multi-act

Deliverable D1.2

Patient Engagement Group (PEG) establishment

"Setup of a multi-stakeholder group on Patient Engagement (PEG) to foster mutual learning discussion and involve the developers of the patient engagement strategies as well as their beneficiaries in the evaluation and gap assessment"

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Short description of the Deliverable (as in the DoA):

This document details the setup of a multi-stakeholder group on Patient Engagement (PEG) to foster mutual learning discussion and involve the developers of the patient engagement strategies as well as their beneficiaries in the evaluation and gap assessment.

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STATEMENT OF ORIGINALITY:

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

TABLE OF CONTENT

Executive summary

The development of innovative and personalized care for people suffering of chronic brain diseases can benefit by a collective impact research framework, in which, besides being deeply coordinated, each interested party has its return of investment aligned with the common goal of developing effective care for patients.

Therefore multi-stakeholder engagement is at the root of MULTI-ACT project. When translating research into practice, engaging the stakeholders is explicitly intended to make the outcomes of translation relevant to its constituency of users. In particular in measuring the impact of the research in brain diseases and Multiple Sclerosis (MS) health research organizations, it is fundamental to consider the patients as key stakeholders and their needs and perspectives throughout the entire measurement process. Starting from this assumption this document aims to introduce the guidelines of Patient Engagement in the MULTI-ACT project in order to assure their contribution, as key stakeholder, in the development of the Collective Research Impact Framework.

Starting from the collection of existing patient engagement procedures in R&I, we aim to:

1) collect and merge existing procedures and guidelines of engagement in R&I and identify main gaps and bottlenecks;
2) update and co-create recommendation and rules together with all the relevant actors involved in R&I;
3) create innovative routes for patient engagement, especially for R&I phases that are missing procedures for patient engagement (strategic agenda planning, evaluation process, exploitation, etc.);
4) ensure that the views, considerations and insights of patients are represented throughout all the work packages;
5) ensure that representation would enable patients to have an equal voice, in partnership with researchers and other experts;
6) ensure that Patient Reported Outcomes and perspectives are designed in partnership with patients and integrated in the development of CRIF as core and transversal dimension of such model;
7) ensure that the use of patient data, including concerns about privacy and intellectual property, is considered from the perspective of the person with MS across Europe.

The word “patient”, in terms of patient engagement, can refer to people living with a condition, as well as caregivers. Patient organizations will be also involved, however considered as a separate stakeholder.

The patient engagement process in MULTI-ACT project will be enable by a consortium of several actors:

1) patients with brain diseases via the Patient Forum (PF)
2) people with MS (PwMS) via patients’ organization at international level as MS International Federation (MSIF) and European MS Platform (EMSP)

Considering that Patient engagement needs to be a strategic and operative group (PEG), its governance will be based on a lean organization, with few individuals working on it (14 persons). However PEG activities will be supervised and exploited by the external advisory bodies (Patient Forum and External

Advisory Board) by applying the innovative stakeholders engagement framework ICEE (Identify, Connect, Engage and Enable) that is core and transversal in the development of the MULTI-ACT project.

Last but not least, considering the information that will be dealt with in the engagement process, ethical compliance will be ensured in order to accomplish with the European and National regulations.

To note, the present version of this document has been modified following the request - included in the letter Ref. Ares(2019)6817961 - 04/11/2019 received from the EC – to "provide academic/authoritative references to the methods that have been used, the I-CEE and ICR" (see section 3.1.1).

Introduction

This document contains the rationale and concept for PEG establishment. In particular, we wants to address specific questions as:

- Why we need a PEG in MULTI-ACT, why is it important and for what purpose?
- How the PEG has been shaped? Who was engaged in the shape?
- Who are PEG final members and how do they address the required expertise?
- What do we expect from PEG? What are the roles, responsibilities, terms of references?
- How is patient engagement addressed in PEG (are PwMS engaged)?
- How have PwMS been engaged? Are ours engagement actions ethical compliant?
- Are all ethical issues addressed in T1.1 (link with WP10)?
- How is PEG collocated in the governance of MULTI-ACT? Which is the communication flow and interaction with advisors (PF, EAB)?
- How is PEG integrated in the overall patients-related stakeholder engagement of MULTI-ACT?

Sections of the document have been shaped considering the above stated questions.

1.1 Purpose of this document

D1.2 document provides an introduction to MULTI-ACT project in order to contextualize the establishment of a Patient Engagement Group (PEG); to set the PEG within the framework of MULTI-ACT; to provide an extensive overview of the PEG rationale; to present the concept of PE process within the PEG and the overall WP1; to introduce PEG individual members as well as their organizations, to describe PEG roles, responsibilities and activities; to describe the communication flow between PEG and MULTI-ACT governing and advisor bodies; to demonstrate that actions related to PEG establishment are ethical compliant and to address other ethical issues.

1.2 Structure of document

The deliverable is arranged in ten sections as follows:

- **Section 1 "Introduction"**
- **Section 2 "Background**" introduces the MULTI-ACT overall project, WPs structures, focus on WP1, KPIs and RRI in relation to the need for a PEG.
- **Section 3 "Rationale and concept for PEG"** describes the rationale for establishing a PEG within MULTI-ACT and describes the concept for Patient Engagement in the PEG.
- **Section 4 "Actions for PEG set-up"** describe actions to set-up the PEG and provides rationale for expertise required in the PEG.
- **Section 5 "PEG individual members"** presents individual PEG members and biographical sketches and how they addressed the rationale stated in Section 4.
- **Section 6 "PEG Term of references"** presents PEG roles and responsibilities, including Term of References (Annex 1. External members acceptance form)**.**

- **Section 7 "PEG and the governance of MULTI-ACT"** describes how PEG is collocated in the Governance of MULTI-ACT and the communication flow (PEG, PF, AEB).
- **Section 8 "Ethical issues"** describes Ethical issues and link with WP10.
- **Section 10 "Conclusion".**

1.3 Glossary

CRIF	Collective Research Impact Framework
EAB	External Advisory Board
EC	European Commission
EU	European Union
GA	Grant Agreement
IAM	Integrated Accountability Model
I-CEE	Identify, Connect, Engage and Enable framework
ICR	Incremental Cross-exchange Roundtables
KPI	Key Performance Indicator
MS	Multiple Sclerosis
NDD	Neurodegenerative diseases
PE	Patient Engagement
PEG	Patient Engagement Group
PF	Patient Forum
PwMS	People with Multiple Sclerosis
R&I	Research and Innovation
RFPO	Research Funding and Performing Organization
RRI	Responsible Research & Innovation
ROI	Return on Investment
WP	Work Package
Entities Acronyms	
EARLS	European Alliance Restless Legs Syndrome
ECHAlliance	European Connected Health Alliance
EFNA	European Federation of Neurological Associations
EPF	European Patient Forum
EUROATAXIA	Federation of European ataxia patient groups
EURORDIS	Rare Diseases Europe
GAMIAN	Global Alliance of Mental Illness Advocacy Networks
IAPO	International Alliance of Patients' Organizations

MSIF	Multiple Sclerosis International Federation
PCORI	Patient-Centered Outcomes Research Institute
Partners Acronyms	
FISM	Fondazione Italiana Sclerosi Multipla Fism Onlus
UNITN	Universita Degli Studi Di Trento
EY	Ernst & Young Financial Business Advisors
UBU	Universidad De Burgos
UTA	Tampereen Yliopisto
EBC	European Brain Council
INTRA	Intrasoft International
EHMA	European Health Management Association
ARSEP	Fondation Pour L'aide A La Recherche Sur La Slerose En Plaques
DiA	Dane-I-Analizy.Pl Sp Zoo
UCP	Universidade Catolica Portuguesa

2 Background

2.1 Overview of the MULTI-ACT project

The MULTI-ACT project aims to foster the diversification of constellations of actors and stakeholders in Health Research and Innovation processes by developing a strategic collective framework where research governance is expanding to a model of a **'quadruple helix'** with patients and their community as a fourth strand.

The framework development will start from reflections on health research outcomes and impact from a comprehensive perspective, involving all the stakeholders. We believe that collective initiatives can be sustainable only if each involved part can see its return of investment and alignment toward a given mission.

So far, most multi-stakeholder initiatives have lacked shared measurements of impact and supporting infrastructures to enable true alignment of efforts and accountability of results discouraging the true engagement of the different stakeholders (Zaratin et al., 2014)[1]. In particular in measuring the impact of the research in brain diseases and MS health research organizations, it is fundamental to consider the patients, as key stakeholder, and their needs and perspectives throughout the entire measurement process.

Conventional metrics related to the excellence dimension will be integrated with new measures related to the economic and financial dimension (efficiency) and to the social dimension that relates to achieving mission success (efficacy; one explicit driver of the MULTI-ACT co-accountability approach). The paradigm should shift from a single stakeholder perspective toward the engagement of all the interested parties in joint discussions for the mutual learning and collaborative understanding and the co-creation of research outcomes measurement.

Innovative metrics developed in MULTI-ACT will be instrumental in enabling the finalization of common objectives (common research agenda), together with the Return On Investment (ROI) by each involved stakeholder and integrated sustainability.

Literature reviews revealed that, where broader policy and practice impacts of research have been assessed in the literature, the vast majority of studies have relied on principal investigator interviews and/or peer review to assess research impact, instead of interviewing policy-makers and other important end-users of research. This would seem to be a methodological weakness of previous research, as solely relying on principal investigator assessments, particularly of impacts of their own research, has an inherent bias, leaving the research impact assessment process open to 'gilding the lily' (Milat AJ, 2015[2], Langella et al., 2017[3]).

[1] Zaratin P, Battaglia MA, Abbracchio MP. Nonprofit foundations spur translational research. Trends Pharmacol Sci. 2014 Nov;35(11):552-5.

[2] Milat AJ, Bauman AE, Redman S. A narrative review of research impact assessment models and methods. Health Res Policy Syst. 2015 Mar 18;13:18.

[3] Pedrini, M., Langella, V., Battaglia, M.A., Zaratin P. Assessing the health research's social impact: a systematic review. Scientometrics (2018) 114: 1227.

Considering the case of chronic brain diseases, the development of innovative and personalized care for people with such diseases can benefit only from a collective-impact research framework, in which, besides being deeply coordinated, each interested party has its return on investment aligned with the common goal of developing effective care for patients (Zaratin et al., 2016).

Starting from the Integrated Accountability Model (IAM) (M. Andreaus and E. Costa, 2014)[4] in its different accountability dimensions (mission, economic and social), new and appropriate metrics to evaluate research impact of health-sector research will be developed in a multi-stakeholder approach, considering in particular the field of brain diseases. Building on the IAM model, MULTI-ACT aims to develop a Collective Research Impact Framework (CRIF) able to measure the multi-dimensional accountability of a multi-stakeholder research organization for a given mission and agenda. CRIF is a prospective model to be implemented at the start of a research initiative, engaging stakeholders in defining metrics in a bottom-up approach, rather than a single performance assessment system. This will be instrumental to enable 'New constellations of Changing Institutions and Actors'. As a first step, the CRIF will be applied to the case study of Multiple Sclerosis (MS) as an accountability tool for evaluating the impact of MS research in a comprehensive manner, with regard to four dimensions of accountability: mission, excellence, economic and social dimensions.

MULTI-ACT foresees patients and their community as new actors and a key stakeholder in the Health Reseach & Innovation (R&I) process. Indeed, the "science of people with MS inputs" will be applied in a transversal modality throughout the four dimensions (M. Anderson and K. K. McCleary, 2016)[5].

Finally, the framework will be also a tool to be adopted by research funding and performing organizations according to their mission toward better and collaborative decision making in the design of policies, agendas, funding programmes, evaluation procedures, etc. The project will include a work package addressing the plan to extend the validation of the collective-impact research framework to the other diseases beyond MS.

This innovative approach will be instrumental to define a broader framework for collaborative initiatives in the health domain and for the evidence-based policies (Westrich KD, 2016[6], Zaratin at al., 2016[7]).

The framework will be based on key requirements that will be jointly analyzed and developed during the first months of the project:

- enabling the science of patient input,
- strategic research global agenda,

[4] Andreaus M; Costa E, "Toward an Integrated Accountability Model for Non-Profit Organizations" in E. Costa, L. Parker, M. Andreaus. Accountability and Social Accounting for Social and Non-profit Organizations, Bradford, United Kingdom: Emerald Group Publishing, 2014, p. 153-176.

[5] Anderson M, McCleary K. On the path to a science of patient input. Sci Transl Med. 2016 Apr 27;8(336):336ps11.

[6] Westrich KD, Wilhelm JA, Schur CL. Comparative effectiveness research in the U.S.A.: when will there be an impact on healthcare decision-making? J Comp Eff Res. 2016 Mar;5(2):207-16.

[7] Zaratin P, Comi G, Coetzee T, Ramsey K, Smith K, Thompson A, Panzara M. Progressive MS Alliance Industry Forum: Maximizing Collective Impact To Enable Drug Development. Trends Pharmacol Sci. 2016 Oct;37(10):808-10.

- strategic funding models,
- new metrics to measure the impact of research on patients and society,
- committed partnership between health research stakeholders that create and oversee cooperative ventures,
- common classification system to uniformly identify types of health research (database),
- mechanism to determine the nature of health research funding on a national level.

The framework will be developed through a mutual learning exercises between international heterogeneous actors such as research organizations (accounting and accountability research centers, research consortia), industry (Pharma, Biotech, Health ICT, consulting), civil society organizations (Patients organizations, diseases networks), and policy makers (Ministries, Regulatory agencies).

MULTI-ACT address some Responsible Research and Innovation (RRI) issues including the **Public engagement** topic, to make a science of patients/public input and research governance, to share a responsible progress in research and innovation with all societal actors – researchers, policy-makers, industry and civil society (see Section 2.4).

