

## **Patient Reported Outcome for Multiple Sclerosis Strategic Intent**

**The Multiple Sclerosis International Federation (MSIF) and the European Charcot Foundation (ECF) will jointly lead and coordinate the Patient Reported Outcome for Multiple Sclerosis (PROMS) initiative. The Italian MS Society (AISM), through its Foundation (FISM) will act as the MSIF Lead Agency for, and on behalf of the Global MSIF Movement.**

### **Mission**

ECF and MSIF will jointly lead and coordinate a multistakeholder initiative<sup>1</sup> on global Patient<sup>2</sup> Reported Outcomes (PROs) for MS with the strategic intent to maximize impact on Science with and of Patient Input<sup>3</sup> on the health, healthcare and quality of life of people affected by MS. The Initiative aims to represent a unified view on PROs for MS to Healthcare Providers, Regulatory Agencies and Healthcare Technology Assessment Agencies (HTAs).

### **Value of the organizations involved**

**ECF** is an independent non-profit organization for advancing Multiple Sclerosis research in Europe. ECF establishes an interface between individuals/institutions involved in MS research and pharmaceutical industries. ECF establishes an interface between pharmaceutical industries and the clinical world. ECF Multistakeholders Initiative is a joint approach to coordinate existing initiatives in MS aims to avoid overlap in the actions and increase the power of representation of the MS world at institutional level in

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<sup>2</sup>Collective governance and transformational governance are instrumental to produce Responsible Research innovation. An important way in which collective and transformational governance is being manifested is in so called multi-stakeholder initiatives. Multi-stakeholder initiatives bringing together government, civil society, and the private sector that become mutually responsive to each other to address complex development challenges that produce an impact on people and society. In so doing, multi-stakeholder initiatives come to complement the role of each stakeholder alone in achieving these ends.

<sup>2</sup> For the purposes of this initiative, the term “patient” refers to the people with the disease: any individual with lived experience of the disease. Whilst the term Patient Reported Outcomes is the term used in relation to the whole healthcare and research sector, in this document we will refer to People with by MS outside the direct context of this terminology. People affected by the disease: any individual or group that is affected by the disease: E.g., family members, caregivers will be also engaged as the other stakeholders in the initiative.

<sup>3</sup> On the path to a science of patient input. Anderson M, McCleary KK. On the path to a science of patient input. Sci. Transl. Med. 8, 336ps11 (2016); <https://www.fastercures.org/programs/patients-count/science-of-patient-input-resources/>

Europe with the ultimate goal of improving MS patients' lives<sup>4</sup>. Its collaborative base consists of 500 MS research institutes and 1500 MS researchers.

**MSIF** is a unique network of MS organizations with 48 members from around the world and links to many others<sup>5</sup>. MSIF has an objective within its Strategic Plan (2017-2021) to explore the feasibility of 'global collaborations for registries or databases in relation to Patient Reported Outcomes' (Italian MS Society MSIF lead agency). MSIF and MS Society members can play a pivotal role to implement a global master framework for systematic engagement of people with and affected by MS in health research and care.

**AIMS**, through **FISM**, has substantial experience in promoting and financing MS Research<sup>6</sup>, in applying framework for Multistakeholder Initiatives (coordinator of EU H2020 Responsible Research Innovation MULTI-ACT project<sup>7</sup>) and on PROs for MS research and healthcare. AIMS is already working on a pilot project to standardize and harmonize PROs between their own PROMOPRO-MS database and iConquerMS (Accelerate Cure Project) network.

## Background

What began as an extension of patient advocacy has now evolved into an emerging 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. The power of the science of patient input relies on sources of patient data and the framework used to involve patients.

PROs and their measurement instruments (PROMs) are tools that ideally are developed in partnership with patients to capture the outcomes that matter most to them (science with Patient Input). Several global initiatives are defining and shaping this developing field. However, despite differences in viewpoint, the different stakeholders agree that PRO and PROMs have not reached their full potential of delivering benefits to patients.

In particular:

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<sup>4</sup><https://www.charcot-ms.org/research-initiatives/multi-stakeholder-initiatives>

<sup>5</sup><https://www.msif.org/about-us/our-members/>

<sup>6</sup> Trends in Pharmacological Sciences, November 2014, Vol. 35, No. 11

<sup>7</sup> [go.nature.com/2mdkqqt](https://doi.org/10.1038/nature20144); Nature. 2018 Jul;559(7714):331

- People with MS are frustrated that functional domains that matter most to them are not addressed by current PROs
- Clinicians acknowledge the importance to include patient reported outcome measures (PROMs) to understand treatment effects or compare treatment options
- Regulatory Authorities (RA) recognize that current outcomes (EDSS, relapse rate, MRI features) do not fully capture the experience of people with MS
- Healthcare Technology Assessment (HTA) Agencies aim to integrate the “patient voice” in coverage decisions
- Pharma acknowledge the importance to include patient PROs in Medicine Life Cycle Management
- Consumer-driven healthcare is gaining ground

Efforts to enable the uptake of PROs and PROMs into clinical practice and regulatory agencies/HTS decision-making processes could be greatly enhanced and informed by a commonly held strategic PRO agenda and roadmap shared by all relevant stakeholders.

