DEFINITION OF R&D MISSION-ORIENTED GUIDELINE IN PREVALENT NEUROLOGICAL DISEASES

neuroATLANTIC Project

This project is co-financed by the Interreg Atlantic Area Programme through the European Regional Development Fund

INDEX

INTRODUCTION

Executive Summary

At present, **neurological diseases continue to be a major problem in Europe**, due to the difficulty of studying, diagnosing and treating these diseases and the progressive increase of the elderly population in our continent. On the one hand, there is the will and the need to research and develop therapies for neurological diseases, and on the other hand, great efforts are being made in Europe to promote research and the development of innovative solutions that will have a positive impact on the society. But it is necessary to align both wills in order to materialize the progress made and improve the quality of life of current and future patients.

In recent years, **new approaches to address current challenges, called Missions**, have become popular. These missions are being promoted by the European Commission because they benefit society as a whole by **favoring the application of innovation**. These initiatives involve all sectors of society in a coordinated, multidisciplinary and cross-cutting manner. The economist Mariana Mazzucato is one of the promoters of the missions, going so far as to propose the creation of a **Mission on Dementia** in 2018.

This document is intended to guide the definition and promotion of a mission-driven initiative specifically in the neurosciences. This initiative requires a great effort, multiple actions and the coordination of multiple institutions and actors, but with this initiative can derive great benefits for all involved.

The progress achieved with the **neuroATLANTIC project, created in the framework of the European Interreg Atlantic Area program**, represents a starting point for the creation of new initiatives at national and European level. The international consortium of neuroscience research groups created by **neuroATLANTIC are in a position to advise public institutions and lead initiatives** to advance the knowledge and treatment of neuronal diseases.

This document gathers:

(1) **European programs** and mechanisms that support research and development as a key to the solution of current challenges,

(2) the **suitability of a mission-style initiative in neurosciences**, with its basic characteristics and requirements, such as an inspiring objective that is broadly relevant to society, clearly framed, focused, realistic in time, attracts public and private funding, and involves all sectors of society.

(3) a **proposed methodology** of the key points to be met by a mission-type initiative in neurosciences in the field of cooperation at the national or European level and **two examples of mission-style initiatives in Alzheimer's disease and stroke**. The key points are:

- The definition of the initiative based on the key criteria of a mission.
- The alignment of the initiative's objectives with the priorities of the European Commission.
- The scale and activities to be developed with the initiative.
- The governance and the role of all the actors involved.
- The attraction of European and national financial resources.

Research and Innovation Funding from the European Commission

We are currently at the beginning of the **Multiannual Financial Framework 2021-2027** (MFF 2021-27). One of the main developments has been the modernization of cohesion policy, the European Union's main political tool for investment.

In May 2018, the European Commission proposed new regulations for the Union's cohesion policy after 2020, including:

- Investment for jobs and growth (IJG), a regulation concerning the European Regional Development Fund (ERDF), the European Social Fund+ (ESF+); and the Cohesion Fund,
- The Just Transition Fund (JTF),
- A regulation on specific provisions for the new European territorial cooperation objective (Interreg), called the European Cross-Border Mechanism,
- Commission managed EU instruments and technical assistance.

The objective of cohesion policy remains the promotion of economic, social and territorial convergence, through sustainable competitiveness, research and innovation, digital transition, the objectives of the European Green Pact and the promotion of the European pillar of social rights. In order to achieve these objectives, the EU has set aside one third of the total EU budget, around EUR 392 billion through the following specific funds [1]:

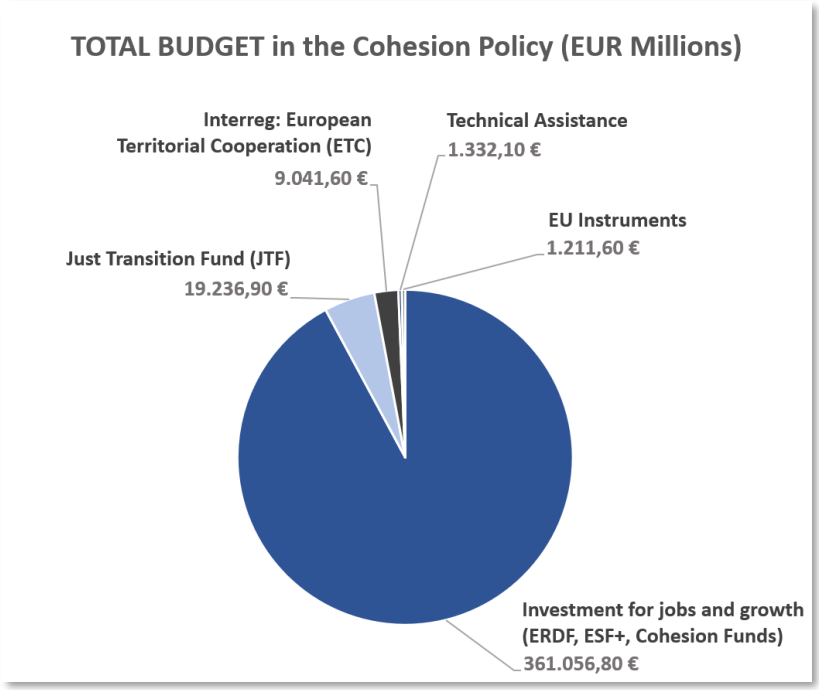

Figure 1: Total budget in the Cohesion Policy for the 2021-27 period

[1] 2021-2027 Cohesion policy EU budget allocations LINK

Another new feature of this new period is the simplification and consolidation of the 11 thematic objectives of the 2014-2020 period into five main Policy Objectives (POs) that will drive EU investments in the 2021-2027 seven-year period:

- **PO1. Smarter Europe**, through innovation, digitization, economic transformation and support for small and medium-sized enterprises;
- **PO2. A greener, carbon-free Europe**, implementing the Paris Agreement and investing in energy transition, renewable energy, circular economy and the fight against climate change;
- **PO3. A more connected Europe**, with strategic transport and digital networks;
- **PO4. A more social Europe**, making the European Pillar of Social Rights a reality and supporting quality employment, education, educational and vocational skills, social inclusion and equal access to healthcare;
- **PO5. A Europe closer to citizens**, supporting locally managed growth strategies and contributing to sustainable urban development (urban, rural and coastal areas) across the EU.

The MFF 2021-2027 spending plan, which is to address the five POs over the next seven years, is made up of 37 programs, funds and mechanisms. Among all of them, the most relevant and recognized in the field of research and innovation are Horizon Europe (the European Union's main initiative for the promotion of research and innovation) and ERDF (a fund that provides financial support to reduce economic imbalances between regions by investing in growth and employment, as well as favoring European Territorial Cooperation).

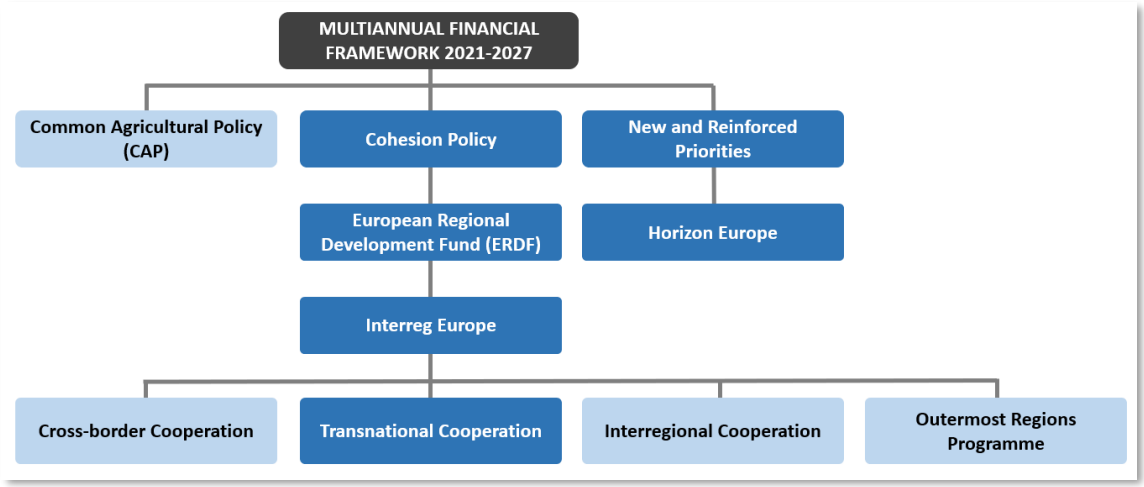

Figure 2: European Commission Financing Instruments

European Territorial Cooperation (ETC)

Within cohesion policies is the ETC instrument, the flagship program for cross-border cooperation at regional and national level, also known as Interreg.