Research impact assessment could be considered as another RRI issue as only research that produces an impact on people can be responsible. Being able to measure the impact of research in a comprehensive manner means to report about the effectiveness and responsibility of research for society.

The mutual learning study will be led by the Italian Multiple Sclerosis Foundation, as member of the International MS Federation, a "boundary organisation" that acts as mediator between science and patients/society with credibility in the eyes of both.

Mapping and analysing structures and policies in international collaborative platforms/initiatives in the Health domain will lead to benchmarking and to develop a broader economic framework.

The final outcome of the project will be a new collective framework where evidence-based good practices and governance models for multi-stakeholder constellations of R&I are disseminated at EU level.

2.2 WPs Structure

MULTI-ACT builds on 9 work packages (see Figure 1). WP8 and WP9 cover cross-cutting activities, namely: Project Management and Dissemination, Communication and Exploitation, while the other work packages are devoted to the design, the development, integration, test evaluation and implementation of the MULTI-ACT action.

WP1 Science of patient input is the intent to make a science of patient input in R&I process and deals with collection and assembling of existing engagement procedures of patient engagement; co-creation of innovative routes, especially for R&I phases that are missing patient engagement procedures, and consequent development of recommendations and rules.

WP2 Development of the information sharing application (MULTI-ACT Toolbox 2.0), intends to create a multi-dimension database format based on the CRIF framework that will be developed in WP3, to be developed and tested as model to be applied at national level for example to RFPOs and public bodies.

The template will be a tool for multi-stakeholder R&I organizations to better classify research, also in relation to a given mission and agenda.

WP3 Collective Research Impact Framework: Development & Assessment – CRIF, extending from the IAM model, aims to develop a collective research impact model to measure multidimensional accountability of a multi-stakeholder research organization for a given mission and agenda. As a first step, the IAM model will be fine-tuned to be applied to the case study of Multiple Sclerosis (MS) as an accountability tool for evaluating the impact of MS research in a comprehensive manner, with regards to four dimensions of accountability: mission, excellence, economic and social dimensions. MULTI-ACT foresees patients and their community as new actors and key stakeholders in Health R&I processes. Indeed, the "science of people with MS inputs" will be applied in a cross-cutting modality throughout the four dimensions.

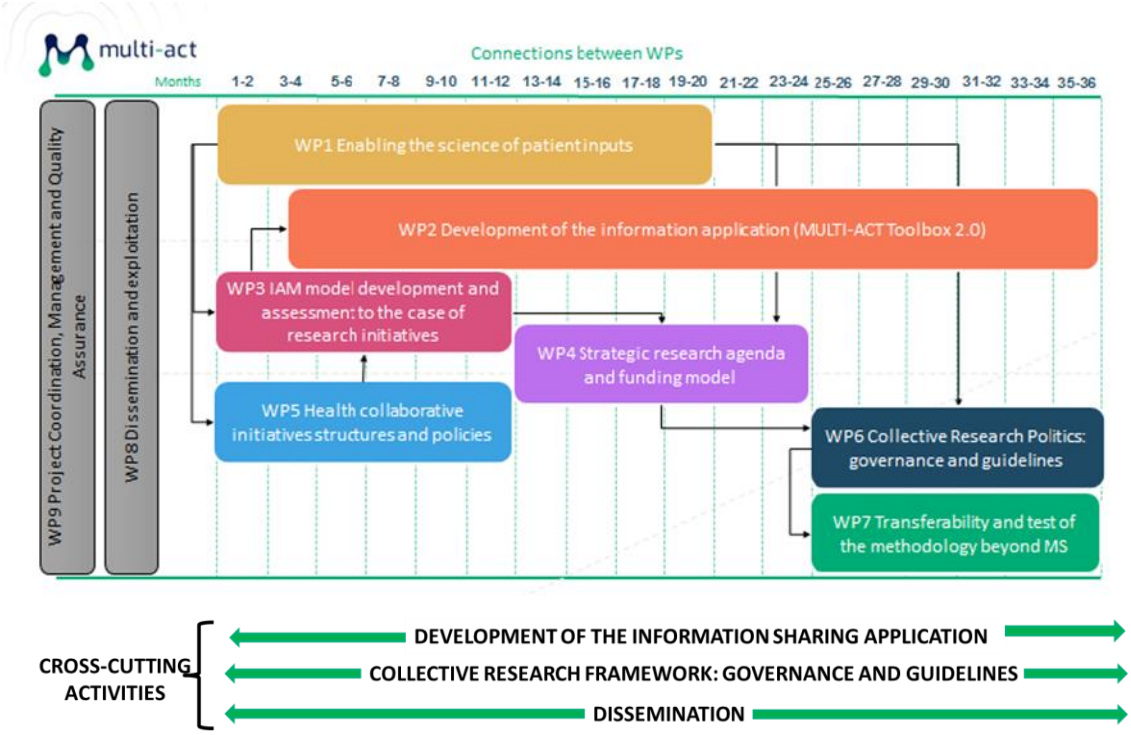


Figure 1: MULTI-ACT Gantt chart and connections between WPs

WP4 Strategic research agenda and funding model aims to implement the CRIF model to strategic planning and funding models. In continuity with the WP3, WP4 will focus on Multiple Sclerosis as first test case study to set a European strategic research and innovation agenda including priorities, actions, instruments, resources and an implementation timeline.

WP5 Health collaborative initiatives structures and policies intends to identify and analyze existing multi-stakeholders collaborative experiences and accountability models in the medical and health-care field and in other economic sectors where these experiences have been more widely applied in order to define the MULTI-ACT governance model for collaborative initiatives and the most suitable tools.

WP6 Collective Research Framework: governance and guidelines links the outcomes of all previous WPs and make them a concrete supporting tool for R&I actors. Politics and recommendations will be

collected and declined in a broad methodology approach and tools (e.g. dedicated online platform supporting research organizations in EU, provision of supporting guidelines, procedures, tools, etc.).

WP7 Transferability and test of the framework beyond MS aims to propose, apply and adapt the developed framework and related politics and methodology to selected organizations/processes OR to a BRAIN disease case-study. Actions will be done to foster the tailoring of the framework to other domains and identify collaborations for post-development work beyond the project life-span.

WP8 Dissemination, communication and exploitation: conventional channels, like exhibitions, meeting, as well as non-conventional ones, like LinkedIn, YouTube, Facebook, are exploited to diffuse the project results. Transfer to industry is evaluated and a business plan derived on pilot data. One of the key elements for success of MULTI-ACT is the early involvement in the project (as well as in the consortium) of end-users and stakeholders. This is aimed to promote shared goals and to foster communication and strong collaboration throughout the project, thus effectively implementing a bidirectional translational research approach and a co-design of functional specifications.

WP9 Project management, coordination, quality assurance provides all support to the project, promoting a shared view, and early detection of risks. A strong emphasis is devoted to ethical issues, through a dedicated ethical review board and to IPR management.

The PEG is expected to work specifically for activities related to WP1 but the concept to have a group dedicated to PE issues implies that it will be instrumental along the overall project development. In particular, the PEG will contribute to the link on PE tools to be downloaded in the MULTI-ACT Toolbox 2.0 (WP2); to the patient-related stakeholder engagement actions planned in WP3; to test the PE guidelines in the selected multi-stakeholder MS research organizations (WP4); to check in a patient oriented vision the politics developed in WP6; to help the scalability of MULTI-ACT beyond MS in WP7; to facilitate the communication of MULTI-ACT evolution and progresses to patient communities (WP8).

2.3 Focus on WP1 “The science of patient input”

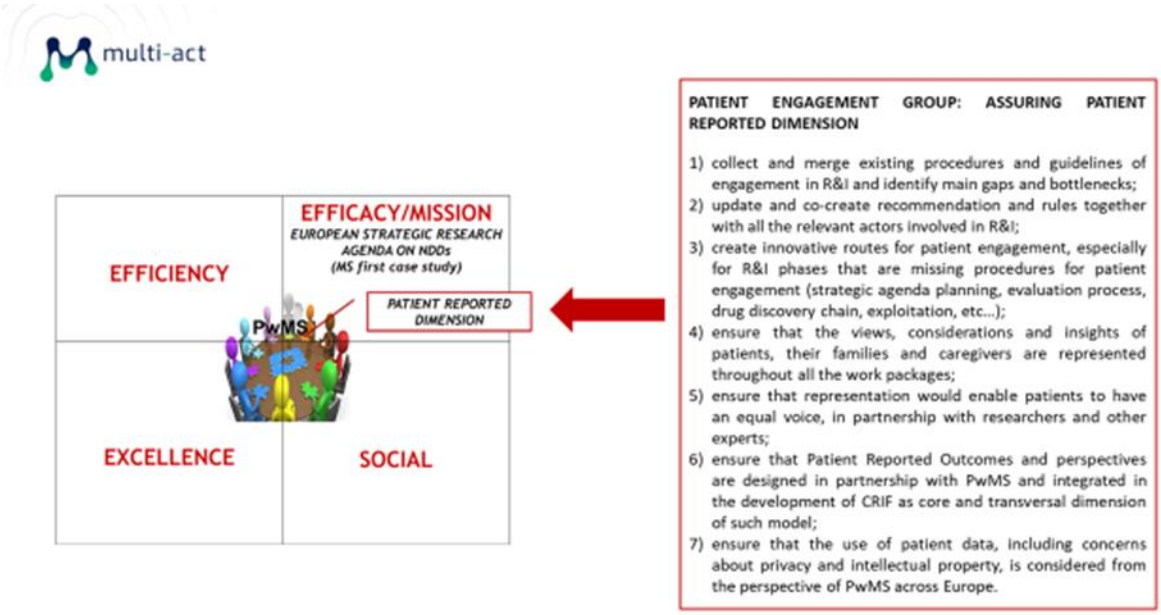


Figure 2. WP1 objectives and aims

The overall WP1's objective is to provide a guidance for all R&I stakeholders about who and how to engage, when and what information is required, to enable 'science of patients input'. Innovative practices, methodologies, tools and strategies for patient engagement is the primary expected outcomes of WP1's activities.

2.4 MULTI-ACT expected outcomes and RRI

A central activity projected in MULTI-ACT is the establishment of a group of experts focused on PE, engaged primarily on WP1 activities but indirectly also engaged to the overall MULTI-ACT project in response to the call for Responsible Research & Innovation (RRI)[8].

[8] https://ec.europa.eu/research/swafs/pdf/rome_declaration_RRI_final_21_November.pdf

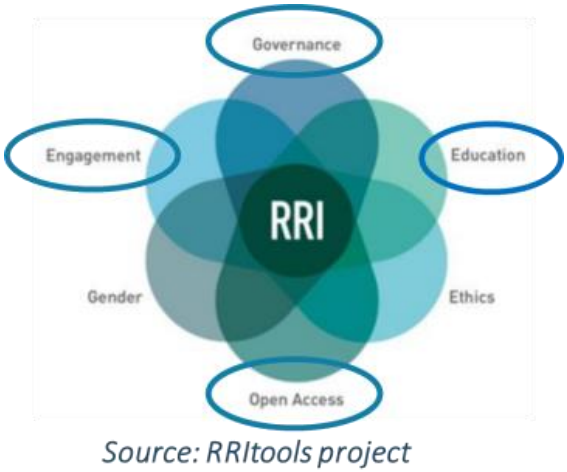


Figure 3. RRI topics, source: https://www.rri-tools.eu/it

As presented in Figure 3, MULTI-ACT responds to the following RRI key themes:

- **Governance**: Innovative governance strategies, methodologies and tools for RRI co-created by engaging R&I multivariate-stakeholders);
- **Education and Open Access**: open access to guidelines for innovative governance strategies and innovative routes for patients engagement;
- **Engagement**: MULTI-ACT overall MULTI-ACT co-creation approach. Involving stakeholders and the public in the processes of R&I, while dealing with Health research, means involve patients and their communities.

This engagement helps to ensure that the results of research match the values, needs and expectations of the primary target as well as society.

MULTI-ACT aims to make patients becoming partners and key stakeholder in the process of co-creation within the overall health RRI. Patients will be engaged in the design of innovative strategies, methodologies and tools for PE across R&I.

The concept for the PEG could be relevant beyond the MULTI-ACT project and, while considering further exploitation, the PEG could set the basis to a broader PEG to be implemented at European level in order to monitoring the European progresses on the PE topic (as sub-topic of Engagement), in strictly connection with RRI evolution.

Patients are engaged, according to guidelines develop by PEG in activities concerning research impact measurement to the construction of consensus among stakeholders. Patients and patient organizations are key stakeholders from a RRI point of view for two reasons:

a) Research outcome measurement is complex, involving different dimensions that are modelled through the CRIF. This complexity calls the attention to the need to consider the values and the perspectives of different stakeholders, in particular those who can input their immediate and personal insight into MS research assessment.
b) Health research involves a degree of uncertainty that suggests the need to extend the assessment of research beyond peer researchers to laypersons, such as patients.

c) Patients and Patients Organizations will be bring valuable, however different contribution to the activities concerning research impact measurement.

PEG will develop different strategies to mediate, negotiate and build shared perspectives on the development of innovative metrics in MULTI-ACT.

2.5 Key Performance Indicators for MULTI-ACT

The MULTI-ACT Description of Action states that at least **300 patients** should be engaged to ensure the development of an appropriate framework (within the 3 years project), as indicated in the KPI table (Table 1).