Taking this into account, MSIF’s strategy for 2017-2021, under its aim of *Better Scientific Understanding Leading to New Ways to Treat, Prevent and Stop MS*<sup>8</sup>, identified the objective to explore the “need for and feasibility of global collaborations for registries or databases in relation to Patient Centered Outcomes. In 2015, the MSIF Research Staff Network identified data sharing<sup>9</sup> as a priority area for research collaboration between MS organizations, particularly in relation to patient reported outcomes. MSIF, in collaboration with AISM, which had agreed to function as a lead agency for this project, organized a meeting in Barcelona in May 2017 bringing together relevant MS organizations (MSIF and member organizations, RIMS and EMSP) and a small number of experts to develop a strategic plan towards a ‘science of people with MS input’ via an international ‘federated network of MS Cohorts’. The meeting concluded on the need to focus on PROs.

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<sup>8</sup> <http://www.msif.org/wp-content/uploads/2017/08/MSIF-Strategy-2017-2021-web.pdf>

<sup>9</sup> For the purpose of this document, Data sharing refers to the collaboration between registries or research databases and making this data available to other investigators (and the public). Sharing data helps researchers to access and build on new information and knowledge. This provides opportunities to accelerate the progress of research and improvements in health. Examples include making clinical trial data available to researchers, linking existing datasets, supporting of post-marketing safety and efficacy studies by regulatory agencies.

In 2018, the ECF in collaboration with AISM organized a second multistakeholder meeting in Lerici with international participants from clinical and non-clinical research backgrounds, pharmaceutical industry and representatives of people with MS. The meeting had the specific goal of reaching consensus on the path forward including:

- To advise relevant stakeholders on appropriate current PROs and PROMs that might feasibly to be used in clinical trial
- To advise relevant regulatory agencies and physicians on appropriate current PROs that might feasibly be collected and used in clinical care, and included in registries
- To identify critical gaps in the knowledge base that are hindering progress toward the development of a clear roadmap for research needs and progress

Following these two meetings, the MSIF and the ECF have agreed to jointly lead and coordinate the multistakeholder PROMS Initiative, with AISM acting as the MSIF Lead Agency for, and on behalf of the Global MSIF Movement.

## **Strategic objectives of the PROMS Initiative**

MSIF, ECF, AISM agree on the following as the strategic objectives of the initiative:

- To provide a scientific value to the voice of people with and affected by MS
- To develop a global master framework for systematic engagement of people with and affected MS in PROMS Initiative global agenda
- To identify functional domains that matter most to people with MS that will lead to the prioritization of functional domains, with inputs of people with MS, clinicians and researchers. This is particularly important for ensuring content validity
- To identify critical gaps in the knowledge base that are hindering progress toward the development of a clear roadmap for research needs and progress
- To promote, coordinate, implement and support initiatives aiming at validating and harmonizing PROs across cultures
- In relation to the strategic objectives listed above, to disseminate outputs to all stakeholders and educate stakeholders in the availability and use of agreed global PROs and PROMs, including:
  - To advise relevant stakeholders on appropriate current PROs and PROMs that might feasibly to be used in clinical trial

- To advise relevant regulatory agencies and clinicians on appropriate current PROs and PROMs that might feasibly to be used in clinical care and collected in registries

### **Multistakeholder Initiative Principles**

The PROMS Initiative recognizes the crucial importance of a framework to guide effective multistakeholder engagement. As such, it will operate with respect for the values of ECF and MSIF, and will learn from best practice of other relevant initiatives (such as <sup>10,11,12</sup>)

Key principles of the PROMS initiative:

1. To ensure the scientific quality of the input from people with and affected by MS because in absence of this quality the PROMS initiative will never have value
2. Clarity of purpose: the mission of the initiative is clearly defined, with people affected by MS at its heart
3. Inclusivity. The initiative will aim to engage all parties/organizations from across the globe that have an interest in furthering the mission of the PROMS Initiative, and will:
  - a. Learn from their relevant experience and work to date.
  - b. Give them opportunity to shape the overall scientific agenda of the initiative.
  - c. Ensure that all stakeholders, including people with and affected by MS, have an equal voice.
  - d. Use a co-creation approach where possible.
  - e. Ensure that, when relevant, people with or affected by other conditions and diseases are involved
4. Impact. The initiative will ensure the mission meets its objectives, through:
  - a. Effective project management/coordination of the overall initiative, including any working groups arising from it.