Since 1990, Interreg has encompassed a number of key EU programs to assist the transnational, cross-border and interregional development and cooperation of both areas within the European Community and bordering external areas. The program focuses on different sectors such as transport, trade, tourism, environment and education, among others. Currently, the Interreg

program is financed with ERDF Funds, within the MFF 21-27, and presents as novelties for this period the inclusion of new areas), or outermost regions and new thematic objectives aligned with the objectives of the ERDF Funds. The new Interreg program has a total budget of EUR 9 billion, distributed as follows [2]:

1. **Cross-border cooperation**, with 60 programs and a budget of EUR 5,8 billion euros.
2. **Transnational cooperation**, made up of 15 programs that promote highly integrated partnerships in a common cooperation area whose impact goes beyond national borders (including the Atlantic Area, Interreg Sudoe and Interreg MED) and EUR 1,5 billion euros at its disposal.
3. **Interregional cooperation**, with 4 programs (such as Interreg Europe) and endowed with EUR 490 million.
4. **Cooperation in outermost regions**, with EUR 281.21 million.

European Territorial Cooperation calls 2022 (ERDF 2021-2027)

New calls for interest for the Interreg EURO-MED 21-27 (Mediterranean) and Interreg Europe programs have been published at the beginning of 2022. Both programs support projects developing innovative concepts and practices and promoting a reasonable use of resources through ERDF Funds. As a novelty, EURO-MED 21-27 has four main themes articulated in the style of the "Missions", very focused on the sustainability of the Mediterranean area. The main policy objectives (PO) of the program include a smarter and greener, social and connected Europe with better governance with positive impact in the society. The Smarter Europe PO focuses in Research & innovation to developing and enhancing research and innovation capacities and the uptake of advanced technologies.

The final budget of the Interreg Euro-MED 21-27 Programme has not been approved yet, but should be endowed with EUR 281 million in total for the next years [3]. The first call for EUR 36 million was opened in February 2022 and will close on May 24 and will finance projects of between EUR 4 million and EUR 5 million.

Territorial Innovation, that include programs such as Interreg Atlantic, Poctep, Sudoe and Poctefa, are currently in the preparation phase and are not expected to open calls for proposals until after the summer period.

Neuroscience innovation projects in the European framework

In the framework of the Interreg B Transnational Cooperation, the Interreg Atlantic Area program for the period 2014-2020 approved the funding of the neuroATLANTIC project, which was focused on neurological diseases. An international platform was created in the neuroATLANTIC project including 9 partners coming from 4 countries (see map below), involving six Atlantic regions (Spain: Galicia and Basque Country; Portugal: Centre and Lisbon; France: Basse-Normandie; and Ireland: South and East), encompassing different types of entities such as research groups and innovative companies. neuroATLANTIC brought together clinical and

[2] Agreement on EU funding for cross-border projects LINK
[3] Interreg EURO-MED Programme 2021-27 LINK

preclinical capabilities focused on neurological diseases associated with aging (mainly stroke and Alzheimer's disease) to accelerate the adoption of new innovations that will revolutionize the treatment of neurological diseases in this field.

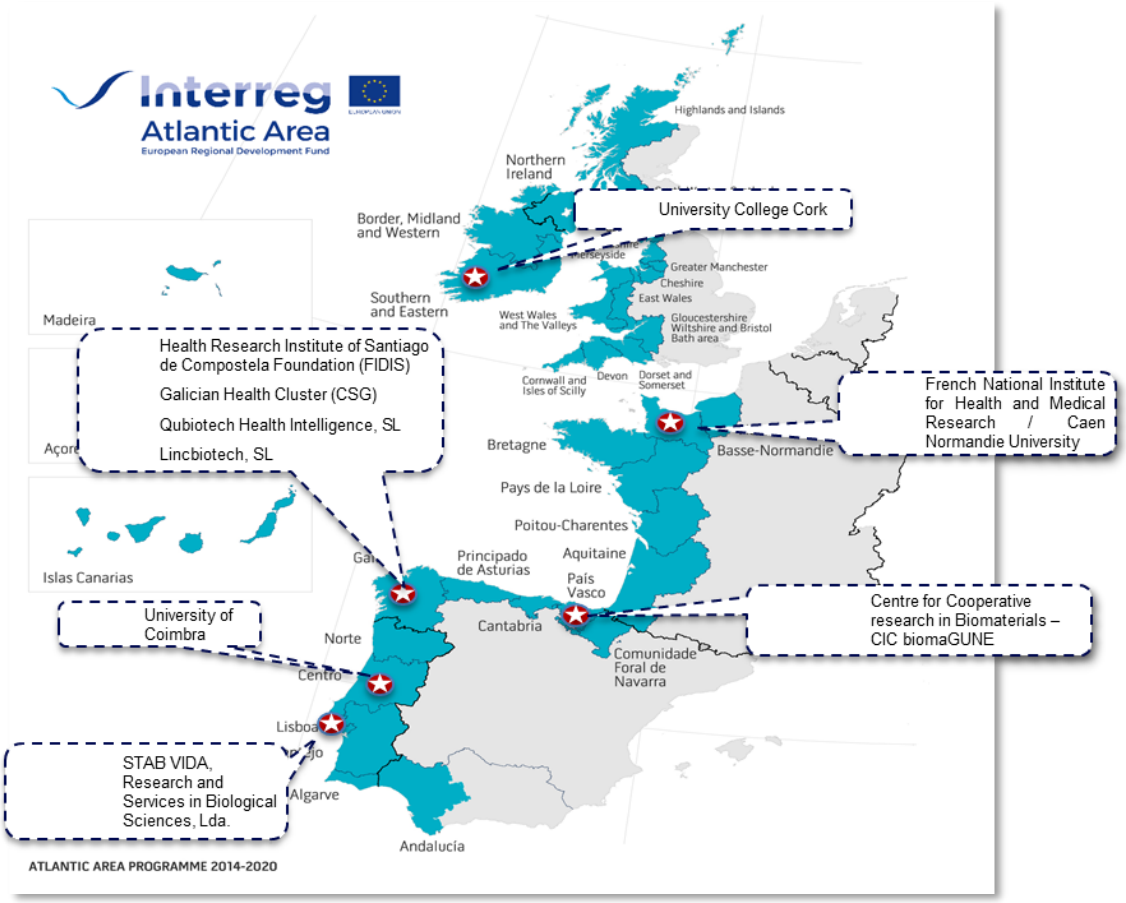

Figure 3: Atlantic regions involved in the neuroATLANTIC project.

SUITABILITY OF A MISSION IN HEALTH IN THE FIELD OF ETC INTRUMENT

Innovation is one of the main vehicles for achieving the major socioeconomic challenges of international scope set out by the EU through the Missions-oriented policies (MOPs). These policies are characterized by the promotion of large strategic technological projects oriented by an objective. They are systemic policies that combines demand-side with supply-side instruments through which the State links public and private actors for the development of sectors, technologies and markets according to strategic objectives [4].

In this regard, selected Missions will help deliver key EU policy priorities such as the Europe's Beating Cancer Plan, NextGenerationEU, the EU Industrial Strategy and a Europe fit for the Digital Age, amongst others.

This approach to innovation support, used for decades in Defense, has consolidated its prominence within innovation policies at national level [5] and is one of the main novelties of Horizon Europe - Framework Program for Research and Innovation for the period 2021-2027. For its successful implementation, it will work in synergy and coordination with other EU funding instruments and policies, so as to articulate a portfolio of actions to be developed under a mission. To achieve this, regional policy makers have an important role to play in shaping the actions included in the missions in their regions, in order to successfully achieve the set objectives within the established timeframe.

Research and Innovation Missions in Horizon Europe

Horizon Europe is the European Union's flagship initiative for the promotion of research and innovation from the conceptual phase to market introduction, and complements national and regional funding. The structure of Horizon Europe consists of three pillars: (1) Excellent Science, (2) Global Challenges and European Industrial Competitiveness and (3) Innovative Europe. In addition, it has a cross-cutting section that provides support measures to the Member States to enable them to make the most of their national research and innovation potential and to consolidate the European Research Area (figure 4).

One of the main novelties of the new Framework Program is the inclusion of "missions" in Pillar 2 "Global Challenges and European Industrial Competitiveness", with the aim of directing R&D&I towards projects of social and economic relevance in areas of interest to the EU and its citizens [6]. These missions are defined as a portfolio of interdisciplinary R&D&I-based actions aimed at achieving a bold and inspiring, yet measurable, goal that has a major impact on society.

