.12213.

Baart IL, Abma TA. Patient participation in fundamental psychiatric genomics research: a Dutch case study. Health Expect. 2011 Sep;14(3):240-9. doi: 10.1111/j.1369-7625.2010.00634.x.

Bouwman MG, Teunissen QG, Wijburg FA, Linthorst GE. 'Doctor Google' ending the diagnostic odyssey in lysosomal storage disorders: parents using internet search engines as an efficient diagnostic strategy in rare diseases. Arch Dis Child.2010; 95(8):642-4. doi: 10.1136/adc.2009.171827.

Brett J, Staniszewska S, Mockford C, Herron-Marx S, Hughes J, Tysall C and Suleman R. Mapping the impact of patient and public involvement on health and social care research: a systematic review. Health Expectations, 17, pp.637–650 (2012)

Brett J, Staniszewska S, Mockford C, Herron-Marx S, Hughes J, Tysall C, Suleman R. Mapping the impact of patient and public involvement on health and social care research: a systematic review. Health Expect. 2014 Oct; 17(5):637-50. doi: 10.1111/j.1369-7625.2012.00795.x.

Cadwallader JS, Lebeau JP, Lasserre E, Letrilliart L. Patient and professional attitudes towards research in general practice: the RepR qualitative study BMC Family Practice 2014, 15:136.
Hesse BW, Hansen D, Finholt T, Munson S, Kellogg W, JThomas JC. Social Participation in Health 2.0 IEEE COMPUTER 2010:43(11) 45-52

Cardoso F, Costa A, Norton L, Senkus E, Aapro M, André F, Barrios CH, Bergh J, Biganzoli L, Blackwell KL, Cardoso MJ, Cufer T, El Saghir N, Fallowfield L, Fenech D, Francis P, Gelmon K, Giordano SH, Gligorov J, Goldhirsch A, Harbeck N, Houssami N, Hudis C, Kaufman B, Krop I, Kyriakides S, Lin UN, Mayer M, Merjaver SD, Nordström EB, Pagani O, Partridge A, Penault-Llorca F, Piccart MJ, Rugo H,
Sledge G, Thomssen C, Van't Veer L, Vorobiof D, Vrieling C, West N, Xu B, Winer E; European School of Oncology; European Society of Medical Oncology. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Breast. 2014; 23(5):489-502. doi: 10.1016/j.breast.2014.08.009.

Cardoso F, Harbeck N, Fallowfield L, Kyriakides S, Senkus E; ESMO Guidelines Working Group. Locally recurrent or metastatic breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2012; 23 Suppl 7:vii11-9.

Caron-Flinterman C. A New Voice in Science: patient participation in decision-making on biomedical research. PhD thesis, 2015, ISBN-10: 90 90 19996 9. Printed by Wöhrmann Print Service, Zutphen
Brett J, Staniszewska S, Mockford C, Herron-Marx S, Hughes J, Tysall C, Suleman R. A systematic review of the impact of patient and public involvement on service users, researchers and communities. Patient. 2014; 7(4):387-95. doi: 10.1007/s40271-014-0065-0
Callard F, Rose D, Wykes T. Close to the bench as well as at the bedside: involving service users in all phases of translational research. Health Expect. 2012; 15(4):389-400. doi: 10.1111/j.1369-7625.2011.00681.x.

Elbaum-Garfinkle S. Close to home: a history of Yale and Lyme disease. Yale J Biol Med. 2011; 84(2):103-8.

Elberse JE, Caron-Flinterman JF, Broerse JE. Patient-expert partnerships in research: how to stimulate inclusion of patient perspectives. Health Expect. 2011; 14(3):225-39. doi: 10.1111/j.1369-7625.2010.00647.x.

Elberse JE, Caron-Flinterman JF, Broerse JE. Patient-expert partnerships in research: how to stimulate inclusion of patient perspectives. Health Expect. 2011; 14(3):225-39. doi: 10.1111/j.1369 7625.2010.00647.x.