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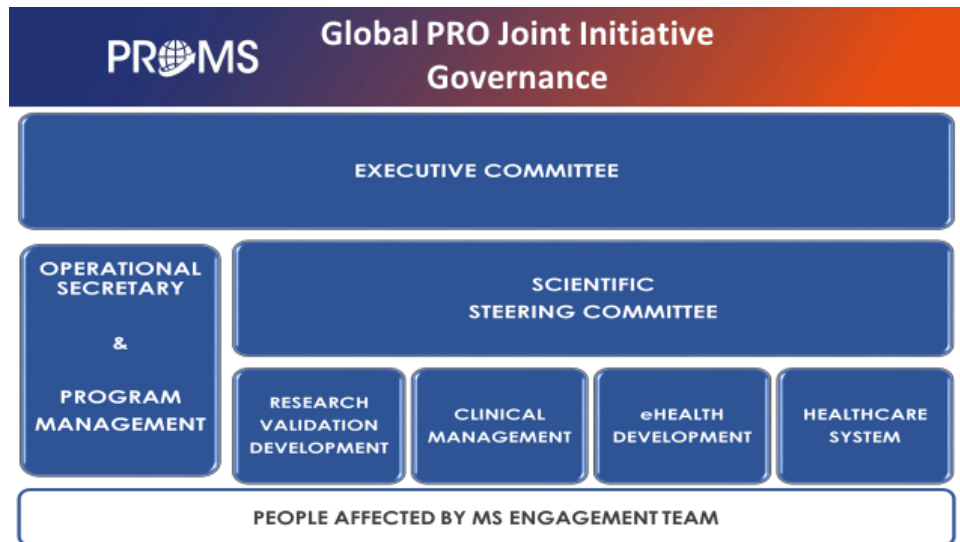
<sup>10</sup> <https://www.progressivemsalliance.org/>;

<sup>11</sup> <https://www.multiact.eu/>

<sup>4</sup><https://www.charcot-ms.org/research-initiatives/multi-stakeholder-initiatives>

- b. Establishing milestones and indicators to monitor progress against objectives, receive feedback from stakeholders, learn from experience, and continuously improve.
- c. Measuring the ultimate impact of the initiative in relation to its mission.

**Governance high level structure**



**Executive Committee**

**The Executive Committee is responsible for:**

- the overall direction of the PROMS Initiative, including agreeing the strategy (agenda) and the Terms of Reference for the Scientific Steering Committee,
- evaluating the functioning of the Scientific Steering Group and of the Working Groups

**Scientific Steering Committee**

- The Scientific Steering Committee (SSC) reports to the Executive Committee. The SSC will be co-chaired by a representative of ECF and a representative of MSIF.
- The Scientific Steering Group will be global and multistakeholders in the composition (e.g. academia, clinicians, industry, patients and patient organizations).

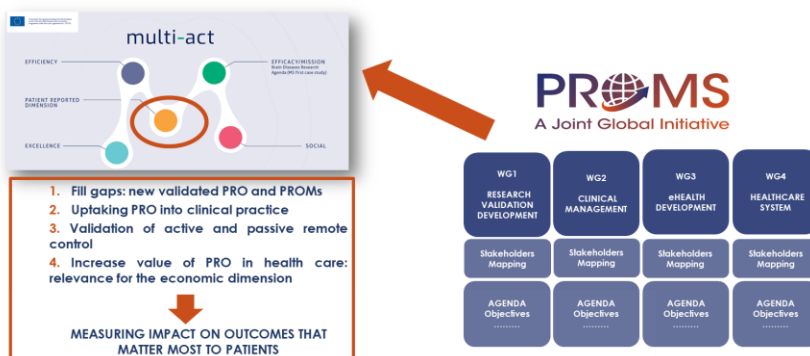
- The Group comprises international stakeholders in the field of PROs for MS and other diseases and is in charge of:
  - the development of the strategic objectives of the agenda
  - engagement of the wider scientific field for consultation
  - recommending appointment of Working Group leads and members
  - recommending resource allocation for Working Groups
  - provision of scientific advice to Working Groups
  - agreeing the high level action plans for the Working Groups

## People affected by MS Engagement Coordination Team (ECT)

- The Engagement Coordination Team (ECT) will lead the design and implementation of the engagement of people with and affected by MS in the agenda design, in the initiative development and in the implementation, monitoring and evaluation phases.
- The ECT will be co-chaired by an MS Society representative and a person with or affected by MS.
- The ECT reports to the EC and interacts with the SC in matters concerning patient engagement.

## Strategic priorities of PROMS Initiative

Building on Lerici's meeting four initial strategic priorities and expected outcomes have so far been identified by the Executive Committee:



## 1) Research, validate and development

- To identify functional domains that matter most to people with and affected by MS that will lead to the prioritization of functional domains, with inputs of people with MS, clinicians and researchers. This is particularly important for ensuring content validity
- To fill critical gaps in the knowledge base that are hindering progress toward the development of a clear roadmap for research needs and progress
- To research, validate and develop relevant PROMs

## 2) Clinical Management:

- To identify current PROs and PROMs to be used in clinical care and collected in registries and advice relevant regulatory agencies and clinicians.
- Meet regulatory agencies position on PRO and PROMs (e.g. MSOAC EMA document)
- To promote, coordinate, implement and support initiatives aiming at validating and harmonizing PROs across cultures

## 3) e-Health:

- To establish current e-Health return of investment for all the stakeholders engaged
- To enable the long-term benefits afforded to patients (active versus passive), clinicians and other stakeholders by e-Health

## 4) Health care system:

- To translate standardized data into a performance measure (PRO-PMs) that captures the results most important for improving long-term wellness.
- To enable PRO-PM in innovative reimbursement models, regulatory frameworks well as their clinical decision support algorithms.