[4] The Importance of Technology Policy. Ergas, H. 1987, Cambridge University Press, 51-96
[5] Mission-oriented innovation policies: Challenges and opportunities, Mazzucato, 2018, October 2018 Industrial and Corporate Change 27(5):803-815
[6] Pillar II - The largest share of Horizon Europe funding LINK

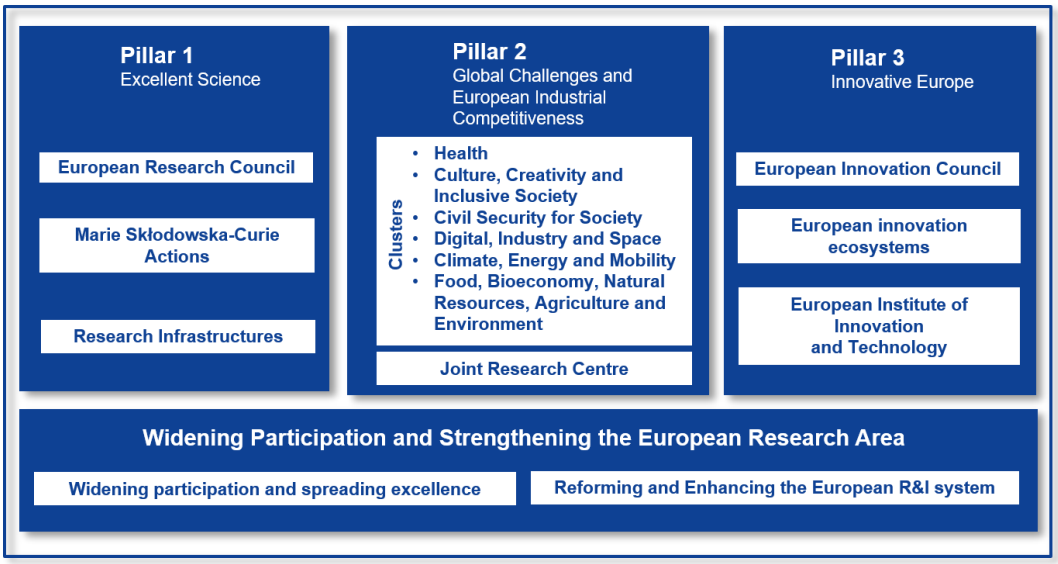

Figure 4: Structure of Horizon Europe

The definition of a mission

A mission is a new way of providing innovative solutions to the major problems of society, by proposing solutions to very ambitious challenges, and by creating an environment around which to articulate all the projects necessary to achieve the main objective [7]. The objectives set by a mission are ambitious since they cannot be achieved through individual actions, they must be achievable and offer concrete results in a given timeframe. In the framework of the Horizon Europe program for the years 2021-2027, missions currently under development are required to deliver results by 2030 [7].

The **EU defines a mission** as: "*A time-bound portfolio of transdisciplinary actions aimed at achieving a bold and inspiring, yet measurable, goal that has an impact on society and policy-making and is relevant to a significant part of the European population and a broad spectrum of European citizenship*" [8,9]. For this reason, the missions are based on four key questions:

1. What are the main challenges facing society?
2. How can concrete missions help to solve these challenges?
3. How can missions be best designed to allow the participation of different actors?
4. Does the mission allow for bottom-up experimentation and innovation throughout the system?

The concept of Mission is associated with the technological development of the Apollo XI mission to take man to the moon. This milestone, which had a clear objective, also meant a great innovative push in many sectors even those not related to space travel. Promoting a mission implies a great technological and scientific advance, inspiring the creativity and talent of research centers and companies dedicated to innovation, creating a favorable scenario that

[7] What are EU Missions? LINK
[8] Mission economy: a space race to change capitalism. Mariana Mazzucato, 2021, Editorial Taurus.
[9] Missions València 2030 LINK

allows them to apply their knowledge, products or services to the projects framed in the mission. In order to achieve the objectives to be solved through a mission, it is necessary that all actors of the society participate, such as the public sector, the private sector, the administrations, the academy and the civil society in general. All this leads to social and economic progress, with MOPs for the projects framed in the mission, providing the necessary tools and funding for it, consolidating an industrial fabric of companies dedicated to innovation.

Fundamental aspects guiding the missions

In order to create a mission, it is essential to identify and select the challenges to be solved. Once identified, it is necessary to evaluate whether it is possible or necessary to apply a strategy articulated as a mission to solve the challenge and, if appropriate, to evaluate the scope and structure of the mission.

Mazzucato described the five criteria **to guide the selection of missions**[10,11]:

1. be bold, inspirational and widely relevant to society
2. be clearly framed: targeted, measurable and time-bound
3. establish impact-driven but realistic goals
4. mobilize resources on EU, national and local levels
5. link activities across disciplines and different types of research and innovation, making it easier for citizens to understand the value of research and innovation investments

The mission consists of three levels or layers, a first level where the major challenge to be achieved is set out, a second where the objective to be pursued is clearly defined, and a third phase where the projects linked under the umbrella of the mission are articulated. Once the mission objective has been established, the projects linked to the achievement of the mission objectives are articulated. The mission's projects are developed in a coordinated and interconnected manner, with the participation of the necessary stakeholders. The achievement of a broad commitment throughout the EU and partner countries, as well as the organization and coordination of the actors involved in the projects is a key process to move forward in a successful way, achieving the best results from each project [12]. These actions will act as vehicles for innovation, so the role of education and training institutions in the development of talent, as well as the private and public sector will also be key elements of the missions.

In 2020 the European Commission selected **five missions proposed** by Mission Boards in different fields such as health, climate and environment to be developed before 2030. The Mission Boards consulted very widely, including a dialogue with specially created expert groups, one for each of the Mission Areas, of the 'shadow' Strategic Configuration of the Horizon Europe Programme Committee. These applications are carefully examined by expert committees, which decide whether they are suitable to be articulated as missions. In the past, some proposals, such as the reduction of the use of plastics given the pollution they generate, were not accepted as

[10] Missions: Mission-Oriented Research & Innovation in the European Union. Mariana Mazzucato. Brussels, Belgic: European Commission, 2018

[11] Mission-oriented innovation policy and dynamic capabilities in the public sector, Kattel and Mazzucato October 2018 Industrial and Corporate Change 27(5):787-801

[12] Horizon Europe mission-orientation to tackle main global challenges LINK

such, but were included in the "*Restore Our Ocean and Water*" mission, which includes this challenge. The selected missions were:

MISSIONS	MAIN OBJECTIVES
Adaptation to Climate Change	Support at least 150 European regions and communities to become climate resilient by 2030.
Cancer	Working with Europe's Beating Cancer Plan to improve the lives of more than 3 million people by 2030 through prevention, cure and solutions to live longer and better.
Restore our Ocean and Waters	The Mission will prevent and eliminate pollution by reducing plastic trash in the sea, nutrient losses and the use of chemical pesticides that pollute the water by 50%.
100 Climate-Neutral and Smart Cities	Deliver at least 100 climate-neutral and smart cities by 2030, and ensure that these cities act as experimentation and innovation hubs to enable all European cities to follow suit by 2050.
A Soil Deal for Europe	Create 100 living labs and lighthouses to lead the transition towards healthy soils by 2030.

Figure 5: The five challenges selected by the European Commission to develop a mission

Articulation of MOPs in cities and/or territories

In recent years, the European Commission has promoted the application of innovation as a tool to solve challenges that benefit society. To this end, the **European Commission implements policies that favor innovation**, such as MOPs in programs like Horizon Europe and other European programs. Thanks to MOPs, projects are promoted that are mission-like in style, with a similar structure, scope, level of commitment, objectives and funding requirements as missions.

As an example of programs that use the style of the missions (Figure 6) is the Interreg EURO-MED, which despite belonging to the Interreg program, imitates many of the characteristics of the missions Europe. In addition, within the program of European missions, we mention the Mission on Climate Neutral Cities and Smart Cities. Despite being a broad mission, given that they are projects and strategies that are applied according to the characteristics of each city, each city has the possibility of articulating its own projects with the structure of the mission.

	Interreg Mediterranean	100 Climate-Neutral and Smart Cities by 2030
THEMATIC	Interreg in EUROMED, focusing on 13 European regions on the northern shore of the Mediterranean, aims at sustainable development and the rational use of resources by promoting innovation. The projects are aligned with the objectives of the Missions and with Europe's priorities for 2030.	The programme's mission is climate neutral cities 2030 with a good life for all within planetary boundaries. The mission aims to accelerate compliance with the Paris Agreement and the 2030 Agenda, promoting innovative projects and strategies in European cities to achieve emissions neutrality
FUNDING	Projects financed by Interreg Funds co-financed with national funds.	Horizon Europe is the main source of funding for this mission, but it must be co-financed with national own funds or with other European programs, such as NextGeneration Europe or the national Recovery and Resilience Plan.
PROJECTS	**AXIS 1:** Green and Blue projects, social and creative (41 projects) **AXIS 2:** Efficient buildings, renewable energy, urban transport (28 projects) **AXIS 3:** Sustainable tourism, biodiversity protection (41 projects) **AXIS 4:** Governance, Strategic projects (5 projects)	Each city decide which projects develop based on their characteristics, capacities and the entities involved. In general, the projects focused on **(1)** Generate sustainable and resilient cities and territories; **(2)** Renovation of buildings to reduce energy consumption; **(3)** neutral and technological mobility **(4)** Evaluate, capitalize and ensure territorial cohesion and solidarity.
STRATEGIES	**(1)** Governance & strategic projects to influence and define policies towards a common goal of territorial development **(2)** horizontal projects to create new methods of cooperation between the various projects in an interdisciplinary manner **(3)** modular projects to study, test or capitalize on **(4)** integrated projects to connect modular projects from study to capitalization phases	**(1)** innovative forms of collaboration between municipalities, regional and national actors, both public and private entities. **(2)** Low Emission Zones (LEZ) and pedestrianized city center streets; **(3)** data collection and analysis for traffic reorganization, city planning and modeling the cities of the future to make them more efficient and sustainable **(4)** new technologies in automotive with hydrogen engines and fuel cells
KEY STAKE-HOLDERS	Specialized agencies, universities, NGOs, local communities, associations and foundations, as well Thematic Transnational Networks and public authorities	Cities, ministries, universities, public and private sector, citizenship, participatory cooperative governance, at local level, scaling up to national and European, with distributed leadership
STATE OF THE DEVELOPMENT	It is the continuation of the completed, INTERREG EUROMED 2014-2020, for the period 2021-27 is expected to start at the end of 2022 and run until 2029..	Some European countries have continued or adapted for this mission technological and urban planning programs that have been developed over the last decade.