Evans BA, Bedson E, Bell P, Hutchings H, Lowes L, Rea D, Seagrove A, Siebert S, Smith G, Snooks H, Thomas M, Thorne K, Russell I; West Wales Organisation for Rigorous Trials in Health (WWORTH). Involving service users in trials: developing a standard operating procedure. Trials. 2013; 14:219. doi: 10.1186/1745-6215-14-219.

Elkjaer M. E-health: Web-guided therapy and disease self-management in ulcerative colitis. Impact on disease outcome, quality of life and compliance. Dan Med J. 2012; 59(7):B4478.

Frost J, Okun S, Vaughan T, Heywood J, Wicks P. Patient-reported outcomes as a source of evidence in off-label prescribing: analysis of data from PatientsLikeMe. J Med Internet Res. 2011; 13(1):e6. doi: 10.2196/jmir.1643

Geest 2010. Patients as co-researchers? Views and experiences in Dutch medical anthropology. https://www.academia.edu/5548669/2010_Patients_as_co researchers_Views_and_experiences_in_Dutch_medical_anthropology._In_S._Fainzang_H.E._Hem_and_M.B._Ris%C3%B8r_eds_The_taste_for_knowledge_Medical_anthropology_facing_medical_realities._Aarhus_Aarhus_University_Press_pp._97-110

Golik M, Kurek M, Poteralska A, Bieniek E, Marynka A, Pabich G, Liebert A, Kłopocka M, Rydzewska G. Working Group Guidelines on the nursing roles in caring for patients with Crohn's disease and ulcerative colitis in Poland. Prz Gastroenterol. 2014; 9(4):179-93. doi: 10.5114/pg.2014.45098.

Hayes H, Buckland S, Tarpey M. INVOLVE: Briefing notes for researchers: Public involvement in NHS, public health and social care research. http://www.invo.org.uk/wp-content/uploads/2014/11/9938_INVOLVE_Briefing_Notes_WEB.pdf

INVOLVE: Promoting public involvement in NHS, public health and social care research. Exploring impact. http://www.invo.org.uk/wp-content/uploads/2011/11/Involve_Exploring_Impactfinal28.10.09.pdf

Jenner MK, Gilchrist M, Gillian GC. Research Involvement and Engagement (2015) 1:3. DOI 10.1186/s40900-015-0002-y

Knox S. The European advocacy perspective on mammography screening. Breast. 2011;20(1):93-5. doi: 10.1016/j.breast.2010.07.003.

Li H, Kuo NT, Liu H, Korhonen C, Pond E, Guo H, Smith L, Xue H, Sun J. From spectators to implementers: civil society organizations involved in AIDS programmes in China. Int J Epidemiol. 2010; 39 Suppl 2:ii65-71. doi: 10.1093/ije/dyq223.

Löfstedt, R. Risk Management in Post-Trust Societies. Palgrave (2005).

Mavris M, Le Cam Y. Involvement of patient organisations in research and development of orphan drugs for rare diseases in europe. Mol Syndromol. 2012;3(5):237-43. doi: 10.1159/000342758.

Mitchell D, Geissler J, Parry-Jones A, Keulen H, Schmitt DC, Vavassori R and Matharoo-Ball B. Biobanking from the patient perspective. Research Involvement and Engagement (2015) 1:4

Mosconi P, Kodraliu G. Italian forum of Europa Donna: a survey of breast cancer associations. Health Expect. 1999; 2(1):44-50.

Mockford C, Staniszewska S, Griffiths F, Herron-Marx S. The impact of patient and public involvement on UK NHS health care: a systematic review. Int J Qual Health Care. 2012; 24(1):28-38. doi: 10.1093/intqhc/mzr066.

Nierse CJ, Schipper K, van Zadelhoff E, van deGriendt J, Abma TA. Collaboration and co-ownership in research: dynamics and dialogues between patient research partners and professional researchers in a research team. Health Expectations, 15, pp.242–254 (2011)

Parsons S, Starling B, Mullan-Jensen C, Tham SG, Warner K, Wever K; Needs Assessment work package of European Patients' Academy on Therapeutic Innovation (EUPATI) Project. What the public knows and wants to know about medicines research and development: a survey of the general public in six European countries. BMJ Open. 2015; 5(4):e006420. doi: 10.1136/bmjopen-2014-006420.