N°	Impact	D/I [48]	Term	Beneficiaries	KPIs	Means of verification
1	Innovative framework used by various R&I stakeholders for their strategic planning	D	M	RFPO, Academia, Industries (Pharma, Biotech, ICT, consultancy), Policy makers (EC, Ministries, Regions, Local Agencies, Insurers), Regulatory agencies (EMA, Medicine National Agencies), Patients organizations, Foundations	Number of innovative validated framework by the end of the project (1)	D3.9, D6.1
					Number of organizations that voluntary ask to adopt the framework after the empirical validation within 12M since project's end/assessment phase (3)	Direct contact
					Number of single stakeholders involved for developing the framework during the project (10)	D3.1-D3.6, D7.1-D7.6
					Number of singles organizations that accept to test the framework during the project (2)	D7.6
2	Increased adoption of best practices standardized policies on patients engagement in Health R&I process (WP1)	D	M	Health RFPO , Patients organizations, Funding organizations	Number of organizations that download the policies during project life (3)	Database template, D2.4, D6.2
					Number of organizations that state a change due to the policy after 3 years since project's end/assessment phase (4)	Survey to who downloads the files
3	Increased patients engagement in Health R&I process	I	L	Patients, family, caregivers	Number of patients engagement procedures published (1) Number of research organizations that downloaded the published patients engagement procedures (40)	D1.8, D6.2, Survey to who downloads the files
					Number of patients engaged for developing the framework (300, via MS Societies' Network)	

Table 1. "Expected impacts, KPIs, target groups" extracted by MULTI-ACT DoA (GA n.787570)

To comply with this KPI, patients are engaged at different levels:

- Patients engaged in activities of MULTI-ACT with operative working role;
- Patients engaged in the governance of MULTI-ACT with advisory role;
- Patient associations, organizations and initiatives engaged in the governance of MULTI-ACT (see Section 7 on EAB, PF);
- Extensive outside Patient Engagement through Patient Organizations (see Section 3.2 on PE in the PEG).

3 PEG rationale and concept

In MULTI-ACT framework the establishment of a dedicated panel of experts in charge to operatively work on WP1 activities and in all activities related to patient engagement is fundamental in order to facilitate the development of all activities that need expertise on PE.

3.1 The science of patient input: the context

Considering the case of brain diseases, the development of innovative and personalized care for people suffering of such diseases can benefit only by a collective-impact research framework, in which, besides being deeply coordinated, each interested party has its return of investment aligned with the common goal of developing effective care for patients (Zaratin et al., 2016)[9]. Starting from this assumption this document aims to present the strategy that will be used to develop the guidelines for Patient Engagement in the MULTI-ACT project in order to assure their contribution in the development of the Collective Research Impact Framework (CRIF) as key stakeholder.

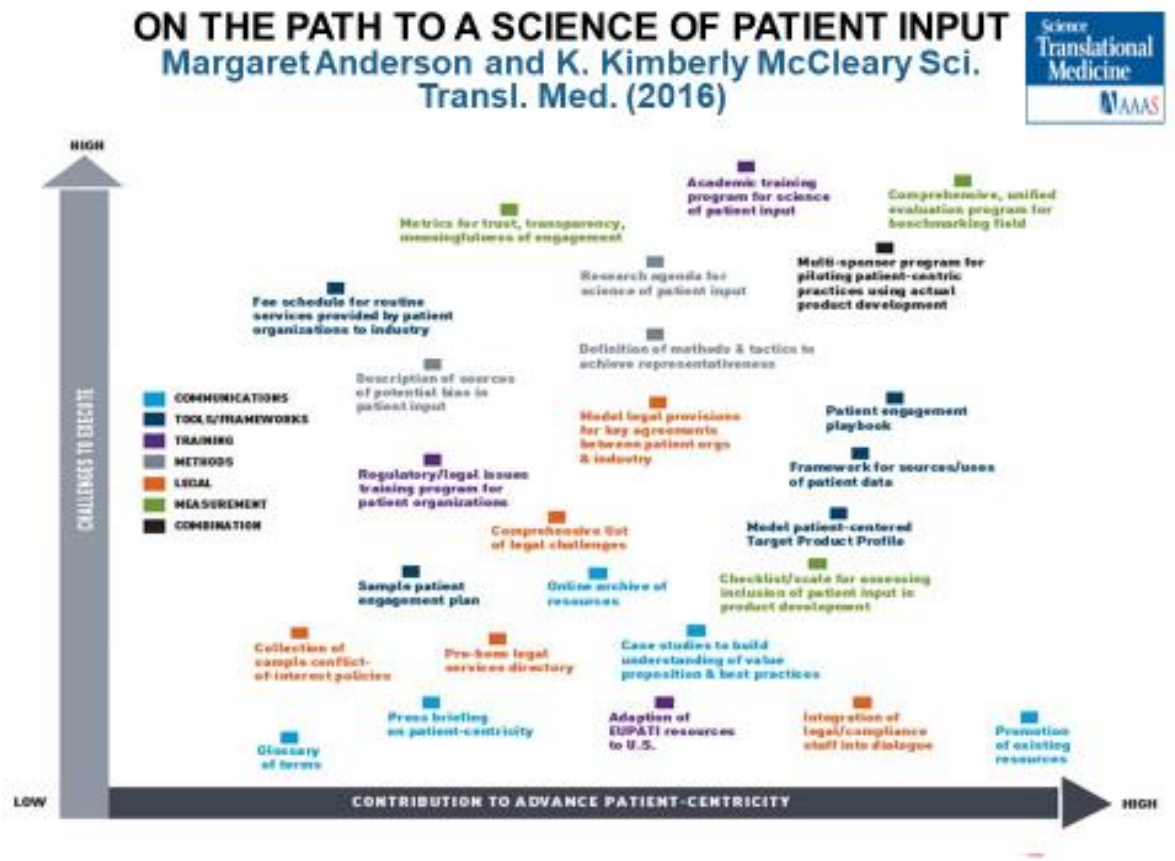


Figure 4. Anderson M, Kimberly McCleary K. On the path to a science of patient input. Science Translational Medicine, 2016

[9] *Zaratin P, Comi G, Coetzee T, Ramsey K, Smith K, Thompson A, Panzara M. Progressive MS Alliance Industry Forum: Maximizing Collective Impact to Enable Drug Development. Trends Pharmacol Sci. 2016 Oct;37(10):808-10.*

What began as an extension of patient advocacy[10] has now evolved into an emerging scientific discipline aimed at understanding and incorporating patient needs and perspectives into the processes of developing, regulating, and delivering new therapies as well as improving care: the science of patient input (M. Anderson 2016) [11].

This field has different and urgent priorities which are effectively summarized and represented in Figure 4, where they are positioned according to their expected contribution to advance patient centricity and how challenging they are to execute.

One of the mail goal of this new field is to develop rigorous methods to better integrate patient perspectives, needs, and priorities across the translational research continuum.

FasterCures tracked more than 70 collaborative initiatives that are further defining and shaping patient-centered practice including patients' data sources and measurement/metrics12. In the United Kingdom, for instance, the involvement of stakeholders in social and health care policy has been well recognized since 1996. The British National Institute of Health recognized that individual and community stakeholders determine important aspects of health care services and research, and the project INVOLVE13 was established to achieve this engagement. In the United States, the Patient Centered Outcomes Research Institute (PCORI) was established in 2010 and placed great importance on the engagement of patients and other stakeholders in the research process14.

The Engage2020 Action Catalogue is an outcome of the Engage2020 project, which is funded by the European Commission. The Action catalogue is an online decision support tool that is intended to enable researchers, policy-makers and others wanting to conduct inclusive research, to find the method best suited for their specific project needs ((http://actioncatalogue.eu/).

Moreover practical guidelines for patient engagement have been developed for European Union (EU) healthcare research projects15 that dealt with patient engagement.

The different initiatives approach this field from a different vantage point. It is essential to perform the work required to create the field of patient input ensuring maximum synergies among all the initiatives focusing on the science patient input. PARADIGM, a public-private partnership, co-lead by the European Patients' Forum (EPF) and European Federation of Pharmaceutical Industry and Association (EFPIA), is working to provide a unique framework that enables patient engagement (PE) in synergism with European Patient Academy on Therapeutic Innovation (https://www.eupati.eu/) and Patients

[10] Patient advocates give a voice to patients on healthcare-related issues, informing the public, the political and regulatory world, health-care providers, organizations of health-care professionals, the educational world, and the medical and pharmaceutical research communities.
[11] Anderson M, Kimberly McCleary K. On the Path to a Science of Patient Input," Science Translational Medicine, 2016 Vol. 8, Issue 336, pp. 336ps11
[12] http://www.fastercures.org/programs/patients-count/science-of-patient-input-resources
[13] http://www.invo.org.uk/about-involve/
[14] https://www.pcori.org/research-results/patient-centered-outcomes-research
[15] http://www.europeanlung.org/assets/files/publications/ubiobookletpip.pdf

focused Medicine Development (http://patientfocusedmedicine.org/). The European Patients' Academy (EUPATI) is a pan-European project implemented as a public-private partnership by a collaborative multi-stakeholder consortium from the pharmaceutical industry, academia, not-for-profit, and patient organisations. The Academy was started, developed and implemented as a flagship project of the Innovative Medicines Initiative (http://www.imi.europa.eu/), and continues to be led by the European Patients' Forum. EUPATI has already trained 96 patient experts on medicines development, clinical trials, medicines regulations, health technology assessment. Additionally, EUPATI offers and maintains the Toolbox on Medicine Development, and coordinates a network of national platforms for patient advocates.

Patient engagement in healthcare research is likely feasible in many settings. However, this engagement comes at a cost and can become tokenistic. Research dedicated to identifying the best methods to achieve engagement is lacking and clearly needed. To make a meaningful shift to patient-centeredness and in the development of science of patients input, quality measurement needs to focus on patient priorities. This is particularly important for ensuring content validity and still remain the main challenge of the field. This is even truer when applied to the development of a collective research impact framework to measure impact of health research on patients and society.

Within this frame, MULTI-ACT Patient Engagement focus Group aims to enable the use of resources that are already available (i.e. outcomes and outputs of already existing PE initiatives, as well as the discovery and all efforts already done at global level on this topic), and to capture a baseline assessment to benchmark growth on PE and identify areas of unmet need to enable patients' engagement in a cross-cutting modality throughout the four dimensions of the CRIF in line with the co-accountability approach of MULTI-ACT. The patients engagement guideline developed by PEG will assure the involvement of patients, as key stakeholder, in line with the cocreation philosophy that is at the root of the project. PEG will be led by the Italian Multiple Sclerosis Foundation, as member of the International MS Federation, a "boundary organisation" that acts as mediator between science and patients/society.

MULTI-ACT PEG deliverables will be both supervised and exploited by two MULTI-ACT advisory bodies: an External Advisory Board (EAB) and a Patients Forum (PF) including representatives from relevant organizations (e.g. EPF and EFPIA organizations). See Section 7 for further details on EAB and PF.

The multi-stakeholders co-creation approach, where patients is a key stakeholder, will be enabled by applying the innovative stakeholders engagement framework ICEE (Identify, Connect, Engage and Enable) that is core and transversal in the development of the MULTI-ACT project.

3.1.1 I-CEE methodology for stakeholder engagement

Multi-stakeholder engagement is at the root of the MULTI-ACT project. When translating research into practice, engaging the stakeholders is explicitly intended to make the outcomes of translation relevant to its constituency of users. In particular in measuring the impact of the research in BRAIN diseases and MS health research organizations, it is fundamental to consider the patients as key stakeholders and their needs and perspectives throughout the entire measurement process. Innovative practices, methodologies and measure for patient engagement is a key expected outcome of MULTI-ACT. Also

building on the outcomes of relevant initiatives[16], stakeholders empowerment in the MULTI-ACT will be carefully carried out based on the I-CEE Methodology and the related technique of the Incremental Cross-exchange Roundtables (ICR).

The I-CEE Methodology was developed by EHMA within the framework of the Horizon 2020 project IC-Health (GA N.727474). The project was focused on improving digital health literacy of European citizens and had a strong focus on engaging with specific categories of stakeholders to deliver the different phases of its implementation. EHMA, as one of the main partners of the project, developed this original strategy composed of four key steps to ensure identification of key stakeholders, structured connection with them, constant engagement and enabling-focused interactions.

Given the success of the I-CEE methodology and how it supported the IC-Health project in its successful implementation, certified by positive reviews by European Commission officers and external reviewers, EHMA has adopted and adapted the I-CEE methodology to support other projects strongly focused on the importance of stakeholder engagement, including MULTI-ACT.

Further reference is available on approved deliverables of the IC-Health project, in particular the deliverable D5.1 – Dissemination Strategy, available on the website ichealth.eu[17]

The ICEE Methodology entails the following four stages: **I**dentifying - **C**onnecting, **E**ngaging and **E**nabling (**I-CEE**) methodology (Figure 5).

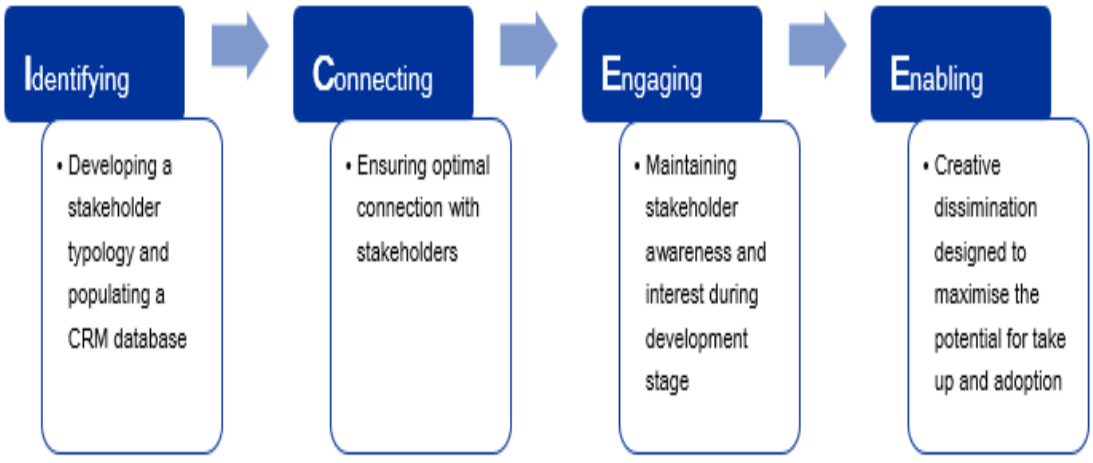


Figure 5. ICEE Methodology

Given the importance of stakeholder engagement in MULTI-ACT, where possible, activities will be organized applying the technique of the Incremental Cross-exchange Roundtables (ICR), which will facilitate the engagement participants, ensuring a high-level interaction and the development of concrete solutions to beforehand identified issues.