Figure 6: Interreg EURO-MED and City Missions particular characteristics

Interreg EURO-MED

As described above, **Interreg EURO-MED** (Mediterranean) for the period 2021-27 will be articulated in the style of a mission, which means that the objectives, thematic projects, external experts, stakeholders and actors involved to participate will be established in the same way as a mission is structured. The Interreg EURO-MED program aims to develop programs in the Mediterranean region with the same philosophy as the missions, solving ambitious and inspiring challenges in order to optimize the conditions for improving territorial and political governance and thus increase the program's contribution (impact) in line with the objectives established by the European Commission. Same as mission, this program will require the participation of specialized entities, universities, NGOs, local communities, associations and foundations, as well Thematic Transnational Networks and public authorities.

The projects included in the program will have horizontal or modular characteristics, so that they are interconnected from a multidisciplinary point of view and involve actors from different fields. Governance will also have the style of missions, so that the different public, private, academic and civil society sectors interact. The programs will have monitoring, management and contact committees with the countries involved, as well as a secretariat to coordinate the committees.

The projects selected in this program will be developed over the next 6 years, starting at the end of 2022. Projects of between 4 and 5 million euros will be financed by Interreg Funds co-financed with national funds.

City Missions

As mentioned in the previous section, the European Commission selected as one of the five relevant current challenges the **Mission on Climate Neutral and Smart Cities** (called City Missions). The objective of this mission is to transform 100 European cities through innovation in order to meet the climate targets set by the European Commission.

Each EU country and each city can develop the strategies and projects they consider most suitable for their cities and their possibilities, as long as they are aligned with the objectives. The fundamental aspect of the mission is the research and development of innovative solutions to be applied to cities. Each country is supported by different innovative and technological centers, so each city will develop projects of a different nature. Part of the funding comes from Horizon Europe, but it must be complemented with other sources of funding. Examples of national agencies that have adopted and tested the Mission Cities model include EcoCités[13] (France, 30 cities), citiES 2030[14] (Spain, 8 cities), Fit4UrbanMission[15] (Austria, 9 cities) and Klimatkontrakt 2030[16] (Sweden, 9 cities).

Decreasing the burden of dementia, an unselected mission proposal

A mission was proposed in the field of neurological diseases: "**Decreasing the burden of demencia**", although it was not selected to be materialized as mission. For this mission proposal (Figure 7), a series of interconnected projects were designed, based on research and innovation, involving all sectors of society (patients, physicians, social workers, families, designers, teachers, programmers, researchers and others). Likewise, the research is multidisciplinary (clinical, technological, big-data, telemedicine, monitoring, medical devices) and is developed in a cross-cutting manner to respond to the challenges posed.

[13] EcoCités, France LINK
[14] CitiES 2030, Spain LINK
[15] Fit4UrbanMission, Austria LINK
[16] Klimatkontrakt 2030, Sweden LINK

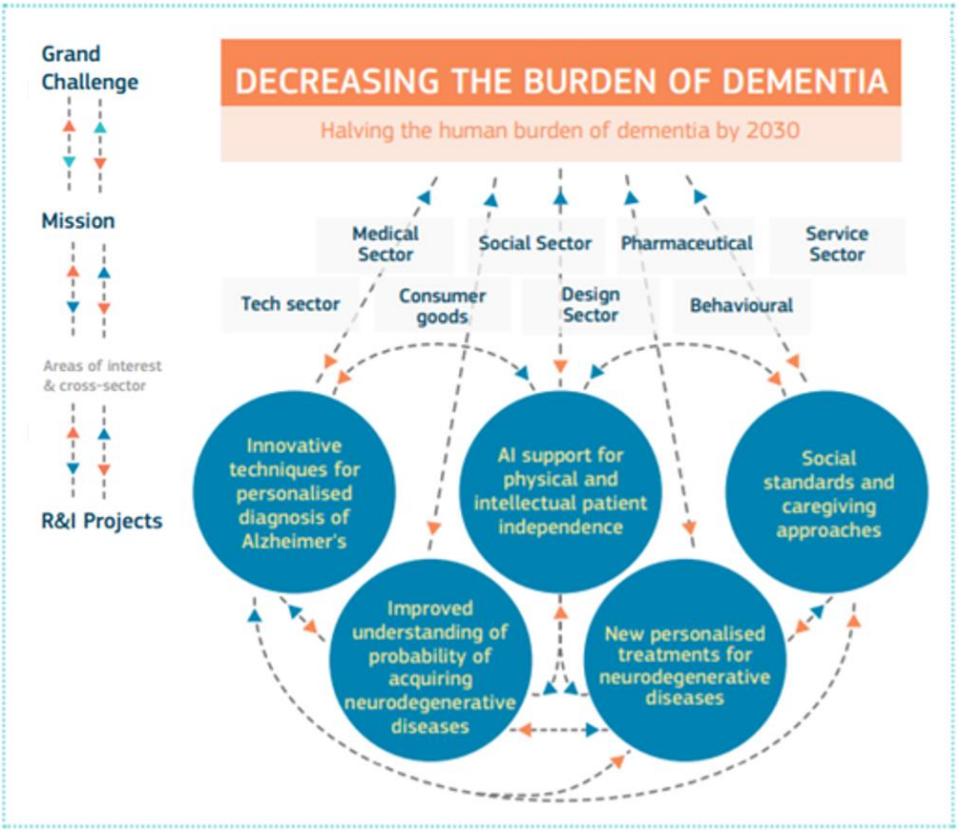

Figure 7: "Decreasing the burden of Dementia" mission structure

PROPOSED METHODOLOGY FOR THE DEFINITION OF MISSIONS-ORIENTED INITIATIVES IN NEUROLOGICAL DISEASES AT THE REGIONAL LEVEL AND IN THE AREA OF COOPERATION.

Neurological diseases are disorders that affect the central nervous system and can impair the brain, spinal cord, peripheral nerves or neuromuscular function[17]. Most of these diseases are directly related to aging, with Alzheimer's disease (AD) and stroke being particularly relevant because of their incidence and the economic burden they entail. More than 7.5 million European citizens suffer from various types of dementia, and these figures will increase in the near future. Neurological diseases are becoming a global challenge, especially in regions with a higher proportion of elderly population over 65 years of age, since neurological diseases are more frequent the older the patients are. These results in a progressive increase in the economic burden related to AD and stroke and other neurological diseases, which must be efficiently managed to ensure the sustainability of health systems in EU countries[18].

[17] David Borsook. Brain. 2012 Feb; 135(2): 320–344. doi: 10.1093/brain/awr271.

[18] Green Paper on clinical guidelines for the management of neurological diseases. neuroATLANTIC: An Atlantic innovation platform on diagnosis and treatment, of neurological diseases and aging 2021.

The report "*Dementia as a European Priority – A Policy Overview*"[19], made in 2020, describes in in detail the current challenges in Europe and the appropriate policies to understand, address and care for patients. Policies must address the fact that in the near future, there will be an increasingly aging population in Europe with longer life expectancy, so the number of patients will increase, aggravating the care, social and economic problem. The social and economic cost associated with dementia was EUR 177 billion in 2008 across Europe, and it is estimated that by 2030 the expenditure will be EUR 250 billion.

Despite all the scientific advances, the lack of treatments and drugs for dementia, some of which are palliative rather than curative as in the case of AD treatments, still poses a difficult challenge. The number of approved treatments for dementia is small, because many potential candidate molecules do not pass clinical trials. Another challenge in neurological diseases is the diagnosis, detection and identification of the disease in patients. Late detection exacerbates the problem of lack of treatment, so efforts in new imaging, genetic and molecular technologies for diagnosis are of great benefit to patients. Awareness of the disease is another challenge to be addressed for the benefit of patients and their families. Disease awareness campaigns can help early detection, anticipate treatment and make the disease more visible in order to reduce or eliminate the social stigma associated with the disease.

In 2018, several proposals were submitted on current challenges that could be solved within the framework of the HE Missions, with the mission on dementia[10] being one of the proposals. The proposed mission on dementia highlights the challenge of neurological diseases today and in the Europe of the future. Although it did not materialize as a Mission, it highlighted the concern about the aging population, the progressive increase in life expectancy and how much remains to be discovered in the field of neuroscience.

Some of the objectives or projects raised in this mission proposal could be developed through regular HE programs or other EU funding programs such as European Territorial Cooperation (ERDF and Interreg funds) and NextGenerationEU. Within the ETC program for the period 2021-27, PO1 aims to create "Smarter Europe", where innovative initiatives at regional level are included as was the neuroATLANTIC project, included in the 2014-2020 period.