Parveen S, Giles S, I Din I. A collaborative approach to patient involvement in health research: challenges and enablers. Research, Policy and Planning (2013/14) 30(3), 167-177

Pietroni P, Winkler F, Graham L. Cultural revolution. BMJ. 2003; 326(7402):1304-6.

Radley DC, Finkelstein SN, Stafford RS. Off-label prescribing among office-based physicians. Arch Intern Med. 2006; 166(9):1021-6.

Røtnes R, Staalesen PD. New methods for user-driven innovation in health care sector. Nordic Innovation Centre. http://www.nordicinnovation.org/Global/_Publications/Reports/2010/New%20methods%20for%20user%20driven%20innovation%20in%20the%20health%20care%20sector.pdf

Schembri G, Schober P. The Internet as a diagnostic aid: the patients' perspective. Int J STD AIDS. 2009; 20(4):231-3. doi: 10.1258/ijsa.2008.008339.

Schembri G, Schober P. The Internet as a diagnostic aid: the patients' perspective. Int J STD AIDS. 2009; 20(4):231-3. doi: 10.1258/ijsa.2008.008339.

Staley K, Buckland SA, Hayes H, Tarpey M.'The missing links': understanding how context and mechanism influence the impact of public involvement in research. Health Expect. 2014; 17(6):755-64. doi: 10.1111/hex.12017.

Staniszewska S, Boardman F, Gunn L, Roberts J, Clay D, Seers K, Brett J, Avital L, Bullock I, O' Flynn N. The Warwick Patient Experiences Framework: patient-based evidence in clinical guidelines. Int J Qual Health Care. 2014; 26(2):151-7. doi: 10.1093/intqhc/mzu003.
358(14):1427-9. doi: 10.1056/NEJMp0802107

Supper I, Ecochard E, Bois C, Paumier F, Bez N, Letrilliart L. How do French GPs consider participating in primary care research: the DRIM study. Family Practice 2010; 0:1–7

Supper I, Ecochard E, Bois C, Paumier F, Bez N, Letrilliart L. Recherche en médecine générale : un tiers des généralistes prêts à participer MÉDECINE janvier 2012 Pages 39-45 (in french) DOI : 10.1684/med.2012.0788.

Teunissen T, Visse M, de Boer P, Abma TA. Patient issues in health research and quality of care: an inventory and data synthesis. Health Expectations. 2011; 16: 308–322

Tang H, Ng JH. Googling for a diagnosis--use of Google as a diagnostic aid: internet based study. BMJ. 2006; 333(7579):1143-5.

Tozzi AE, Mingarelli R, Agricola E, Gonfiantini M, Pandolfi E, Carloni E, Gesualdo F, Dallapiccola B. The internet user profile of Italian families of patients with rare diseases: a web survey. Orphanet J Rare Dis. 2013; 8:76. doi: 10.1186/1750-1172-8-76.

Van der Geest S. Patients as co-researchers? Views and experiences in Dutch medical anthropology In: S. Fainzang, H.E. Hem & M.B. Risør (eds) The taste for knowledge: Medical anthropology facing medical realities. Aarhus: Aarhus University Press, pp. 97-110

van Staa AL, Jedeloo S, Latour LM, Trappenburg MJ. Exciting but exhausting: experiences with participatory research with chronically ill adolescents. Health Expectations, 2009, 13, pp.95–107

Wicks P, Massagli M, Frost J, Brownstein C, Okun S, Vaughan T, Bradley R, Heywood J. Sharing health data for better outcomes on PatientsLikeMe. J Med Internet Res. 2010; 12(2):e19. doi: 10.2196/jmir.1549.

de Wit MP, Berlo SE, Aanerud GJ, Aletaha D, Bijlsma JW, Croucher L, Da Silva JA, Glüsing B, Gossec L, Hewlett S, Jongkees M, Magnusson D, Scholte-Voshaar M, Richards P, Ziegler C, Abma TA. European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects. Ann Rheum Dis. 2011; 70(5):722-6. doi: 10.1136/ard.2010.135129.