[16] Bradley P, Akehurst R, Ballard C, et . lTaking stock: A multistakeholder perspective on improving the delivery of care and the development of treatments for Alzheimer's disease. Alzheimers Dement. 2015 Apr;11(4):455-61. Epub 2014 Apr 21.
[17] https://ichealth.eu/results/project-deliverables/

The ICR technique entails the following steps:

- Introduction and topic-oriented presentation: the ICR Moderator introduces the ICR methodology, rules and objectives. The session is opened with thematic presentations, addressed to the audience, introducing the topics of discussion. Presentations are followed by a structured discussion with the audience aimed to identify problems/questions that participants will have to find concrete answers/solutions to in the subsequent phase.
- Small roundtable cross-exchanges: participants are divided into tables, each of which led by a Table Facilitator and assigned one of the questions/problems identified during the initial phase. Each table has a fixed amount of time (on average 20 minutes) to collectively find a single answer/solution to the question/problem posed, which will be recorded by the Table Facilitator. At the end of the given time, participants will rotate and participate in another table, finding a collective answer/solution to another question/problem. The process will be repeated until each participant has attended each table.
- Preliminary results presentation: each Table Facilitator has collected the answers/solutions identified by their participants. The questions/answers, which may be identical, similar or divergent, will be presented to the audience without mediation from the Table Facilitator, who will just provide context and background on the discussion held which led to the specific outcome. The audience can ask questions to the Table Facilitators.
- Collective wrap up: the audience will have to collectively agree on a single solution/answer for each of the questions/problems posed. The audience may decide to pick one of the proposed solutions, to develop a new one combining those proposed or to disregard the outcomes and come up with an alternative solution/answer.

The above stakeholder engagement methodology will be conceptualized in a prototype information sharing and decision support tool, the MULTI-ACT Toolbox, demonstrating the MULTI-ACT models and providing advice to healthcare policy makers on the best methods to achieve engagement. The Toolbox portal-type tools will enable policy makers to experience the results of the project and also serve as a blueprint of future healthcare research integrating patient perspectives as one of the key stakeholder. The MULTI-ACT Toolbox will provides link with the methods objectives of deliverables of WP1.

3.2 Patient Engagement in the PEG

During the MULTI-ACT Kick-off Meeting, held in Camogli on the 14th and 15th May 2018, it emerged that MULTI-ACT should grasp and build upon on both the personal perspective of the real individual patients as well as the 'advocacy' experience of the organizations who represent them. However, this approach is to be carefully managed taking into account that the patient as an individual is expressing his/her personal opinion while the patients' organizations are giving voice to the whole community of patients suffering from a certain disease. The ideal would be to find a happy medium between patients reported perspectives that work at population level and the ones that can be individualized for use in care and treatment. Also, having non-experts patients chairing in advisory bodies or operative working groups would make the discussion about certain topics difficult to manage. The conclusion was that the ideal configuration for the overall approach is having both views represented identifying members of patients' associations (who can provide the long term vision due to their advocacy role) and patients

themselves (thus bringing their short term view too). In support to this view, several representatives of patient organizations are people with the disease as concrete example of how the two perspectives can match.

It is also interesting to mention that the scope of European Patients' Academy (EUPATI), represented in the PEG, is indeed to make patients experts on research topic. Although EUPATI primary scope is concentrated on making patients aware of the drug discovery and development process rather than understand patients' priorities in measuring research impact, EUPATI graduates are very much involved in several European projects, like PARADIGM, as well as many patient engagement activities to show that the EUPATI training is an excellent basis to become patient advocates at 360 degrees.

PEG establishment is the first step that deals with PE and related ethical issues. FISM engaged the Ethical manager to assess and verify that all ethical regulations are applied, with particular regard to privacy in the disclosure of information related to PEG's goals (see Section 8).

3.2.1 Patient engagement via Patients Organizations

The preliminary concept for engaging patients in MULTI-ACT through the PEG is to engage them via the Patients Organizations. An example is presented in Figure 6 with the case of Multiple Sclerosis International Federation (MSIF). The engagement approach will be defined together with PEG members during the next months and will be finalized and better described in the following deliverables.

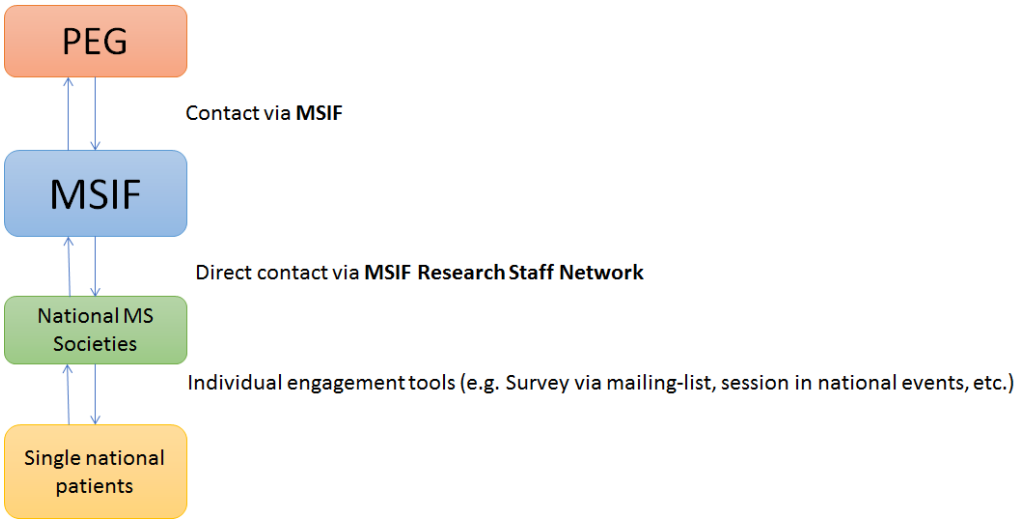


Figure 6. Preliminary concept of PwMS engagement via Patients Organizations (via MSIF as example)

Figure 6 highlights the example of engagement of PwMS via MSIF: FISM, ARSEP and the US National MS Society (as members of the PEG) could interact with MSIF and MSIF Research Staff Network in order to leverage the engagement of national MS societies worldwide. Each single national MS Society could in turn engage national patients by its individual engagement tools.

This approach, via MSIF Research Staff Network, can assure geographical coverage of engagement (Figure 7).

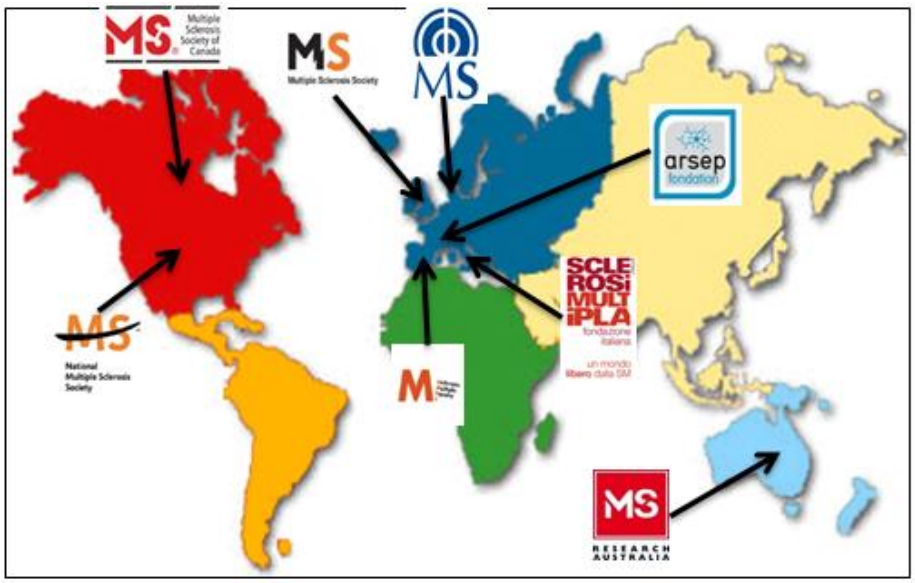


Figure 7. Multiple Sclerosis International Federation: MS Societies members of the Research Staff Network

4 Actions for PEG setup

The idea was to set-up a working group with an extensive expertise on PE across geographical areas, diseases, health domain and topics, integrating MULTI-ACT consortium expertise with eventual external expertise in order to have a wide representation of PE experts.

The MULTI-ACT consortium is composed by 10 partners from 7 European countries (IT, ES, PT, FI, BE, LUX, FR, PL), forming a multidisciplinary combination of specialist on different areas, that perfectly fits with the MULTI-ACT concept and needs. The collaboration among academia and research organizations (UNITN, UBU, UCP, ATA), consulting companies (EY), other companies (INTRA, DiA), European organizations (EBC, EHMA), RFPOs (FISM, ARSEP and the linked MSIF, EMSP, PMSA), policy makers and governmental institutions (ministries and municipalities linked to EHMA and DiA), makes it possible to create innovative concepts for research impact assessment and accountability of R&I processes and actors, considering the point of view of all the different stakeholders involved. Being the focus on R&I actors, the consortium is composed of a **quadruple helix approach** where the expertise in economics research (UNITN, UBU, UCP, UTA, EHMA) is combined with the institutional dimension (research funding, healthcare services), represented by the public municipalities/ministries linked with EHMA and DiA, the market oriented approach (EY, INTRA, DiA) is completed with the expertise in diseases and patients field (FISM, ARSEP, EBC). Society is represented as well by patients' organizations and ministries/municipalities while industry's interests are put forwards by representative organizations in the External Advisory Board (e.g. EFPIA, ECHAlliance).

Activities related to PE will of course benefit from all this expertise but the idea is to strengthen the expertise linked to PE as patients are expected to be the **core and key stakeholders** to be transversally involved and deserve attention also with respect to **ethical issues** (see Section 8).

The internal expertise is integrated with external expertise considering different levels of engagement. In particular we wanted to integrate the expertise on the specific MS case study, already on board with FISM, ARSEP and their membership to European and International MS organizations (i.e. EMSP, MSIF) with expertise on PE in general and across diseases.

To engage expertise across diseases we identified main initiatives on PE and finally decided to involve EUPATI, Consumer Involvement Laboratory of the Mario Negri Institute and Engage2020.

A summary of the engagement levels are:

1) Disease specific expertise (focused on MS as a case study):

International MS Federation MSIF (disease specific at international level)

European MS Platform EMSP (disease specific at European level)

2) Across diseases:

European Patient Academy EUPATI

Mario Negri Institute, Laboratory of Medical Research and Consumer Involvement

Engage2020

For each of the mentioned entities and initiatives we have identified an individual expert on PE that will bring his/her personal expertise and experience in the PEG and that will also represent the organization in the PEG (see Section 5 for individual members).

4.1 Internal expertise

Internal expertise is primarily represented by partners with expertise focus on management of health, diseases and patients. In particular FISM, ARSEP representing people with MS (PwMS) and MS disease, EBC representing different brain diseases and link with related patients and EHMA representing Health management issues (final users of outcomes).

4.1.1 Partner #1 Italian MS Foundation FISM

The Italian Multiple Sclerosis Society (AISM), through its Foundation (FISM), is the leading funding agency of research in Multiple Sclerosis (MS) field in Italy and the third funding agency worldwide (after US and Canada MS Societies) to better understand the causes of the disease, to improve the quality of life of people with MS (PwMS) and to provide better treatments toward a definitive cure for a MS. The overall goal of the MS Society is to make the bridge walkable between PwMS and health care government agencies and thus to support people with MS in making decisions for their treatments and quality of life.

Italian MS Society advocates and campaigns to raise public awareness and understanding of MS by uniting the national MS movement though campaigning and advocate for the interests and rights of people affected by MS, in order to improve their quality of life. Information and communication activities of the Italian MS Society aim to empower PwMS by providing information, which meet the needs of people affected by MS.

Italian MS Society, through its Foundation, finances, influences and promotes research via extramural research projects, fellowships and infrastructures; performs research in the areas of rehabilitation, public health and health related socio-economics (intramural research supported by public funds); promotes information, communication and training for healthcare and social professionals as well as for the patients and the general public.

Since 1987, extramural research projects and programmes have been funded on MS domains such as pathogenesis, risk factors, disease classification and diagnosis, new treatments, neurorehabilitation, neurophysiology, quality of life, advocacy, networks, infrastructures (e.g. MRI and neuroscience lab facilities). On the other side, intramural research projects includes 1) Rehabilitation: health monitoring, innovative ICT-based treatments and personalized protocols, predictive medicine, personalized medicine, anatomo-functional correlates, enabling technologies, functional outcomes, patient-centred outcomes research, rehabilitation treatment effectiveness, sport, well-being and physical activities for people with MS; 2) Public Health: cost of illness studies, registers of disease, epidemiological studies (i.e. prevalence/incidence, unmet need, work and disability, quality of life studies); 3) Socio-Economics: innovative non-profit organizational and funding models, innovative research impact measurements, etc.