In the following sections, we will describe the fundamental component that a mission in neuroscience must fulfill to be successful and the essential requirement to articulate a mission or a mission-like initiative in the cooperation area.

Definition of a mission-style initiative in neurosciences

Creating a European Mission is not an easy task, especially since it is necessary to take many initiatives at the institutional and social level before launching a mission proposal. In addition to the size, the shape and scope, defining the objective is a crucial step, since the problem to be solved can be recognized, but it is necessary to narrow it down and design how to address it. Not all of the challenges identified may be grounds for articulating a mission within the specific HE program that funds the established Missions. It is possible to fully/partially articulate mission-

[19] Dementia as a European Priority – A Policy Overview LINK

style projects based on health and innovation through the HE program or other European funding programs.

To launch an initiative of great relevance in neuroscience, in addition to specifying the challenge to be achieved, requires the interest and commitment of the main actors in society, making it a key actor in the creation of an ecosystem of policies and instruments that favor innovation. However, there is a need for a working group to act as a technical office that will make a major effort to coordinate and seek funding to mobilize the public sector related to the challenge.

The accepted European Missions focus on very different issues and challenges, although they all have some key characteristics in common that give them the mission entity[20]. To promote a mission-style initiative, the following requirements must be met:

1. **Bold, inspirational with wide societal relevance**: the ultimate goal of the missions is to improve the daily life of a significant part of European society. The objective of a mission-style initiative in neurosciences must actively involve all the sectors of the society to solve the challenge. It must involve bold and innovative actions at the level of the European continent, giving a positive impact in the actual and future patients, their families and the healthcare sector.
2. **A clear direction: targeted, measurable and time-bound:** the missions should be clearly framed over a long period of time, with a clear and measurable goal. As the Dementia Mission proposal includes, reduction in the number of strokes or significant improvement in the diagnosis or quality of life of AD patients could be two of the objectives among others. However, missions are time-limited and need a clear timeframe within which actions should take place in order to measure progress and be successful.
3. **Ambitious but realistic research & innovation actions** to achieve the stated objectives. Although research and innovation involve taking the high risks inherent in innovation, actions must be realistic and feasible so that they can be implemented in a timely manner. The development of innovative solutions (such as those requiring technological development) attracts private agents for collaboration, making it easier for the public sector to acquire the good or service.
4. **Cross-disciplinary, cross-sectoral and cross-actor innovation**: The mission aims to bring together teams and actors with different backgrounds, who contribute their expertise to solve the established challenge, promoting interaction and collaboration between different industrial sectors. In the case of the neuroscience disease challenge, in addition to physicians and scientists, engineering teams, software developers and artificial intelligence, among others, must be included, whose contribution will benefit the public service.
5. **Multiple, bottom-up solutions:** the challenges addressed are not achieved with a classical approach, but with the application of multiple technologies to achieve different types of solutions with unexpected results. These solutions must be bottom-up, being

[20] EU Missions in Horizon Europe LINK

applicable in multiple fields in an effective and innovative way, even beyond the objectives of the mission. Solutions could be applicable to other diseases or medical processes, or allowing the creation of new unexplored lines of research.

In summary, to articulate a mission proposal, it is essential to establish an objective (or objectives) of great social relevance at the present time, inspiring and stimulating, causing a great scientific and social impact. Later, it is necessary to anticipate multi-disciplinary approaches, providing innovative solutions applicable to various sectors of society, leading to new advances in other fields. A good design of the timing, scope and key sectors involved is required for the mission to be successful.

Alignment with European MFF programs 2021-2027

Of the challenges proposed to be developed as Missions, the European Commission selected those that were aligned with one or more of the priorities established by the EU for the period 2021-2027. Similarly, new initiatives to be promoted must also be aligned with these priorities in order to be funded and implemented. For the coming years, the EU is strongly promoting policies that favor the application of innovation in all sectors of society, as a means for economic and social growth. The five policy objectives (PO) of the **MFF 2021-2027**, especially PO1 (called "Smarter Europe"), promote the implementation of solutions applying innovation, digitalization, and economic transformation with support to SMEs. In line with the established priorities, the EU favors policies that allow improving the health of citizens, promoting research and development of treatments or with policies that promote better quality of life in aspects such as food, lifestyle habits and healthy environments.

As described above, the **Horizon Europe program** is structured in Pillars, with Pillar 2 focusing on knowledge generation, intensifying the impact of research and innovation (R&I) in the different clusters of the pillar. The main objectives of the Health Cluster are to improve and protect the health and well-being of citizens of all ages by developing and integrating innovative solutions to prevent, diagnose, monitor, treat and cure diseases. In the case of neurological diseases, due to the limited number of treatments available, prevention, diagnosis and monitoring are key factors for patients. In addition, Pillar 2 of HE aims to make public health systems more equitable and sustainable and to improve their cost-effectiveness by introducing tools, technologies and digital solutions for health and care, including personalized medicine.

It is possible to articulate mission-type projects within the HE program even if it is not funded by the specific framework for Missions. A mission-type initiative could be also financed (in its entirety or complementing other sources of financing) within the framework of the **cohesion policies, mainly through the ERDF, Interreg and NextGenerationEU programs**. It is necessary to be familiar with the characteristics of each program in order to design an initiative to increase the chances of it being accepted and funded by the program. Cohesion policies are aimed at promoting the development of specific EU regions through social and industrial transformation, with the objectives of boosting the region's economic growth and fostering territorial cooperation. These programs have their own PO, so it is essential that projects are aligned with the objectives, characteristics and particular policies of each program.

Scope and activities of the mission-style initiative in neurosciences

For the design of an initiative, it is necessary to define the scope, objectives, activities and projects to be included, the geographic extension and the number of participants required. Taking the European Commission Missions as an example, these are large in scope with a high degree of complexity. A mission-style initiative could be planned with a very specific scope, carried out in a specific city or region, and depending on how it develops, the involvement of the actors or the funding, it can increase in scope.

To promote new mission-style initiatives, it is necessary to involve the public administration and the public health system. The public sector can establish policies that favor innovation, such as MOPs, and can support the search for funding for the initiative [11,21]. MOPs and mission-style projects should be adapted according to the challenge to be solved, the scale of the initiative, the objective, the region or countries involved and the sectors or entities involved [8]. The Health System is a key actor in the creation of health policies, reflected in the National health plans, based on the health priorities and recommendations of the EU. However, despite the intermediation of the public administration, an entity, acting as dedicated working team or technical office, should be set up to take on the role of leader and coordinator of the initiative. It is possible to create teams or entities to coordinate the initiative at the local or national level, such as research centers of great relevance or similar public entities (e.g. Health Knowledge Agency[22]).

Mazuccato brings together several considerations about how the **public system** should proceed in the implementation of innovation and how to relate to the private sector[10]. She proposes that governments should lead proactively in guiding society to solve problems rather than offering solutions reactively or correcting problems as they arise. The public sector must create value through its competencies and channel it to society. Examples of this are the technological advances that resulted from space or military programs, or the scientific advances in health driven by the projects of health research institutes. The public sector should not limit itself to administering and regulating according to the social situation, nor should it try to imitate the private sector in the way it operates, but should take the initiative in constructing policies with a view to redirecting society to solve current problems. It should not be understood that the private sector should not be dispensed with at all, but rather that the role of public institutions in society should be rethought. Finally, the public sector must ensure equal opportunities and competition, and freely choose the actors it considers most appropriate for financial support [8].

As seen above, missions must meet certain criteria to be selected for the Horizon Europe program and the same criteria are valid for the design of a mission-style projects funded by European programs. There are key aspects to consider when creating an initiative as are the activities and the design of various implementation plans that it should include. Some of the aspects pointed out by the European Commission are:

[21] *Capacidades institucionales en políticas de innovación orientadas por misiones en México: Estudios de caso sobre elección, diseño y evaluación de las políticas.* Dutrénit, Gabriela et al., March 2021, DOI: http://dx.doi.org/10.18235/0003154. Edited and published by IDB

[22] The Health Knowledge Agency (ACIS) LINK

- **Actions with a multidisciplinary and multisectoral perspective**, so that they are approached from multiple thematic sectors. As a novelty, the European Commission requires that the gender dimension be taken into account in the research and innovation methodology.
- The **implementation plan** must be feasible, robust and likely to achieve the planned objectives. The implementation plan must convincingly describe what work plans and actions (research and innovation actions, deployment actions, possible policy actions, etc.) are to be carried out throughout the mission and by whom.
- **Adequate and robust mission milestones and indicators** should be included in the implementation plan.
- **Outcomes and impacts:** It is mandatory to show how the project could contribute to the outcomes and impacts described in the work program (the path to impact). It is also important to maximize the impact of the project to design a good dissemination and **exploitation plan including communication activities,** to publicize the project and effectively disseminate its results to the target audiences and maximize its impacts, its integration and its further use also after the end of the project.