de Wit MP, Kvien TK, Gossec L. Patient participation as an integral part of patient-reported outcomes development ensures the representation of the patient voice: a case study from the field of rheumatology. RMD Open. 2015; 1(1):e000129. doi: 10.1136/rmdopen-2015-000129.

de Wit M, Campbell W, Orbai AM *et al*. Building Bridges between Researchers and Patient Research Partners: A Report from the GRAPPA 2014 Annual Meeting. The Journal of Rheumatology. 2015; 42:6, 1021-1026

Annex

QUESTIONNAIRE USER INVOLVEMENT

IN PROCESS OF RESEARCH AND DEVELOPMENT OF DRUGS AND DEVICES

Each questionnaire started with the following introduction:

The questionnaire you will find below is part of the EU Project ASSET-Science in Society (Action Plan on Science in Society related issues in Epidemics and Total Pandemics) www.asset-scienceinsociety.eu, funded by the European research programme FP7.

The questionnaire's aim is to identify examples of involving users in the process of research and development of drugs and devices / other tools (citizens, patients, physicians, and any association or organisation not usually involved in the research and innovation process in health). The input from the questionnaire will serve to identify and establish best practices on how and when to involve users in the health Research and Innovation process and in the drug development. Based on this, the project will transpose relevant practices from other medical fields to the field of pandemics and epidemics. Your input will be treated confidentially.

The questionnaires were slightly diversified to be adapted to two kind of stakeholders: professional of health, and representatives of civil society.

Answers by: Richard Stephens

Name: Richard Stephens

Position: Consumer Lead

Company/Organisation: NCRI

Your field of health or link to health: Cancer Research

Questions :

1. To what extend and according to which conditions user-driven innovation and research is possible in your field? **[NOTE: with the term user we mean a person or organisation / association not normally involved in research and innovation of drugs and devices: citizens, patients, physicians, associations of citizens, patient associations, associations of physicians, health assurance and other health organizations, etc...**

   User-driven research is possible but depends on context. User-driven innovation in the research process has become quite common in UK cancer research.

2. Are you aware of cases (not involving your institution/company/organisation) of such user-driven innovations? If yes, please give details/links/references and your opinion.

   In the UK cancer research, users ("consumers") sit on research funding committees, on major strategic bodies, and have input into national strategies and decisions. There is also increasing consumer involvement with industry, including very early stage study design (especially with some Astra Zeneca studies).

3. Have you had experiences involving physicians/ citizens, patients or other associations/organisations not normally involved in research and innovation in health (either as an individual or within an association) that pushed to research innovation?

Yes. NB Because my group has been embedded in UK Cancer Research for 15 years, it is impossible to answer your questions 3.1-3.5 in the detail you require. Every single cancer study now launched in the NHS in the UK has had user-involvement at some point, and many have had user

involvement at several stages, with some having continuous involvement as more consumers now sit on Trial Management Groups

If you answered yes on question 3, please provide details by answering the questions 3.1 to 3.5:
If you answered no on question 3, please go to question 4.

3.1 How did the interaction begin? Who launched the need for a new "product" (vaccine, drug, medical devices, medical or public health service etc.) or an easier route of administration of an existing product - the citizen, patient, physician or the industry?

3.2 What were the different steps of interaction to launch and, where applicable, then implement a Research and Innovation process?

3.3 Was your experience successful (i.e. it led to research and/or new product or services)?

3.4 Did the interaction with citizens/patients / physicians (or their associations) lead to publications/reports? If yes, please provide the reference.

3.5 If you would again take part in a Research and Development project involving physicians/ citizens, patients or other associations/organisations, what would you change in the way of proceeding?

4. *If you answered "No" on question 3*:

Would you be happy to be involved in a process of user-driven research? If yes, what in your opinion are the benefits of user-driven innovation & research? How would you proceed?