Italian MS Society Foundation is member of the International MS Federation (MSIF), international umbrella organization, established in 1967, that links the activities of more than 85 national MS societies worldwide stimulating international cooperation.

Italian MS Society Foundation is member of the International Research Staff Network, which includes staff from all the key MS organizations amongst the membership that have common research agendas and dedicated research infrastructures and of the International Medical and Scientific Board (IMSB), that has the role to advise on matters related to international MS research, and to form a professional link between the MS medical and research community and the MSIF.

MSIF and MS member organizations focus their efforts on actions that contribute to a world in which people with and affected by MS are able to benefit from.

Italian MS Society and its Foundation is also one of the managing member of the International Progressive MS Alliance. In 2012 the PMSA (Fox et al., 2012) was established as a collaboration between leaders from MS societies around the globe, volunteer experts, academics, and the industry to expedite the development of disease-modifying and symptoms management therapies for people living with progressive MS. The managing members of the Alliance are MS Research Australia; Multiple Sclerosis Society of Canada; Italian MS Society; UK MS Society; USA National MS Society and Multiple Sclerosis International Federation. In an unprecedented manner, through advocacy organizations that represent them worldwide, people with MS were demanding a renewed focus on progressive MS with the goal that relevant stakeholders work together to maximize their collective impact (P. Zaratin et. al. 2016,) on developing new treatments for this form of MS. Through a series of scientific and strategic

planning meetings, the PMSA identified and developed a strategic research agenda, launched research funding initiatives and a multistakeholders review process.

4.1.2 International Multiple Sclerosis Federation MSIF (FISM, ARSEP membership)

MSIF (www.msif.org), established in 1967, is a unique global network of MS organisations that links the activities of some 108 MS organisations in 95 countries worldwide, stimulating international cooperation. Their mission is to lead the global MS movement to improve the quality of life of people affected by MS and to support better understanding of the treatment of MS.

They bring together the work of more than 100 MS organisations to deliver programmes to help people affected by MS around the world. They strengthen those organisations in countries where there is little support for people with MS. Together they lead the fight against MS and work to improve the quality of life of people affected by MS in more than 90 countries. MSIF, as an umbrella organization of MS organisations, through cooperation with and among its Members and the International Research Staff Network (which includes staff from all the key MS organisations amongst the membership that have common research agendas and dedicated research infrastructures) and with their advisors from their International Medical and Scientific Board, stimulates, supports and partners international collaborations in areas of greatest need and promise for people with MS.

MSIF and MS members organizations focus their efforts on actions that will contribute to a world in which people with and affected by MS are able to benefit from. In order to foster collaboration among relevant stakeholders towards the common goal to “Better scientific understanding of MS and more ways to treat it - leading one day to prevention and a cure”.

Patients’ engagement and measuring impact of research are at the root of the 2017 - 2021 MSIF strategy (Ensure people affected by MS are part of strategic research decision making processes across the Federation: http://www.msif.org/wp-content/uploads/2017/08/MSIF-Strategy-2017-2021-web.pdf).

4.1.3 European MS Platform EMSP (FISM, ARSEP membership)

EMSP (www.emsp.org) brings together MS activists from across Europe, relying on a growing network of 40 member organizations from 35 European countries. We are the only MS specific organization that can influence health and other EU policies. This capacity was proven again in 2014, when EMSP received a European Commission grant to produce and promote a Pact for Employment supporting people with MS and other neurodegenerative diseases. At the same time, EMSP continues to strengthen ties with other patient organizations and federations – such as the European Patients’ Forum (EPF), the European Federation for Neurological Associations (EFNA) and the European Brain Council (EBC). They are also in a position to leverage their direct access to the European regulator for pharmaceutical products, the European Medicines Agency (EMA).

4.1.4 Partner #6 European Brain Council EBC

EBC, taking advantage of its longstanding advocacy experience and networking in the area of brain disorders, will facilitate and stimulate the dialogue among the various actors involved in the project.

EBC is a non-profit organisation founded in 2002 aiming to promote brain research in Europe, improve treatment, care and quality of life of people living with brain disorders. It is a coordinating council for European organisations with an interest in the brain. Its members are: FENS - Federation of European Neuroscience Societies; Pan European Regional Committee (PERC) of the International Brain Research Organization (IBRO); EAN - European Academy of Neurology; EFNA - European Federation of Neurological Associations; ECNP - European College of Neuropsychopharmacology; GAMIAN-Europe - Global Alliance for Mental Illness Advocacy Networks; EPA - European Psychiatric Association. It also has observers from the WHO. It includes delegates of the pharmaceutical and device industry. EBC thus represents a vast network of patients, doctors, scientists, and along with its industrial partners make it eminently suited to work in partnership with the EU. The EBC stimulates dialogue between scientists, society and all interested parties by promoting collaboration of member organizations with the European Commission, the European Parliament and other relevant EU and international institutions. EBC has been involved in a number of EU funded projects and took a lead in work packages in some of them. Most relevant projects include PARADISE (dissemination WP leader) and NERRI (promoting RRI, involving policy makers).

4.1.5 Partner #8 European Health Management Association EHMA

The European Health Management Association is a Belgium based non-profit membership organisation that focusses on enhancing the capacity and capability of health management to deliver high quality healthcare. EHMA has been in existence for 35 years and has a strong tradition as an organization for healthcare-providers, universities and others, providing learning and meeting-places for scientists, managers and policymakers. EHMA operates at an international, European and national level, with a Membership of over 80 organisations and individuals and a broader network covering the WHO Europe Region. EHMA's vision is to see the spread of knowledge on effective practice delivering improved health and wellbeing for Europe's citizens and communities. Built around a dynamic European Health Network of managers, educators, researchers and policy makers and experts, EHMA achieves its goal by making knowledge about effective practice more accessible and by facilitating improvement activities to take place. Within this framework of activities and objectives, patients engagement represents a cross-cutting priority for EHMA. To improve health management at all levels, from research to practice, EHMA work with its membership and broader network to ensure that all the key stakeholders involve patients with right methodology, procedures, tools and activities, to guarantee the development of patients-oriented research and evidence-based practice. In addition, EHMA has been traditionally involved in several European Projects with a strong patients-focused orientation: currently the Association in involved in IC-Health, a H2020 project that aims at co-creating MOOCs (Massive Open Online Courses) with citizens and patients to improve their digital health literacy; and SUSTAIN, a H2020 project with the objective of improving integrated care for older people towards sustainability, patient-centeredness and safety.

4.1.6 Partner #9 French Multiple Sclerosis Research Association ARSEP

ARSEP was founded in March 1969. In 2010, ARSEP became a Foundation. It is recognized as a public utility. ARSEP Foundation is the leading funding agency of research in Multiple Sclerosis (MS) field in France. Its objectives are to better understand the causes of the disease, to improve the quality of life

of people with MS (PwMS) and to provide better treatments toward a definitive cure for a MS and to support people with MS in making decisions for their treatments and quality of life.

Information and communication activities of ARSEP Foundation aim to empower PwMS by providing information which meets the needs of people affected by MS. It has two primary missions. ARSEP Foundation is member of the International MS Federation (MSIF), international umbrella organization, established in 1967, that links the activities of more than 85 national MS societies worldwide stimulating international cooperation.

ARSEP Foundation is member of the International Research Staff Network, which includes staff from all the key MS organisations amongst the membership that have common research agendas and dedicated research infrastructures.

Indeed, ARSEP Foundation promotes relevant international initiatives and networks as the Progressive Multiple Sclerosis Alliance (PMSA), established in 2012 to speed up the development of treatment for progressive MS. ARSEP Foundation's resources include researchers in the areas of Neuroscience, Rehabilitation, Public Health, Epidemiology, Bio-statistics, Bio-engineering, Neurobiology, and Psychology. Moreover, ARSEP Foundation is linked to the French MS Federation, which organizes campaigns to sensitize the public, the media and governmental health agencies, explain the MS and defend the interests and rights of those affected by the MS in order to improve Their quality of life.

The collaboration with national and international multi-disciplinary partners and academic departments makes the ARSEP Foundation an effective research infrastructure where experts on different domains can perform joint research programmes while exchanging expertise and facilities. ARSEP, taking advantage from its international network, including the International MS Federation (MSIF) and the Progressive MS Alliance (PMSA), will have the role to enable patient reported dimension throughout then proposal and to communicate/disseminate scientific results to people with Multiple Sclerosis, families, friends, and caregivers.

4.2 External expertise

4.2.1 European Patients' Academy EUPATI

EUPATI (www.eupati.eu) is a pan-European project implemented as a public-private partnership by a collaborative multi-stakeholder consortium from the pharmaceutical industry, academia, not-for-profit, and patient organisations. The Academy was started, developed and implemented as a flagship project of the Innovative Medicines Initiative, and continues to be led by the European Patients' Forum. EUPATI has already trained 96 patient experts on medicines development, clinical trials, medicines regulations, health technology assessment. Additionally, EUPATI offers and maintains the Toolbox on Medicine Development, and coordinates a network of national platforms for patient advocates. They focus on education and training to increase the capacity and capability of patients to understand and contribute to medicines research and development and also improve the availability of objective, reliable, patient-friendly information for the public. They ran two English language Patient Expert Training Courses in 2014 to 2016 and a web-based toolbox, hosting educational material in English, Italian, Spanish, Polish, German, French, Dutch, Romanian, Portuguese, Danish and Russian for use by the patient community across Europe and beyond. Ongoing projects of EUPATI include rigorous content development for patient education, the furthering of advocacy skills of patient experts, and

the strengthening of a European patient movement, and a continuously updated inventory of possibilities for patients to get involved in biomedical research and development. EUPATI is engaged in PARADIGM.

PARADIGM, a public-private partnership, co-lead by the European Patients' Forum (EPF) and European Federation of Pharmaceutical Industry and Association (EFPIA), is working to provide a unique framework that enables patient engagement (PE) in synergism with EUPATI and Patients focused Medicine Development (http://patientfocusedmedicine.org/).

4.2.2 Mario Negri Institute - Laboratory of Medical Research and Consumer Involvement

IRCCS-Mario Negri Institute for Pharmacological Research (www.marionegri.it) is a scientific organisation for research and education in the biomedical field. The aim of the Institute is to improve the quality of human health and life. The Institute's three main fields of interest are: cancer, mental and nervous system disorders and cardiovascular diseases. The Institute consists of about 30 Research Laboratories organised in 50 units and a 12 of administrative and service facilities. A total of 750 people work.

The Laboratory of Medical Research and Consumer Involvement promotes research activities aimed at developing the participation of citizens, patients & their representatives to the health decision process. The Laboratory coordinates consensus conferences, citizens' juries, and ad hoc surveys, and a training course dedicated to representatives of associations of citizens and patients that allows to deal effectively with the medical and scientific world. Moreover the Laboratory is involved in projects for the assessment of the type of information provided on diseases and treatments, and the development of health information internet portals. Main research projects: Partecipa Salute: a strategic alliance between patient groups, citizens and scientific medical communities; Jury of citizen on cystic fibrosis carrier screening; IN-DEEP project developing research-based health information applicable to decision making and self-management by people with multiple sclerosis (funded by FISM); FP7 ECRAN project on European communication on research awareness needs project; Gynecological cancers and Mattioli Foundation

4.2.3 Engage2020 (pending confirmation)

Engage2020 is a project funded by the European Commission (DG Research) looking at research, innovation and related activities and exploring how members of society are involved today, and perhaps more importantly how they could be in the future. The project mapped how, where and why members of the public, stakeholders, consumers and other groups are engaged in the research process, from early policy development to the delivery of research activity. With the European Commission's Horizon 2020 Research and Innovation programme being the largest to date with nearly €80 billion of funding available over 7 years it is clear that the stakes for engagement are very high. Engage2020 aims to increase the use of engagement methods and policies by mapping what is practiced and spreading awareness of the opportunities amongst researchers, policy makers and other interested parties. The project mapped existing policies, structures, methods, approaches, tools and instruments, as well as highlighting promising new or adapted approaches we would like to see in the future. The European Commission has identified seven Grand Challenges -key issues where focused research is needed -ranging from demographic change to security. The Engage2020 project highlighted

engagement policies and methods which are suited to engaging members of society in Research and Innovation activities related to these six Grand Challenges.

Engage2020 looked at the involvement of members of society in research and innovation activities in many different roles, including as consumers, affected parties and citizens. Public engagement in European research and innovation activities is relatively high by international standards, but it is unevenly distributed, both geographically and based on issue areas. Engage2020 spreads participative practice from the pockets of excellence, such as the foresight community and Science Shops, to wider groups.

5 PEG individual members and bio-sketches

PEG members have been engaged considering their professional and personal expertise on PE, evaluating their CVs and possibility to concretely operate for the project.

A short bio-sketches for each is presented below.

1. Paola Zaratin (F), FISM MULTI-ACT Coordinator

Paola Zaratin, PhD in Neuropharmacology, joined the Foundation of Italian MS Society (FISM) on February 2010, where she currently holds the position of Director of Scientific Research on Research Programme in Biomedical Research, Research in Public Health, Research in Rehabilitation and Communication in Scientific Research. Paola has 28 years of experience working in Neuroscience Research and in the last 18 years in the field of Multiple Sclerosis. She also has 21 years of experience working in Drug Discovery and Development in the Neuroscience area. Bridging scientific results to people affected by neurological diseases (translational and advocacy research) has always been Paola ' s guiding research and professional interest. She has experience (Business Leadership MIT Sloan School of Management, Cambridge, Masschusetts, USA) in leading national and international multidisciplinary and multistakeholder teams and developing collaborative networks in Public, Profit and non-Profit sectors. She is author of more than 60 original papers, published on international peer reviewed journals and 6 patents. Paola is currently member of the International Medical and Scientific Board of the International Multiple Sclerosis Federation. She is also member of the Scientific Committee and of the Industry Forum of the International Progressive Multiple Sclerosis Alliance. As director of scientific research of the Italian MS Society Foundation, Paola has developed a management model for the Italian MS Society portfolio that also allows effective programs of technology transfer aimed at developing new therapies (pharmacological and rehabilitation) for people with MS.. Under Paola's leadership the Italian MS Society has published the first 'Manifesto' of Scientific Research development by people with MS.