The governance of innovation missions in the cooperation area

The governance structure of all **European Missions** has many aspects in common at the European level (e.g. mission implementation, coordination, execution, advice among others) regardless of the challenge they aim to solve. At the local level, depending on the mission, the actors, the region and the type of committees may vary. A series of committees are established at the European and regional level for the implementation, coordination and execution of the five missions approved for development within the framework of the HE Missions program, as is depicted in Figure 8.

Figure 8: example of Mission governance (from the *Restore our Ocean and Waters by 2030* Mission[23]).

[23] Restore our Ocean and Waters by 2030 Mission LINK

The governance structure of a project under the **ETC program** consists of several committees and entities. In general, the different Interreg programs have very similar governance with some minor variations. Some of the committees are specific to each country in the region, while other entities are common to all countries in the region. Taking the Interreg Atlantic program[24] as an example, each country in the region has a **Monitoring Committee** which is the main decision making body of the Programme (Figure 9). The Monitoring Committee is composed of representatives of all Members States and regions, Program authorities, representatives of other administrations and civil society organized as advisory members. In addition, each country has its own **National Correspondents**, which is the body that ensures the representation of the Member State in the management structure of the Program and supports the partners at the national level. It is responsible for the dissemination, implementation and management of the Program at the national level. Other entities such as the Managing Authority, the Joint Secretariat, the Certifying Authority, the Audit Authority and the Group of Auditors are common to all participants in the region.

	SPAIN	FRANCE	IRELAND	PORTUGAL	UNITED KINGDOM
MONITORING COMMITTEE	Ministerio de Hacienda Xunta de Galicia Gobierno de Navarra	Préfecture de la région Pays de la Loire Agence nationale de la cohésion des territoires Conseil Régional de Bretagne Conseil Régional Normandie Conseil Régional Nouvelle Aquitaine	Northern & Western Regional Assembly Eastern & Midland Regional Authority Department of Public Expenditure and Reform	Agência para o Desenvolvimento e Coesão I.P. Comissão de Coordenação e Desenvolvimento Regional do Alentejo Região Autónoma dos Açores	Welsh Government Department of Levelling Up, Housing and Communities Scottish Government European Union Division Department of Finance
NATIONAL CORRESPONDENTS	Ministerio de Hacienda y Función Pública	Préfecture de la région Pays de la Loire	Northern and Western Regional Assembly	Agência para o Desenvolvimento e Coesão I.P.	Department of Levelling Up, Housing and Communities
MANAGING AUTHORITY	Comissão de Coordenação e Desenvolvimento Regional do Norte (CCDR-N)				
JOINT SECRETARIAT	Comissão de Coordenação e Desenvolvimento Regional do Norte (CCDR-N)				
CERTIFYING AUTHORITY	Agência para o Desenvolvimento e Coesão I.P.				
AUDIT AUTHORITY	Inspeção Geral de Finanças				

Figure 9: Structure and entities bodies of the Interreg Atlantic Area

The role of the public administration is crucial even if it is not the one driving the initiative (Figure 10). Public entities are involved, encompassing many sectors that are very relevant to the success of the mission, such as the public health system or universities and research centers. The support of the public sector is decisive to achieve a value proposition to apply for European funding programs. For the mission-style initiative to be successful, it is not only necessary to involve the public sector, but also the private sector, with which partnerships can be established with the public sector for the development of innovative solutions. The public sector can also attract other social entities or partners, such as foundations or NGOs, financial networks, philanthropy or citizenship, who can be consulted periodically on specific aspects of the mission-

[24] Programme bodies. Interreg Atlantic Area LINK

style initiative. In short, the participation of all sectors of society is necessary to carry out this type of mission-style initiative.

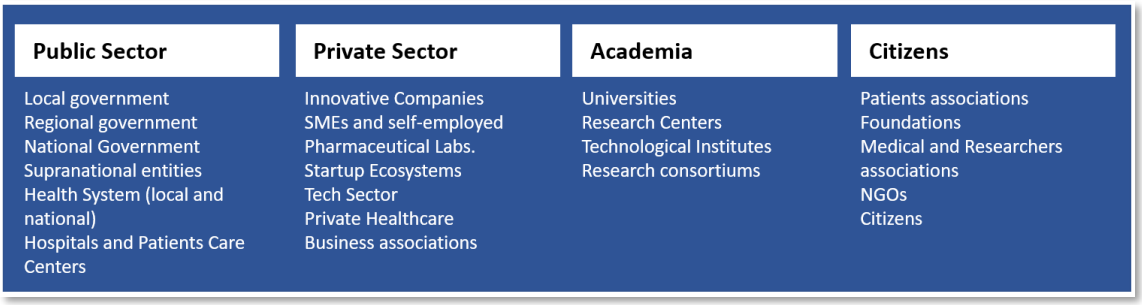

Figure 10: Actors and entities required for a mission-style initiative in neurosciences

European funds and instruments facilitating the creation of a mission-style initiative in neurosciences

After describing how a mission-style initiative should be articulated, its scope and organizational structure, the last key point is its financing. Understandably, the initiative must be designed in such a way that it is attractive and ambitious, attracts interest from multiple sectors and, as a result, is financed with European funds. However, the initiative must be realistic and bankable, and it must comply with the bankable conditions of each European program. As described above, the first step is the **creation of a working team** with sufficient experience and capabilities to promote a mission-style initiative. This working team will be in charge of designing the key aspects discussed above and will contact the public administration to get their support. The involvement of the public administration is indispensable in many aspects, one of the main ones being the attraction of funding.

The promotion of policies and instruments that favor innovation will attract the necessary actors for the initiative, and will therefore be indispensable for the design of the initiative and for obtaining the necessary funding. As an example of public sector initiatives, the Spanish government promoted in 2021 ***SpainNeurotech***[25], a call for interest to create an innovation ecosystem in neurotechnology. The aim is to create a consortium of research institutes with an international perspective, attract companies focused on innovation and favor the application of artificial intelligence in neurosciences. Initiatives such as this one is aligned with the priorities of the European Commission and are financed with funds from the NGEU plan.

The public administration can implement **instruments based on supply and demand**, as shown in figure 11. Public procurement, regulation or systemic policies are the main demand-driven innovation policy instruments. These instruments make it possible to optimize public resources to promote innovation, as well as to find solutions to various social challenges. This instrument has numerous advantages, such as the integration and acquisition of a customized innovative solutions to the buyer's needs, the promotion of companies with innovation as their main

[25] SpainNeurotech, a neurotechnology innovation ecosystem in Spain LINK

activity, favoring visibility, new opportunities and international markets, and the sharing of the risks involved in innovation, among others.

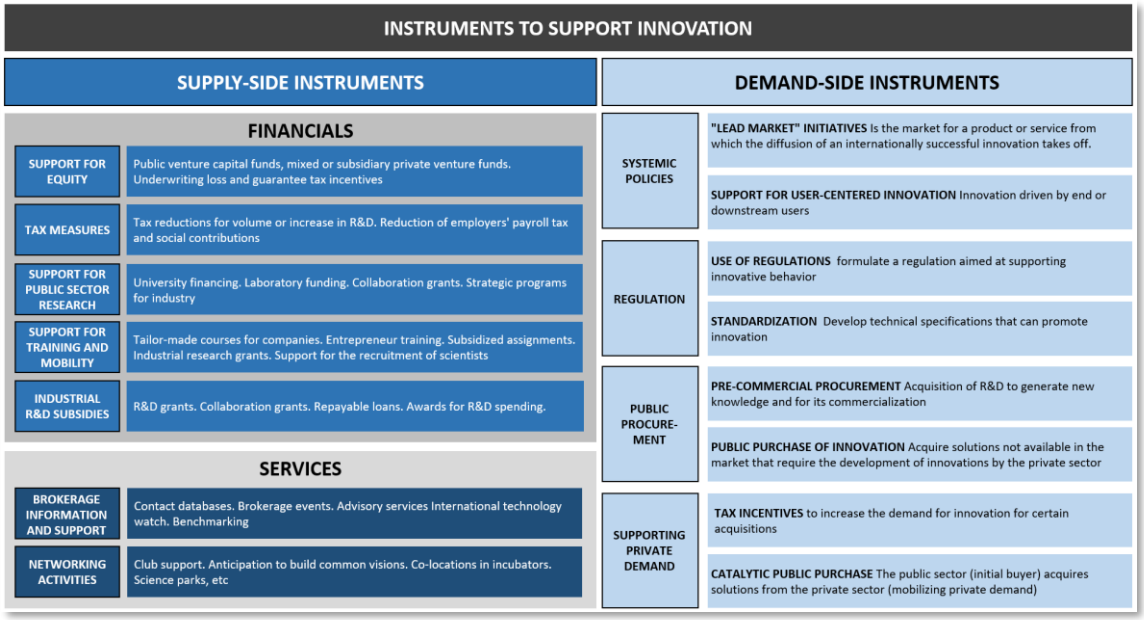

Figure 11: Instruments to support innovation (adapted from Edler 2013[26], Sanchez-Carreira MC[27] *et al*, 2017)

As an example of demand-side instruments, the **PPI4MED project** aims to create and demonstrate a model for transferring results from National Research Centers (NRCs) and companies to public purchasers through the Public Procurement of Innovation (PPI) instrument[28]. This project is part of the **European Territorial Cooperation**, within the Cross Border Cooperation program[29], which promotes cooperation between EU countries and neighboring countries that share a land border or sea crossing. PPI can be a transformational instrument for scientific policy and R&D results financed by the public sector. It will be initiated in 5 national and 1 cross-border living laboratories (Spain, Italy, Tunisia, Egypt, Jordan) for the implementation of 12 real Public Innovative Procurement processes. The **INTECMED** project is an example of a supply-side instrument. This project targets all innovation disciplines and aims to help coordinate their actions by creating regional partnerships, meeting points, mentoring

[26] EDLER, J. 2013. Review of policy measures to stimulate private demand for innovation. concepts and effects. Nesta Working Paper No. 13/13. Manchester Institute of Innovation Research.
[27] Las políticas de demanda en el proceso de innovación fundamentos e instrumentos, RIPS: Revista de investigaciones políticas y sociológicas, ISSN 1577-239X, Vol. 16, Nº. 2, 2017, págs. 229-248 LINK
[28] Technological transfer and commercialization of public research results through PPI in the Mediterranean region (PPI4MED) LINK
[29] Cross Border Cooperation (CBC) LINK

programs and innovation exhibitions, where investors and innovators have the opportunity to exchange their ideas and business opportunities [30].