5. How can/should the different kinds of user best influence the different types of research and innovation?

By being involved as partners from the earliest possible stage.

6. If you are involved in a research area, what do the different types of users care about?

In cancer, it is (a) cure and (b) quality of life, during and after treatment, with or without cure.

7. In your opinion, Is there a need to better align drug research priorities to social need (versus only profit)? In such a case, how could one address needs of minority or special communities?

Yes, surely that is blindingly self-evident? And why assume the needs of minority communities are any different in the context of this particlar question? (NB These answers refer to cancer only!)

8. How developers and manufacturers can incorporate practitioner feedback, to lead to better devices or delivery mechanisms?

I think the UK NIHR Industry Alliance is a very good example of how it can be done.

Answers by: Claire Stephenson

Name: Claire Stephenson

Position: Research Support Network Manager

Association: Parkinson's UK

Your field of health or link to health: Developing patient involvement in Parkinson's research

Questions

1. To what extend and according to which conditions user-driven innovation and research is possible in your field? **[NOTE: with the term user we mean a person or organisation / association not normally involved in research and innovation of drugs and devices:**

citizens, patients, physicians, associations of citizens, patient associations, associations of physicians, health assurance and other health organisations, etc...

My interpretation of 'user-driven research' is research that fosters the collaboration of patients, carers and the public with researchers to design and deliver research.

This is not just possible, but essential in Parkinson's research. Parkinson's, like many other conditions, is complex. The experience of people living with the condition is invaluable and can be the difference between research success and failure.

Deciding which are the right research questions to ask, ensuring that study teams have a thorough understanding of Parkinson's and that studies are designed to accommodate people with Parkinson's is essential right from the beginning. Furthermore, this should not just be done as a consultation but in **partnership** where all stakeholders are considered equal in this process.

Researchers working with people affected by Parkinson's on planning effective recruitment strategies, designing a participant feedback strategy and putting mechanisms into place to encourage retention to the studies will help make the research a success.

2. Are you aware of cases (not involving your associations) of such user-driven innovations? If yes, please give details/links/references and your opinion.

The National Institute of Health Research is a leader in the field of involving patients, service users and the public in research. They recently conducted a review http://www.nihr.ac.uk/get-involved/Extra%20Mile2.pdf

They work with (and fund) INVOLVE (http://www.invo.org.uk/)which supports patient and public involvement in NHS research and works with other organisations to promote patient involvement in research.

NIHR also fund Devices for Dignity (http://www.devicesfordignity.org.uk) which works with patients, carers and the public, clinical and healthcare staff, industry, academics and charities to bring solutions to areas of unmet clinical and patient need. They focus on four key areas: Renal Technologies, Assistive and Rehabilitative Technologies, Urinary Continence Management and Paediatric Technologies

The Health Research Authority has produced a strategy for how it will develop patient and public involvement in the ethics of research (http://www.hra.nhs.uk/documents/2013/10/hra-public-involvement-strategy-circulation-september-2013.pdf)

Internationally, Parkinson's Disease Foundation is a strong advocate of involving people affected by Parkinson's in research and they offer awards to researchers who do this well (http://www.pdf.org/en/grant_funding_apt)

3. Have you had experiences where your association was involved in research and innovation in health that pushed to research innovation?

Yes.

Parkinson's UK worked with the James Lind Alliance to determine what the top ten unanswered questions were for people affected by Parkinson's in the day to day care and management of Parkinson's. The process is an innovative one and has been published in BMJ (http://bmjopen.bmj.com/cgi/content/full/bmjopen-2014-006434?ijkey=2CawT40q3q3chhJ&keytype=ref)

In addition, we have recently started a project that is led by people affected by Parkinson's and supported by the Parkinson's UK research team to determine any potential drug candidates for further investigation that have been used for another condition, but could potentially offer hope in thetreatment of Parkinson's. Also known as drug repurposing/repositioning.

If you answered yes on question 3, please provide details by answering the questions 3.1 to 3.5:

If you answered no on question 3, please go to question 4.