2. Deborah Bertorello (F), FISM WP1 Leader

Deborah Bertorello joined the Italian MS Foundation (FISM) on Apr 2014, where she is in charge of European projects' coordination and monitoring. She is 35 years old and has over than 7 years of experience in clinical studies coordination in the field of Neuroscience and Patients Centred Research. She started her carrier in 2010 acting as coordinator for research projects for the Paediatric Hospital IRCCS G. Gaslini - Neuroscience Department of the University of Genoa. In the meantime she has also worked for Italian national patients associations "ARTeMio - Research and therapies for Myopathies Association" and "AIRett - Rett Syndrome Association", dealing with coordination of patient-centred research projects. In 2013 she worked for the Italian Institute of Technology (IIT) in Genoa, being in charge of projects expenditures monitoring, financial reports and statements redaction, research contracts management, documents collections for inspections and audits, coordination and support for internal departments/centres and external partners for projects management. Deborah has a relatives with MS and is personally engaged in this topic.

3. Elisa Ferrara (F), FISM Ethical Manager

Elisa Ferrara joined Italian MS foundation in January 2018 where she covers the role of funding researcher and project writer.

Her study back ground is in Law and International relations, with two different degrees achieved on these topics.

From April 2013 to December 2017 she has been cooperating at DITEN (Department of Naval Electrical and Telecommunication Engineering) at University of Genova in research activities concerning design and assessment of sociological technology services in the field health / rehabilitation : her research topics were concentrated on International regulation and protocol for health data management, interaction and assessment of sociable technologies in health care and rehabilitation technologies, driven by user centered methods.

She is co-author of more than 10 papers presented at international conferences and she is reviewer in international conferences based on interaction of health technologies and users Technology transfer and lean technology in health care are other topics related to her expertise that are of her interest.

4. Gabriele Dati (M), FISM

Gabriele Dati, PhD, joined the Italian MS foundation with over 12 years of experience in academic and

pharma company research on MS and peripheral neuropathies. Prior to joining the Foundation he was Researcher at Istituto di Neurologia Sperimentale (INSPE) IRCCS San

Raffaele Hospital (Milan, Italy), where he was responsible for the development, implementation and application of advanced imaging technologies to models of neurodegenerative diseases, with the aim of understanding the molecular basis of neurodegeneration and facilitating the pre-clinical development of lead molecules in partnership with Pharmaceutical Companies. Prior to that he was for approximately 6 years, Multiple Sclerosis Pharmacology Senior Scientist, Neuropharmacology Unit, Pharmacology Department, Merck Serono (former Serono), where he was in charge of managing neuropharmacology projects aimed at developing drugs for MS and Peripheral Neuropathies (PN) indications. Gabriele received his Ph.D. from the Open University of London, working in the laboratory of Biology of Myelin, DIBIT, H San Raffaele, Milan, Italy (Advisor: Dott. M.L. Feltri and Dott. L.Wrabetz) on a project aimed at generating and characterizing new models of Hereditary Motor and Sensory Neuropathy (HMSN).

5. Federica Balzani (F), Italian MS Society - EMSP

Federica Balzani was elected on EMSP's Executive Committee in May 2016 to represent the Italian MS Society (AISM). She has seven years of experience with AISM, at the beginning as a member of the Board of Directors at the provincial level and in activities and committees at the national level. Since May 2015, she works for AISM managing the provincial offices of Emilia Romagna – Marche of the Italian MS Society. In 2011, Federica joined the Youth Advisory Committee ExCom of EMSP. In October 2015, she participated in the MSIF's Global Networking Meetings in Barcelona. She graduated with a law degree from the University of Bologna, then attended a Master for lawyers, consultants and business professionals at the same university. In January 2016, she passed the State examination for the qualification to the legal profession. Before working for AISM, Federica worked as a lawyer, as HR Consultant with two societies and as a Tutor in Comparative Public Law in the University of Bologna.

6. Giovanni Esposito (M), EBC

Giovanni Esposito is the Research Project Manager of the European Brain Council since March 2015. Prior to this position, he was a postdoctoral researcher at the VIB in Leuven (Belgium), where he worked for five years. His research at VIB focused on molecular events leading to Parkinson's diseases. Giovanni holds a Master's Degree in Biology and a PhD in neurobiology from the University 'Federico II' of Naples (Italy). Within the EBC, Giovanni is responsible for the coordination of research projects addressing science and health policies in the area of brain.

7. Marijan Scholte (M), EBC

Marijn Scholte works as a Policy Officer at the European Brain Council (EBC) since November 2017. He is primarily responsible for monitoring EU policy processes relevant to the advocacy work of the EBC. Specific areas of interest include Horizon Europe, Health Technology Assessment (HTA), therapeutic innovation, off-label use of medicines and e-health. Prior to this position, Mr. Scholte studied International Relations at the University of Groningen.

8. Donna Walsh (F), EBC

Donna's training is in journalism but she has spent her career working in patient advocacy in the neurology field – including roles at the Migraine Association of Ireland and the European Headache Alliance. In 2012, she set up her consultancy company and was contracted by European Federation of Neurological Associations [EFNA] to act as its Executive Director. Since joining EFNA, Donna has been responsible for overseeing and developing many of its activities on patient empowerment and engagement. This includes EFNA's Training Initiatives for Neurology Advocates and MEP Interest Group on Brain, Mind and Pain. Donna also regularly represents EFNA externally – amongst others – at the European Brain Council, European Academy of Neurology, Societal Impact of Pain Platform and European Society of Radiology. As well as her work with EFNA, Donna has also acted as a consultant to other patient organisations/non-profit associations and, on occasion, to the pharmaceutical industry as part of advisory boards or steering committees, particularly in relation to patient centricity and involvement.

9. Emmanuelle Plassart (F), ARSEP

Emmanuelle Plassart-Schiess joined ARSEP on January 2005, where she was in charge to create the Scientific Department of ARSEP. Today, she is in charge of the funding of research,

the scientific and medical communication (meetings and documents), and of the coordination of research activities with the other societies. Emmanuelle is 50 years old and prior to joining ARSEP she worked many years as a biomedical research scientist. From March to August 1992, she was a trainee at Institute of Molecular Genetics, CNR, Pavia, Italy. From September 1992 to December 1999, Emmanuelle worked as a mater degree, a PhD, and a post-doctoral fellow at Pitié-Salpétrière Hospital, Paris on neuromuscular diseases and multiple sclerosis. From January 2000 to October 2004, Emmanuelle was as researcher at Kremlin-Bicêtre Hospital, and worked on proteins involved in neurological aging. During her PhD trainee, Emmanuelle was a teacher in genetics for students in Bachelor at the University of Denis Diderot. During a postdoctoral fellow, she taught genetics to master and medicine students.

10. Khan Usman (M), EHMA

Usman Khan was appointed Director at EHMA in April 2016. He is currently Managing Director of Modus Europe a European Public Policy Consultancy, an organization providing strategic public policy advice and undertakes related economic and policy studies with a particular focus on health and social care. He has held Board Director positions in public, private and not for profit organizations and has experience of leading significant change management projects in a number of countries. He currently holds a non-executive position within the NHS and is Professorial Lecturer in Health Policy and Management at George Washington University and additionally holds a visiting post at New York Universtity (London). Dr. Khan has over 30 years of general professional experience, of which 20 years in the sector of Health Policy and Management.

Dr Khan has significant expertise within the field of public and patient engagement. His PhD completed at Sheffield University in 1990, was on the subject of Public and User Involvement in Public Services. He went on to establish the Centre for the Study of Public Participation at Bedfordshire University in 1996 and is author of Participation Beyond the Ballot Box (UCL Press 1999). At the EHMA Dr Khan has developed and introduced the ICEE (Identify, Connect, Engage and Enable) framework for stakeholder engagement, which has subsequently been adopted within MULTI-ACT as overreaching project framework for stakeholder engagement.

11. Timothy Coetzee (M), US National MS Society (external member)

Tim Coetzee, Ph.D., serves as the US National MS Society's Chief Advocacy, Services and Research Officer. In this capacity, he leads the Society's work in the areas of state and federal advocacy, services and connection programs for people with MS, healthcare professional engagement and training, as well as the Society's global research programs. Most recently, he served as the president of Fast Forward, a venture philanthropy of the National Multiple Sclerosis Society where he was responsible for the Society's strategic funding of biotechnology and pharmaceutical companies as well as partnerships with the financial and business communities. Prior to Fast Forward, Dr. Coetzee led the Society's research initiatives on nervous system repair and protection in multiple sclerosis as well as the Society's fellowship and faculty award programs. He is a member of the Society's Executive Leadership team and the Progressive MS Alliance's Scientific Steering Committee. In addition, Dr. Coetzee serves on the US National Institutes of Health's National Advisory Neurological Disorders and Stroke Council, the International Advisory Committee on Clinical Trials in MS, the National Academy of Medicine's Forum on Neuroscience and Nervous System Disorders, and the Board of Directors of the American Society of Experimental Neurotherapeutics. Dr. Coetzee received his Ph.D. in molecular biology from Albany Medical College in 1993 and has since been involved in the field of multiple sclerosis research. He has been with the National MS Society since the fall of 2000.

12. Paola Kruger (F), EUPATI (external member)

Paola Kruger has a background in EU Public Affairs and has worked in London, Brussels and Rome. Since being diagnosed with chronic disease in 2010 she has turned her attention to Patient Advocacy and she has been working with the Multiple Sclerosis Centre of a large hospital in Rome helping

healthcare professionals to participate in EU initiatives and developing patient-centric projects, as well as focusing on having more empowered and proactive in their care path. She has participated in the IMI-funded project EUPATI (European Patient Academy on Therapeutic Innovation) whose aim is to train patients on the R&D of medicines and graduated in 2016. Since then she has been officially listed by EMA as an EMA Expert and she is speaker at numerous national and international events especially on the subject of patient involvement in clinical research. She also represents patients in several boards and Scientific Committees.

13. Mosconi Paola (F), Mario Negri Institute (external member)

Paola Mosconi is a biological scientist (1982 University of Milano) with a post-doctoral degree in Pharmacological Research (1984). She is at present Head of the "Laboratory for medical research and consumer involvement"- established in 1996 initially as research unit and then in 2005 as Laboratory - of the department of Public Health at the IRCCS Mario Negri Institute.

Paola Mosconi coordinated several research projects on issues pertaining the involvement of consumers and patients in health care aspects and outcome research. She published articles in leading international and national journals. Paola Mosconi has participated as teacher, or coordinator, to the realization of training course on "Methodological aspects of clinical research" or "Evaluation of quality of life" for health care professionals and representatives of voluntary associations. Significant experiences:

- development of research methods and strategies to involve lay people, patients or their associations, such as consensus conference, jury of citizens, online surveys and development of shared educational tools
- training for patient's organizations on methodological aspects of clinical research and quality of information
- studies for estimate the type of information on diseases and treatments received by patients; set-up of websites targeted on consumers and patients, such as www.partecipasalute.it, www.fondazionemattioli.it; www.ecranproject.eu; http://indeep.istituto-besta.it/
- studies for evaluate the consumers' level of satisfaction with the health services and cure; projects on the assessment of Quality of Life in randomised clinical trials or in epidemiological survey; translation and cultural adaptation of questionnaires for Quality of Life.

Paola Mosconi is the co-founder of the Italian Forum of EUROPA DONNA, she served as vice president and European delegate. At present she is president of Fondazione Nerina e Mario Mattioli Onlus for gynaecological oncological research; member of the board of EUPATI Italia, Fondazione AIOM (Italian Association of Medical Oncology), Fondazione Pofferi, and member of Scientific Committee of Acto-Italian Alliance against ovarian cancer.

Paola Mosconi has been member of two Italian Ethical Committees, in one served as president.

14. Engage2020 representative (external member invited)

We have invited the Coordinator of Engage2020, Dr. Lars Kluver.

A short bio sketch extracted online is presented below:

Lars Kluver is the director/CEO of the DBT Foundation, he has led a turn-around of the organisation from being a public institution to becoming a self-sustaining private common-good corporate foundation. The DBT Foundation is especially strong in Technology Assessment; Foresight; Policy Advice on issues pertaining to the impact of science, technology and innovation on society. One of his personal main interest is the development of new engaging methods for Deliberative Democracy, Open Governance, Co-Creation and other forms of open, democratic, participatory ways for engaging society in solving its own problems. The 30+ employees of DBT have special skills in making citizen participation on a local, regional, national, EU and global level. We do that for municipalities, regional councils, the government, the parliament, EU institutions, EU research, and international organisations / UN. He see large perspectives for the future in making use of this engaging way of working in new areas, such as Open Parliament/Government, CSR, member relations in large member organisations and in developing global dialogue on globally important topics. His responsibility is to develop the DBT Foundation to make that happen.

6 PEG appointment procedure

6.1 PEG formal invitation

PEG members have been requested to proactively support the execution of project activities related to PE and in particular those carried out in the **WP1 Science of Patient input**.

In order to facilitate the collaboration between the consortium and the PEG, PEG members are asked to take part to:

- Max 8 virtual meetings
- N.2 face to face meetings

The effort estimated to afford these duties is of 5 working days along first 20 months of the project (which is the duration of the WP1).