The **Horizon Europe program** (figure 12), as well the **ERDF, ETC and NextGeneration programs** finances projects, generally in transnational collaboration, in all phases of the process leading from research to the market: research, technological development, demonstration and innovation activities (including social and non-technological innovation), as well as horizontal activities in support of research and innovation. Any legal entity, be it a company, university, research center, association, public administration, or any other type of entity, that wishes to develop an R&D&I project whose content is adapted to the conditions, lines and priorities established in the work program or the calls for proposals, may participate in the Horizon Europe program actions. In addition, Horizon Europe applies new funding instruments such as prizes, innovative public procurement actions or equity and debt financial instruments, to maximize the chances that project results will successfully reach the market.

Figure 12: Funding modalities in the Horizon Europe program

A large part of the activities of this program are developed through consortium projects, which must be constituted by at least three independent legal entities, each of them established in a European Union (EU) member state, or different associated country, with at least one EU entity. For the financing of projects it is important that they have a European dimension, since local, regional or national projects are not financed. In any case, the calls for proposals or work programs may establish additional conditions to those mentioned above, depending on the nature and objectives of the action to be developed, and may even limit the participation of entities from certain countries for strategic or EU security reasons. The consortium must designate one of its members to act as coordinator, who will be the main interlocutor between the consortium members and the European Commission.

In general, Horizon Europe awards non-refundable grants to participants covering up to 100% of the eligible costs of the project (including direct costs plus 25% for indirect costs). In the case of innovation actions the grant will be limited to a maximum of 70% of the eligible costs, except in the case of non-profit entities where the percentage will remain at 100%. In the case of

[30] Incubators for innovation and technological transfer in the Mediterranean (INTECMED) LINK

program co-financing actions, the subsidy will have a minimum of 30% of the total eligible costs, and may reach up to 70% in certain duly justified cases. Confirmed national/regional/private funding sources shall be added to the proposal, understood as contributions included in a proposal or decision, as well as whether it is compatible to apply other possible sources of additional funding in the future.

NextGenerationEU is a temporary recovery instrument endowed with more than 800 billion euros that will help repair the immediate economic and social damage caused by the coronavirus pandemic. This plan aims to inject funds through the Recovery and Resilience Mechanism, the ERDF and additional funds to other European programs or funds, such as projects included in the Horizon 2020 program, InvestEU and the Just Transition Mechanism (JTM).

EXAMPLES OF MISSION-STYLE INITIATIVES IN NEUROSCIENCES

The potential of the neuroATLANTIC platform

Within Interreg Atlantic, the **neuroATLANTIC project** was financed with ERDF funds 2014-2020. It has established a **collaborative network at regional level** that includes several research groups focused on neurosciences in different European countries. The objective of neuroATLANTIC was to bring together remarkable scientific and technological capabilities of the Atlantic Area in the field of neurological diseases. This project acted on clinical, preclinical and capitalization aspects by accelerating the adoption of new innovations that will revolutionize the way neurological diseases are treated in the countries included in the Atlantic Area. The working team focused on the creation of a transnational strategy and platform for the development of new early diagnostic agents for the treatment and early diagnosis of these devastating and prevalent diseases. It was considered necessary to join efforts between the different regions of the Atlantic Area, which could be extended to other European countries, to address the health and social problem posed by neurological diseases, so that common action plans can be established to tackle this problem.

Thanks to the collaboration with several **clusters of companies**, a collaborative network has been created that encompasses innovation companies, patient care centers, biotechs and other research groups that have in common a strong innovation component and a focus on neurosciences. This collaborative network has an interdisciplinary character, since it brings together collaborators with experience in numerous sectors such as diagnostic imaging, the use of artificial intelligence for patient management, the development of software and medical devices, genetic and molecular techniques for the diagnosis and prevention of diseases, the development of new molecules and the care and rehabilitation of patients.

Projects of the characteristics of neuroATLANTIC are an example of the need to advance in the research of neurological diseases, searching for new treatments, diagnostic methods and better clinical practices that will benefit current and future patients. It is reasonable to propose initiatives that apply the methodology of missions at national or European level that give continuity to the work initiated in the neuroATLANTIC project. These initiatives, multidisciplinary and involving all sectors of society, would allow the creation of new research projects, scientific and social activities or business opportunities. This could benefit many sectors of society, starting with the patients, the research groups involved or the companies that have innovation as their main activity.

The platform created in the neuroATLANTIC project is in a position to promote and elevate initiatives with the capacity to solve the current challenges in the field of neurological diseases. The main objective of the initiative and the platform is to promote and strengthen research programs in the field of neurological diseases that allow the development of collaborative, cross-cutting and innovative projects aimed at solving the defined health challenges and aligned with the capabilities of the region. The role of the neuroATLANTIC team would be that of a working group or energizing agent, which would drive and shape the implementation of the mission-style initiative, supporting the design of the structure and governance. In addition, it would be in charge of implementing the activities, evaluating the progress of the initiative according to the

objectives and finding sources of funding for the activities to be carried out. In a way, the neuroATLANTIC platform can become an entity that acts as a technical office, contacting and organizing the agents involved.

The main aspects to start a mission-based initiative in neurosciences

A specific mission-style initiative in the field of neurological diseases requires the **creation of an advisory committee** to lead and coordinate the other committees composed of various specialists and stakeholders. It can also actively participate in the design of research initiatives and projects of various types of basic and clinical research, as well as in the development of solutions by private innovative or technological development companies. It is important that the advisory committee take into account all social agents when defining the initiative's projects. In order to get public and social entities involved, periodic initiative presentation days, awareness-raising days and presentations to citizens will be organized to bring them closer to the initiative and involve them in it. All these initiatives, among others, will be included in a communication plan.

Those responsible for the mission-style initiative will be the corresponding public health systems and public administrations. The neuroATLANTIC platform, with its vast experience in neurosciences, could support the working team in charge of promoting the initiative. Each region will have to promote and raise with their respective government bodies and health entities the desirability of creating initiatives that will lead to beneficial plans for society as a whole. Through multiple interviews and workshops, the current challenges, the structure of the initiative and the strategic plan with the challenges, objectives and projects to be carried out before 2030 will be transferred to the public administrations. It would be understandable to start at a local level (in one country of the alliance) and move towards a multinational level, coordinating efforts in projects and programs common to the members of the region. In coordination with public administrations, it is necessary to take into account key aspects such as:

- Establish and create the **steering committee**, which will be the maximum responsible for the governance and the projects included in the initiative. This committee will include the highest representatives of the public administrations participating in the initiative.
- Create a **Scientific Advisory Committee** for the projects included in the initiative.
- Establish a **management and scientific steering body** for the initiative to direct the activities and ensure interaction with the different stakeholders.
- Establish the **working group(s)** that will be in charge of the different operational areas, such as economic and financial management, communication and dissemination of the initiative and project management.
- Organize **periodic meetings** to review the implementation process.

The public administration, through the corresponding departments (health, innovation, economy, social affairs among others) is in charge of implementing plans and policies that favor the creation of multisectoral initiatives that promote programs and projects in the field of neurological diseases. The public administration, with the support of the corresponding committees of the initiative, will contact and attract the innovative agents and entities involved, both public and private. In addition, as described above, public administrations are responsible for articulating supply and demand instruments (see Figure 11) that favor innovation as a fundamental tool for solving society's challenges.

The structure of the initiative must be aligned, at a general level, with the priorities established by the EU for the period 2021-2027. As described above, the main European programs to which it could apply are Horizon Europe, NextGenerationEU and European Territorial Cooperation. In particular, each European funding program has its own characteristics, which must be taken into account when designing the objectives and scope of the initiative in order to obtain funding from the European program to which it applies. The public administration will also be responsible for facilitating the attraction of funding from European programs to develop the initiative. The governing bodies of the public administration will be responsible for channeling European funds and providing their own sources of financing to complement European funds.