3.1 How did the interaction begin? Who launched the need for a new "product" (vaccine, drug, medical devices, medical or public health service etc.) or an easier route of administration of an existing product - the citizen, patient, physician or the industry

It is part of our research strategy to determine any candidates for drug repurposing, however, we share our research strategy with people affected by Parkinson's and in particular a team of volunteers with an interest in research. They were particularly interested in drug repurposing and felt the patient community would be a helpful place to begin this project. The volunteers developed a project plan and are currently recruiting other volunteers to work with them on different aspects of the project.

3.2 What were the different steps of interaction to launch and, where applicable, then implement a Research and Innovation process?

We haven't launched the project yet, we are still in the planning phase.

3.3 Was your experience successful (i.e. it led to research and/or new product or services)?

The project is ongoing.

3.4 Did the interaction between you association and the research isntitutions/industries lead to scientific publications/reports? If yes, please provide the reference.

Not yet but we are hoping to publish.

3.5 If you would again take part in a Research and Development project, what would you change in the way of proceeding?

4. *If you answered "No" on question 3*:

Would you be happy to be involved in a process of user-driven research? If yes, what in your opinion are the benefits of user-driven innovation & research? How would you proceed?

See question 1.

5. How can/should the different kinds of user best influence the different types of research and innovation?

As I mentioned earlier, service users, patients and carers should be working in partnership with researchers of all research. There are many varied and different roles and ways they can become partners in research.

With research that is more basic or fundamental, this does become more of a challenge. Although, working with people affected by Parkinson's to ensure that your research team understand Parkinson's as a condition is the first step. Researchers can also work with people affected by Parkinson's to ensure that the importance of the research to people affected by Parkinson's is represented in the funding application.

6. What do the different types of people in your association care about?

We care about ensuring the voice of people affected by Parkinson's is at the core of Parkinson's research. We care about using our position as a patient organisation to influence the research community.

7. In your opinion, Is there a need to better align drug research priorities to social need (versus only profit)? In such a case, how could one address needs of minority or special communities?

Absolutely yes. Drug development should be done with extensive consultation AND in partnership with the patient community.

8. How developers and manufacturers can incorporate practitioner and user associations' feedback, to lead to better devices or delivery mechanisms?

There are many ways that this could be done. My suggestion would be that developers and manufacturers work with patient organizations in the first instance to explore this further.

Answers by : Julien Biaudet

Name: Julien Biaudet

Position: Project Officer, PhD

Company/Organisation: Cancéropôle CLARA

Your field of health or link to health: Health, illness and medical sociology

Questions

1. To what extend and according to which conditions user-driven innovation and research is possible in your field? **[NOTE: with the term user we mean a person or organisation / association not normally involved in research and innovation of drugs and devices: citizens, patients, physicians, associations of citizens, patient associations, associations of physicians, health assurance and other health organisations, etc...]**

Sociology, and social sciences more generally, underlines the multiplicity of point of view, representations and uses about a device (or a physical object) and helps developers to conceive more useful products. The main condition is to really let the users “speak” by putting away producers or developers conceptions which are often disconnected from the “real world” and daily life.

2. Are you aware of cases (not involving your institution/company/organisation) of such user-driven innovations? If yes, please give details/links/references and your opinion.

Not in drugs/devices research. Hygée Center (based in St-Étienne, France) works on people behavior relative to cancer with user-inclusive methods, like intervention mapping.

3. Have you had experiences involving physicians/ citizens, patients or other associations/organisations not normally involved in research and innovation in health (either as an individual or within an association) that pushed to research innovation?

No, not directly.

If you answered yes on question 3, please provide details by answering the questions 3.1 to 3.5:
If you answered no on question 3, please go to question 4.

3.1 How did the interaction begin? Who launched the need for a new "product" (vaccine, drug, medical devices, medical or public health service etc.) or an easier route of administration of an existing product - the citizen, patient, physician or the industry

3.2 What were the different steps of interaction to launch and, where applicable, then implement a Research and Innovation process?

3.3 Was your experience successful (i.e. it led to research and/or new product or services)?

3.4 Did the interaction with citizens/patients / physicians (or their associations) lead to publications/reports? If yes, please provide the reference.