Each external member has been formally engaged with an email by the Coordinator including:

- MULTI-ACT Bilateral Confidentiality Agreement
- MULTI-ACT PEG Appointment Letter
- Annex of Appointment Letter: Patient Engagement Group (PEG) - Terms of Reference (Annex 1)
- MULTI-ACT PEG Acceptance Form (Annex 2)

6.2 PEG Terms of Reference

A preliminary Terms of Reference (ToR) has been prepared in order to engage external members. However, the ToR will be updated and tailored to the stakeholders engagement power matrix in relation to PE, upon agreement of all PEG members and in line with the other WPs' needs.

PEG members are expected to provide strategic and operational support to the activities of WP1, supporting the brainstorming, discussion and development on WP1 issues and deliverables.

PEG members are expected to take part to:

- Max 8 virtual meetings (one for each deliverable D.1-D.8)
- Max 2 F2F meetings (in relation to internal milestones related to WP1)

The ToR format is included in the appointment letters of each member and is presented in Annex 1.

Patient Engagement Group (PEG) - Terms of Reference

MULTI-ACT Project foresees the set-up of a Patient Engagement multi-stakeholder Group (PEG), in charge of providing strategic and operational support to the activities of Work Package n°1 (WP1) and thus to the other WPs. The set-up of the PEG is itself an official deliverable **(D1.2, M3).** The PEG will be engaged in the development of the activities of WP1 in a concrete manner, collaborating with MULTI-ACT consortium and supporting the development of WP1 deliverables. Here below the list of activities where MULTI-ACT team envisages to involve and consult the PEG.

WP1 - Enabling the science of patient inputs [Months: 1-20]

Task 1.1 Evaluation of patient engagement (PE) procedures across R&I

(M1-M8)

- To map and collect of existing PE procedures and initiatives across R&I by:
  - defining the scope of the mapping exercise,
  - listing relevant PE projects and initiatives according to the scope,
  - creating a specific database for case study collection to be linked to MULTI-ACT digital tool box,
  - mapping PE initiatives with different tools: direct contact with projects, surveys, questionnaires (to be decided in a dedicated meeting),
  - evaluating benefit and exchange from WP5 analysis,
  - drafting a report on the mapping exercise **(D1.1, M4)**
- To identify gaps, useful actions and prioritization of R&I processes needing PE procedures and draft connected reports **(D1.3, D1.4, M6)**

Task 1.2 Expectations, criteria and rules for PE co-developed by R&I stakeholders [M4-M8]

- To define minimal expectations for PE in RRI (who, when, what, how), based on the outcomes of previous tasks (virtual or F2F meeting)
- To co-design criteria, recommendations and rules for engagement and capabilities required for patients, researchers/sponsors (*E.g. review of standard capabilities and toolbox to support patients, conflict of interest; appropriate disclosure to ensure transparency; code of conduct; model of compensation, etc.)* and draft report **(D1.5, M8)**

Task 1.3 Empirical assessment and validation of criteria and rules [M8-M20]

- To implement the preliminary PE guidelines into the "Collective Research Impact Framework" (CRIF): apply to selected CRIF engagement processes and initiatives the identified criteria and rules to verify their usability, relevance, effectiveness and eventually propose adaptations, coming up with a final "Patient Engagement" guidelines validated within MULTI-ACT.
- To connect with WP3 activities, monitor the application and draft updated guidelines **(D1.6, M20)**

Task 1.4 Innovative path of engagement action in R&I [M4-M20]

- To join a meeting of relevant multi-stakeholder research organizations to review and endorse the "MULTI-ACT Innovative route for PE in RRI", building on the findings collected in D1.2-D1.5. Lay the foundation for the inclusion of MULTI-ACT PE guidelines into other RRI projects (H2020, Horizon Europe FP9).
- To collaborate to the development of a white paper to be submitted to the relevant actors of R&I **(D1.7, M20)**.

Task 1.5 Integration of Patient Reported Outcomes (PROs) and perspectives in the CRIF [M4-M20]

To collaborate to the integration of PROs designed in partnership with PwMS in the CRIF as core and transversal dimension and as proof of concept on how patient input can be scientifically relevant for research. The task will take into consideration the outcomes of the international Patient Reported Outcomes initiatives (an MSIF-Italian MS Society co-leaded effort) and the European Charcot Foundation initiative on integrating PROs into clinical and research perspective. **(D1.8, M20)**.

LIST OF DELIVERABLES

D1.1: Scoping of existing procedures and initiatives for patient engagement across R&I [M5]

D1.2: Patient engagement focus group (PEG) establishment [M3]

D1.3: Report on evaluation and gaps identification [M6]

D1.4: List and prioritization of R&I processes needing patient engagement procedures [M6]

D1.5: Set of preliminary criteria, recommendations and rules for patient engagement in R&I [M8]

D1.6: Patient engagement in R&I guidelines: final report on criteria, recommendations and rules for patient engagement in R&I [M20]

D1.7: White paper for innovate route for patient engagement [M20]

D1.8: Report on the integration of Patient Reported Outcomes and perspectives into the CRIF [M20]

7 The PEG and the governance of MULTI-ACT

MULTI-ACT foresees two specific advisory bodies: a Patients Forum (PF) and an External Advisory Board (EAB) and PEG will benefit from both the bodies.

7.1 Patient Forum (PF)

A Patient Forum (PF) will be establish in order to engage people with different diseases in order to have a broader representation beyond MS and to consider issues related to the transferability of the model to other diseases since the initial phases of the MULTI-ACT project. To make a meaningful shift to patient-centeredness and in the development of science of patients input, quality measurement needs to focus on patient priorities that will be initially focused on MS on WP1 as starting action.

PEG activities are focused on PwMS as the MS is the first case study but the outcomes will be submitted to the PF in order to be adapted as much as possible to other disease conditions. Although specific actions directed to exploitation, transferability and scalability of the outputs related to PE will be addressed in WP7, validation and advices from PF is needed since the early stage of development. D1.7 "White paper on Innovative routes for PE", although focus on MS, will be validated by PF in order to reflect patient priorities also for other brain diseases.

The PF will be directly involved in the identification of patients' needs and priorities while considering the impact of research. PF will be asked to work closely with the External Advisory Board (EAB) to contribute to project development, formulating research questions on project findings, monitoring research conduct and progress. The PF chair will be member of EAB. PF will collaborate in the implementation process, identifying the steps of health research processes where patients input is essential and identifying communication channels for patients community and selecting specific applications for information and social awareness. The PF will be asked to monitor research conduct and progress and consequently to formulate research questions on project outcomes. Both the PF and the EAB members will be fully informed on the project to decide autonomously and spontaneously whether to participate or not and will sign a nondisclosure agreement before participating in any meetings. All patient-related tasks within the project will be quality assured by the PF, which is directly involved for the identification of patients' needs and priorities while considering the impact of research.

PF will be asked to meet virtually, review and providing online inputs to 6/8 draft documents/deliverables.

The term "patient", in the PF membership will refer to people living with a condition, as well as caregivers. Patient organizations will be also involved, however considered as a separate stakeholder.

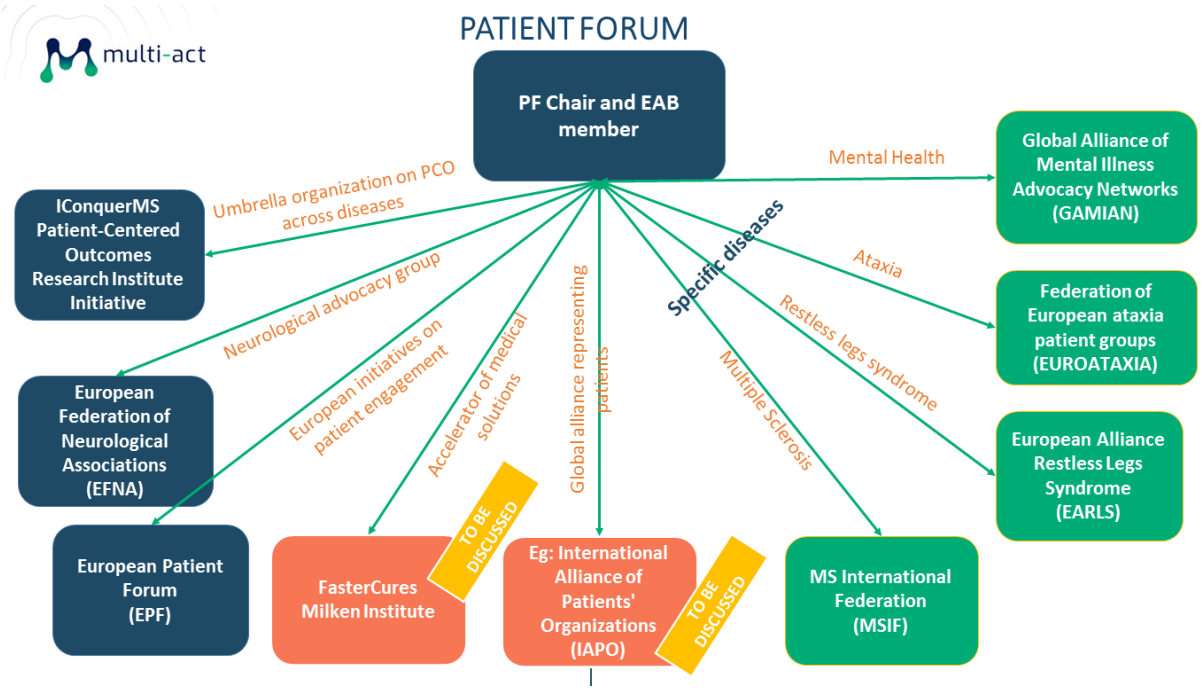


Figure 8. Preliminary Patient Forum composition

A representation of PF invited members is presented in Figure 8 and includes **umbrella organizations on patient centered outcomes** (iConquerMS, an initiative of the Patient-Centered Outcomes Research Institute initiative); **neurology advocacy groups** (European Federation of Neurological Associations, EFNA); **European initiatives and projects on patient engagement** (European Patient Forum, EPF); **accelerators of medical solutions** (FasterCures); **global alliance representing patients** in Europe and beyond (International Alliance of Patients' Organizations, IAPO); **disease specific groups** (MS International Federation, MSIF; European Alliance Restless Legs Syndrome, EARLS, Federation of European ataxia patient groups, EUROATAXIA, Global Alliance of Mental Illness Advocacy Networks, GAMIAN).

7.2 External Advisory Board (EAB)

An External Advisory Board (EAB) has been established in order to engage a larger set of stakeholders in the fields of brain-NDDs domain, Health Research Management, Accountability, Impact measurement, governance development and policy making to ensure effective and expert monitoring of progresses and the exploitation of project results. The EAB will ensure the effectiveness and level of innovation of the project as well as provide help in project quality management and problem solution and in the diffusion of project results envisioned under the specific dissemination activities. The EAB involves persons representing both the Health domain (e.g. managers and representatives of patients organizations, health research consortia, clinicians, health professionals, etc.), the final users sector (e.g. RFPO directors and committees, research and educational ministries, health and social systems, policy makers, research initiatives and consortia, PPPs initiatives, etc.) and other stakeholders (e.g. industry, hospitals, payers, purchasers, health insurers, etc.) that will provide their professional

experience to guide the project development, assuring a comprehensive and relevant stakeholder representatives involvement. Moreover, the chair of the PF is member of the EAB, providing advices and contributing to assure project adherence to patient's needs and rights. The EAB will also collaborate in the implementation process, identifying the health market of the project and communication channels for end-users and applications for post-developments and transferability of the project results (i.e. Framework). The EAB will be asked to monitor research conduct and progress and consequently to formulate research questions on project outcomes and to submit on a yearly basis a "project progress assessment report" to be discussed via a conference with the PSC and to be presented to the yearly consortium meeting.

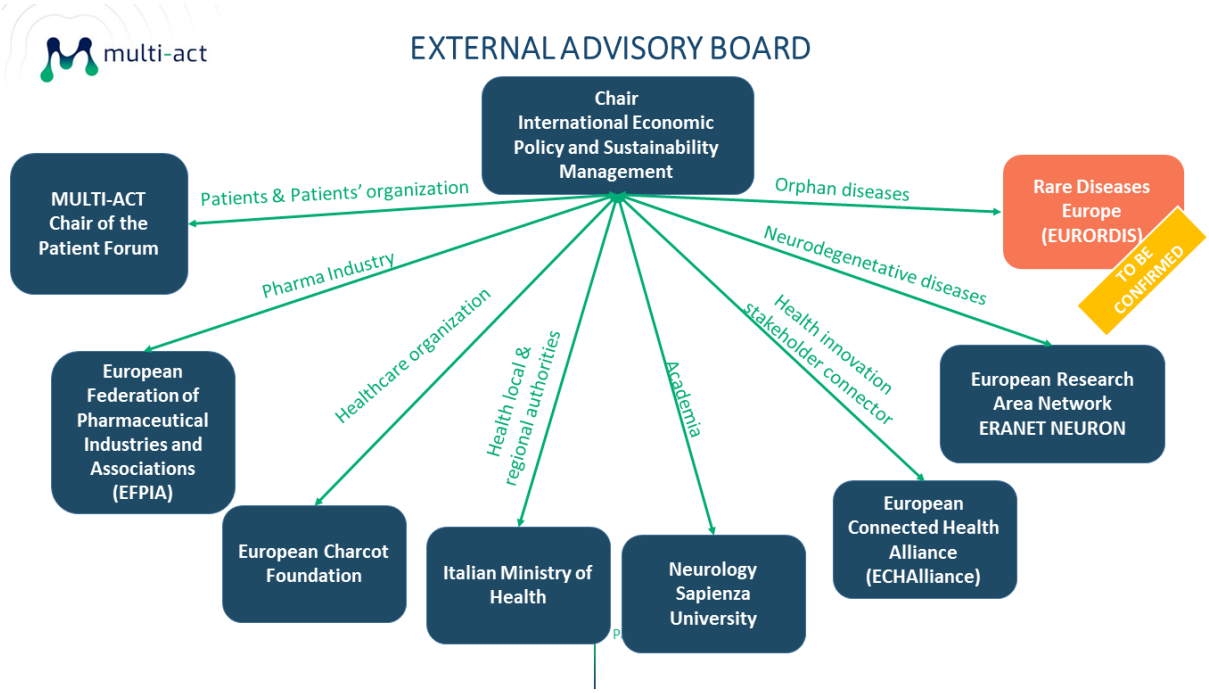


Figure 9. Preliminary External Advisory Board composition

A representation of EAB invited members is presented in Figure 9 and includes experts on **Economics and Sustainability Management of R&I** (Department of Management, Economics, and Industrial Engineering, Politecnico di Milano); **Pharma Industry** (European Federation of Pharmaceutical Industries and Associations, EFPIA); **Healthcare organizations** (European Charcot Foundation), **Healthcare local authorities** (Italian Ministry of Health); **Academia** (Sapienza University, Department of Neurology); **Health innovation connector**s (European Connected Health Alliance, ECHAlliance); research initiatives on **neurodegenerative diseases** (ERANET NEURON) and on **orphan diseases** (Rare Diseases Europe, EURORDIS).