Figures 13 and 14 show two possible initiatives based on the style of the missions to solve two neuroscience challenges, with the objectives, agents involved and projects to be included in the initiatives. Figure 15 lists the most relevant indicators to be taken into account to evaluate the progress of the initiative to successfully achieve the objectives.

Challenge example 1: Reduce the burden of the Alzheimer's disease

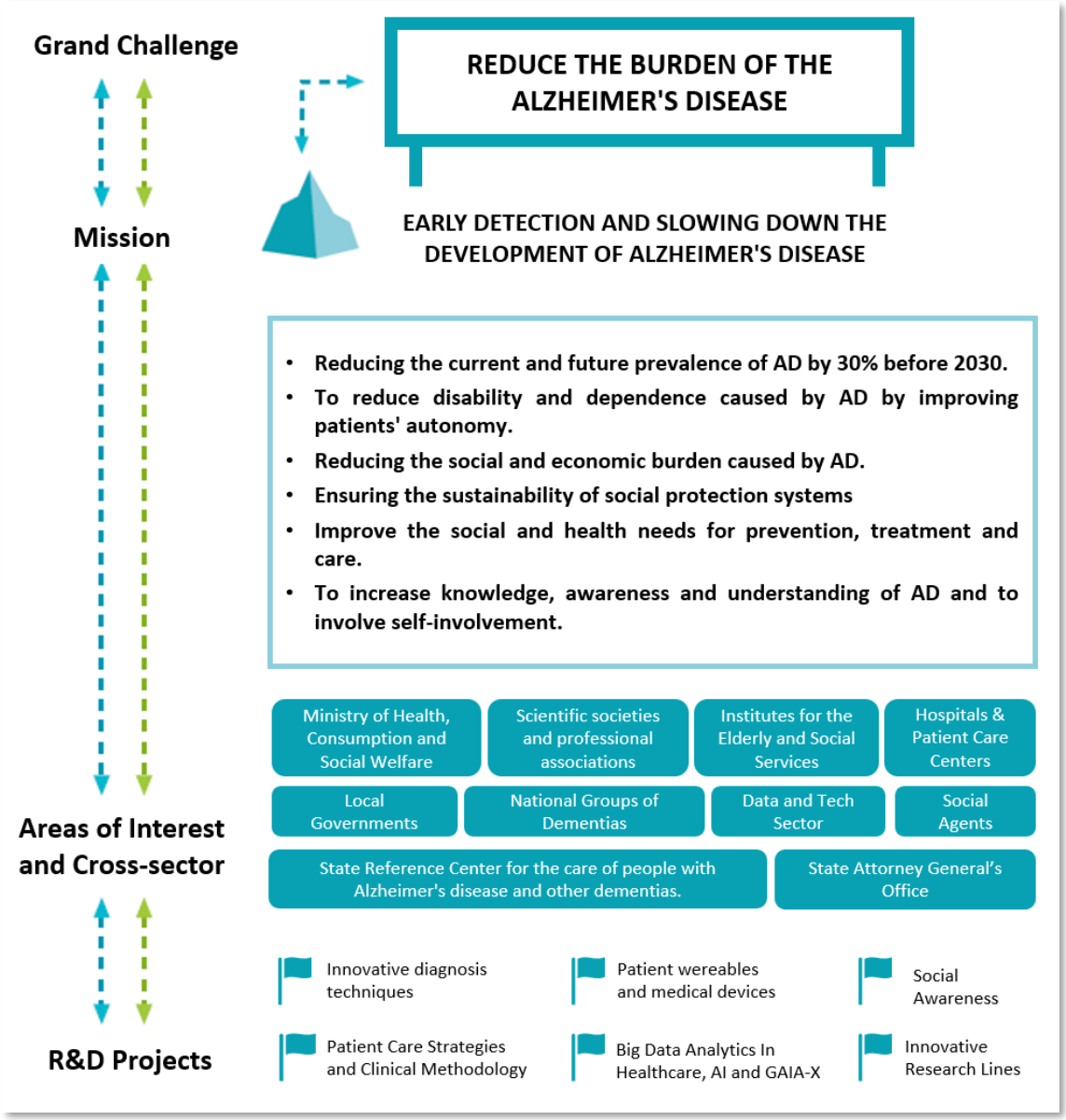

Figure 13: Reduce the burden of the Alzheimer's disease initiative structure

Challenge example 2: Preventing strokes deaths

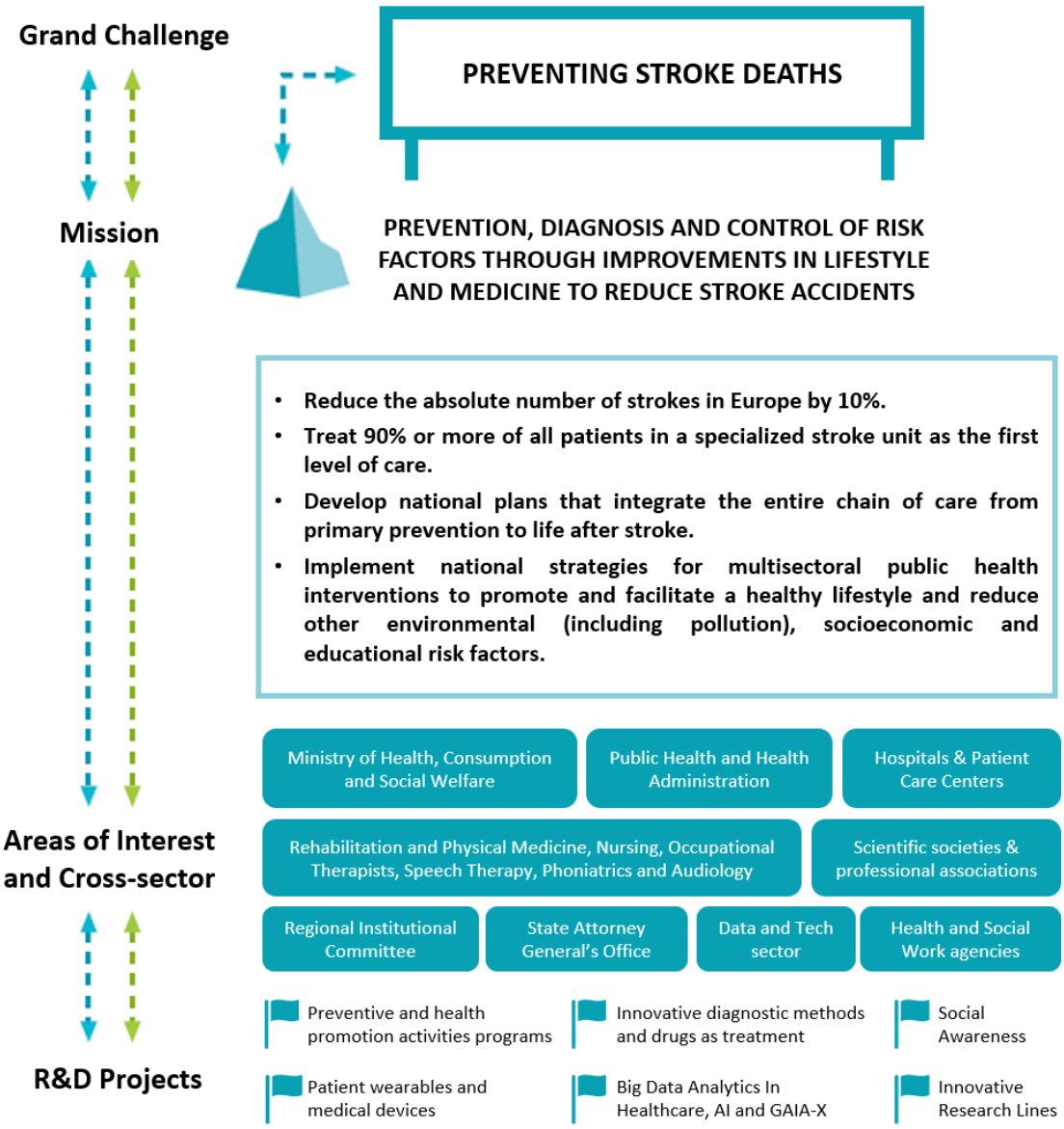

Figure 14: Preventing strokes deaths initiative structure

INDICATOR	DESCRIPTION
Degree of implementation of the initiative	Objectives achieved
Configuration of the Governance	Components of Governance
	Steering and operational management committees
	Nº of entities participating in the mission
Scientific Projects	**Nº R&D projects launched**
	Nº collaborations established between research institutions and companies
	Nº publications resulting from the projects
	Nº transfer initiatives
	Nº licensing agreements or service contracts established
Communication and outreach	Presentation days of the mission-style initiative
	Events, workshops, scientific conferences with the participation of the scientific, technological and business environment
	Awareness-raising sessions with society
	Participatory workshops with agents of society
	News in the media and impacts in social media
Funding	Competitive funding obtained at the public level
	Non-competitive funding obtained
	Funding for the recruitment of research talent

Figure 15: Indicators of the initiative implementation