3.5 If you would again take part in a Research and Development project involving physicians/ citizens, patients or other associations/organisations, what would you change in the way of proceeding?

4. *If you answered "No" on question 3*:

Would you be happy to be involved in a process of user-driven research? If yes, what in your opinion are the benefits of user-driven innovation & research? How would you proceed?

It seems very interesting to me. Including in the very early stage of research program users' point of view and practices, benefits are to avoid waste of time and wrong ways of developing devices. Anthropology and ethnology methods allow to study real people uses and reduce the gap between them and producers' and developpers' ungrounded conceptions.

5. How can/should the different kinds of user best influence the different types of research and innovation?

I don’t know enough drugs research and development to answer this question…

6. If you are involved in a research area, what do the different types of users care about?

Not involved in a research area anymore.

7. In your opinion, Is there a need to better align drug research priorities to social need (versus only profit)? In such a case, how could one address needs of minority or special communities?

NA..

8. How developers and manufacturers can incorporate practitioner feedback, to lead to better devices or delivery mechanisms?

NA.

Answers by Marc Essodagui

Name : Marc Essodagui

Position: Business Developer

Company/Organisation: ONDODIAG

Your field of health or link to health: Antiviral Drugs, Vaccine, diagnostics

Questions

1. To what extend and according to which conditions user-driven innovation and research is possible in your field? **[NOTE: with the term user we mean: citizens, non-research-related physicians, associations of citizens, associations of non-research-related physicians]**

Our organization is specialized in the development of new tools and solutions to improve the current methods for endometriosis' diagnosis. Due to the lack of accurate and reliable epidemiological data regarding this condition in France, we have set-up the first observatory of endometriosis in France, together with several patient advocacy groups.

2. Are you aware of cases (not involving your research group) of such user-driven innovations? If yes, please give details/links/references and, if you think useful, your opinion.

I can mention a great initiative supported by Breast Cancer patients, called Seintinelles (www.seintinelles.com) designed to proactively inform a large patient population on the current and upcoming clinical trials, contributing to significantly shortening the recruitment time in clinical trials, and ultimately benefitting the patients themselves by helping the development of new therapies.

3. Have you had experiences involving physicians/ citizens (either as single or as associations) that pushed to research innovation in your field?

Our organization is involved in such a process, but it's too early to present innovations yet.

If yes, please provide details by answering the following:

3.1. How did the interaction begin? Did you ask users (i.e. physicians and/or citizens) about their needs for a new "product" (vaccine, drug, medical devices, medical or public health service etc.)/ easier routes of administration of an existing product ? Or did they contact you in order to express their needs?

We first worked with patient advocacy groups. The physicians' community, i.e. gynaecologists in our case, have been involved in a second step.

3.2. How did you proceed?
We have launched an observatory supported by an e-Health platform (www.oz2020.com)

3.3. Was your experience successful (i.e. it led to research and/or new product or services)?
Ongoing process

3.4. Did your interaction with citizens/physicians (or their associations) lead to publications/reports? If yes, please provide the reference.

Not yet

3.5. In the case you ought to deal again with similar situation, what would you change in the way of proceeding?

Hard to answer at this stage

4. If the answer to question 2 is "No", would you be happy to be involved in a process of user-driven research? And WHY ought one to begin a process of user-driven innovation & research? And how would you proceed?

5. How can/should the different types of user best influence the different types of research and innovation?

5.1 In your research area, what do the different types of users care about?
Transparency and clear explanation regarding the utilization of their personal data is a major source of concern and questions from the users.

6. In your opinion, Is there a need to better align drug research priorities to social need (versus only profit)? In such a case, how could we address needs of minority or special communities?

Involving them directly and collecting a clear list of their current needs is central in my opinion. That's the only way to get them strongly bound to the project.

7. How developers and manufacturers can incorporate practitioner feedback, to lead to better devices or delivery mechanisms?

By asking them and providing them easy-to-use, social network-like solutions to report their answers.