7.3 Internal workflow

PEG will support the activities of WP1. **PF** will provide orientation and inputs considering the perspective of **different brain diseases** and together with the **MULTI-ACT consortium** and **EAB** will provide final approval on outcomes and deliverables. The PEG will be engaged in all the PE-related

activities along the MULTI-ACT project. All partners are aware of this "facility" and will ask to the Project Coordinator to mediate the interaction with the PEG when needed.

Communication channels:

- Emails, one-to-one calls for daily organization
- Teleconferences (a monitoring teleconference every 2 weeks, extra teleconferences in preparation of deliverables final version)
- Face-to-face meetings in relation to milestones and important/critical issues that need to be discuss face-to-face.

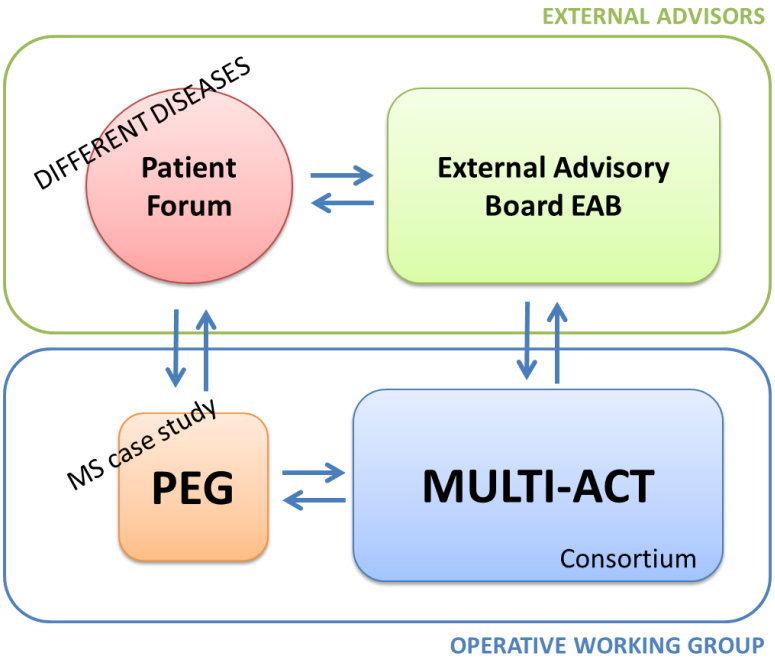


Figure 10. PEG, PF, EAB workflow

8 Ethical issues

8.4 Ethical compliance of PE in the PEG

PwMS, have voluntary agreed to join the PEG and have expressed their enthusiasm for the project, recognizing the need to engage patients in

- the development of a prospective CRIF to measure impact and accountability of Multi-stakeholder Health Research Initiatives
- to identify best-practices and procedures, as well as MULTI-ACT potential to address this need.

They have been selected among those patients more interested in scientific research, considering the following inclusion criteria:

- a cultural background that allows a full understanding of project design, activities and scientific terminology
- an overall good assessment of their possibility to participate to the work, considering the workload and a good level of interaction and work management abilities of these two persons.

Network with patients community and patients engagement initiatives (they will be engaged in the exploitation of patients engagement as for the chart reported in Figure n.8 “Preliminary concept of PwMS engagement via Patients Organizations” (see Section 3.2).

PwMS engaged in the PEG will be asked to **meet virtually or F2F**; all their intervention will be considered according to their specific preferences, both virtually or in F2F meetings, taking into account locations and technical aspects in order to promote at best their participation in relevant procedures of the project.

A specific list of these meetings is reported in section 6.1 of this document.

Their attendance will be requested for the following specific activities:

- to provide their feedback on the actual patient engagement procedure, for co-creating valuable engagement criteria and procedures with other stakeholders
- to verify their usability, relevance, effectiveness and eventually propose adaptations.
- to co-create innovative route for patient engagement in R&I, proposing R&I process where they think it would be relevant to be engagement.
- to provide their feedback to the final reports produced.
- to provide their view also on Patient Reported Outcomes and perspectives designed to be integrated in the CRIF as core and transversal dimension (T1.5.) (see Section 6.2).

Each specific task will be agreed according with their actual situation and with the effort necessary to accomplish the punctual activity in order not to overwork people engaged.

In Section 6.2 of this document, it is state the precise term of reference for all participants that will drive the work for all participants, with a particular attention to voices and engagement of PwMS.

In order to accomplish with all principal European and national regulation, a list of the principal ethical regulation addressed will be exposed in D10.1.

Template of all informative and consent modules will be reported in D10.3

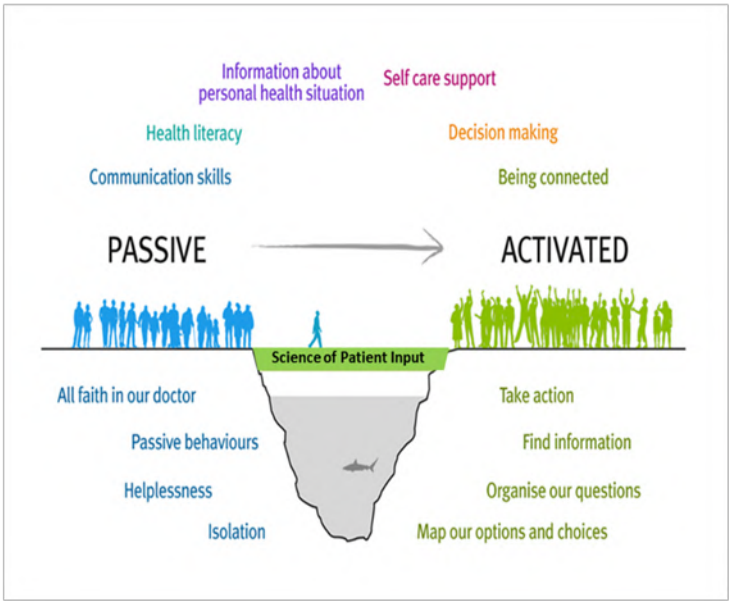
Since there is no direct involvement of patients in clinical trials and their involvement is only on voluntary bases and on PRO, it is not necessary to proceed with an ethical committee at this stage.

8.5 Gender balance

The PEG is composed by n. 14 members: n. 6 males (considering a male for Engage2020) and n. 8 females and gender balance is respected as per Project Grant Agreement art.33. The selection of relevant members tries as much as possible to keep a balanced distribution of genders. The gender analysis has been seriously taken into account, during PEG nomination, in order to get a balanced distribution among genders.

9 Conclusions

The MULTI-ACT project has been inspired by Collective Impact framework, a methodology to tackle deeply entrenched and complex social problems. Collective Impact is an innovative and structured approach to making collaboration work across government, business, philanthropy, non-profit organizations and citizens to achieve significant and lasting social change. The approach calls for multiple organizations or entities from different sectors to abandon their own agenda in favour of a common agenda, shared measurement and alignment of effort. Unlike collaboration or partnership, Collective Impact initiatives have centralized infrastructure – known as a backbone organization – with dedicated staff whose role is to help participating organizations shift from acting alone to acting in concert. The mission of the PEG is to ensure the contribution of the central stakeholder of the project: patient. In fact, the CRIF next to the four dimensions (excellence, efficiency, mission and social) has a fifth cross-cutting dimension: "patient reported dimension" that we consider a core point of our model. The central role of patient reported dimension does not signify that patients are more important than other stakeholders but that the whole research process, and the health research impact assessment, has to be done with an active participation of patients.



MULTI-ACT - Science of Patient Input to help in bridging the gap (adapted from David Somekh , European Health Management Association, 2016)

Figure 11. The science of patient input to help in bridging the gap

Annex 1

SCLEROSI MULTIPLA fondazione italiana

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Patient Engagement Group (PEG) - Terms of Reference

MULTI-ACT Project foresees the set-up of a Patient Engagement multi-stakeholder Group (PEG), in charge of providing strategic and operational support to the activities of Work Package n°1 (WP1) and thus to the other WPs. The set-up of the PEG is itself an official deliverable **(D1.2, M3).** The PEG will be engaged in the development of the activities of WP1 in a concrete manner, collaborating with MULTI-ACT consortium and supporting the development of WP1 deliverables.

Here below the list of activities where MULTI-ACT team envisages to involve and consult the PEG.

WP1 - Enabling the science of patient inputs [Months: 1-20]

Task 1.1 Evaluation of patient engagement (PE) procedures across R&I (M1-M8)

- To map and collect of existing PE procedures and initiatives across R&I by:
  - defining the scope of the mapping exercise,
  - listing relevant PE projects and initiatives according to the scope,
  - creating a specific database for case study collection to be linked to MULTI-ACT digital tool box,
  - mapping PE initiatives with different tools: direct contact with projects, surveys, questionnaires (to be decided in a dedicated meeting),
  - evaluating benefit and exchange from WP5 analysis,
  - drafting a report on the mapping exercise **(D1.1, M4)**
- To identify gaps, useful actions and prioritization of R&I processes needing PE procedures and draft connected reports **(D1.3, D1.4, M6)**

Task 1.2 Expectations, criteria and rules for PE co-developed by R&I stakeholders [M4-M8]

- To define minimal expectations for PE in RRI (who, when, what, how), based on the outcomes of previous tasks (virtual or F2F meeting)
- To co-design criteria, recommendations and rules for engagement and capabilities required for patients, researchers/sponsors (*E.g. review of standard capabilities and toolbox to support patients, conflict of interest; appropriate disclosure to ensure transparency; code of conduct; model of compensation, etc.)* and draft report **(D1.5, M8)**

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Task 1.3 Empirical assessment and validation of criteria and rules [M8-M20]

- To implement the preliminary PE guidelines into the "Collective Research Impact Framework" (CRIF): apply to selected CRIF engagement processes and initiatives the identified criteria and rules to verify their usability, relevance, effectiveness and eventually propose adaptations, coming up with a final "Patient Engagement" guidelines validated within MULTI-ACT.
- To connect with WP3 activities, monitor the application and draft updated guidelines **(D1.6, M20)**

Task 1.4 Innovative path of engagement action in R&I [M4-M20]

- To join a meeting of relevant multi-stakeholder research organizations to review and endorse the "MULTI-ACT Innovative route for PE in RRI", building on the findings collected in D1.2-D1.5. Lay the foundation for the inclusion of MULTI-ACT PE guidelines into other RRI projects (H2020, Horizon Europe FP9).
- To collaborate to the development of a white paper to be submitted to the relevant actors of R&I **(D1.7, M20)**.

Task 1.5 Integration of Patient Reported Outcomes (PROs) and perspectives in the CRIF [M4-M20]

To collaborate to the integration of PROs designed in partnership with PwMS in the CRIF as core and transversal dimension and as proof of concept on how patient input can be scientifically relevant for research. The task will take into consideration the outcomes of the international Patient Reported Outcomes initiatives (an MSIF-Italian MS Society co-leaded effort) and the European Charcot Foundation initiative on integrating PROs into clinical and research perspective. **(D1.8, M20)**.

LIST OF DELIVERABLES

D1.1: Scoping of existing procedures and initiatives for patient engagement across R&I [M5]

D1.2: Patient engagement focus group (PEG) establishment [M3]

D1.3: Report on evaluation and gaps identification [M6]

D1.4: List and prioritization of R&I processes needing patient engagement procedures [M6]

D1.5: Set of preliminary criteria, recommendations and rules for patient engagement in R&I [M8]

D1.6: Patient engagement in R&I guidelines: final report on criteria, recommendations and rules for patient engagement in R&I [M20]

D1.7: White paper for innovate route for patient engagement [M20]

D1.8: Report on the integration of Patient Reported Outcomes and perspectives into the CRIF [M20]

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Annex 2

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Name: _____

Organization: _____

Dear Paola Zaratin,

Thank you for your invitation to serve on the Patient Engagement Group (PEG) of the H2020 project "MULTI-ACT – A Collective Research Impact Framework and multi-variate models to foster the true engagement of actors and stakeholders in Health Research and Innovation" (GA no. 787570) from 01/05/2018 to 30/04/2021.

I am pleased to accept the appointment.

Yours sincerely,

Signed: _____

Name: _____

Organization: _____

Role: _____

Date: _____

Stamp (if available):

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