

# JPND Research Strategy

Tackling the challenge of Alzheimer's and other neurodegenerative diseases in Europe



**JPND**  
research

EU Joint Programme – Neurodegenerative Disease Research

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# Foreword from the Chair

Over seven million people in Europe suffer from neurodegenerative diseases, yet treatments that prevent or stop the progression of neurodegeneration are still lacking. This places a heavy burden on the individuals with disease, their relatives and society as a whole; a problem that will only get worse as the European population inexorably ages. Tackling this 'grand' challenge is clearly beyond the scope and resources of any one country. Enhanced co-ordination of national efforts is required to stimulate research by bringing together funding bodies, researchers and other stakeholders to consider the existing research evidence, build a common vision, and facilitate sharing of tools, techniques and other resources more efficiently. Only by maximising our collective potential can we confront this common challenge. The difficult economic climate in which Europe finds itself at the moment reinforces the need for European states to structure and optimise what should be the foundation for their future growth and economic resilience: research and innovation strategy.

The EU Member States, through the EU's Competitiveness Council and research and higher education ministers, endorsed in December 2008 a new concept of research collaboration: Joint Programming. This was defined as a process by which countries would develop common visions and strategic research agendas in order to address major societal challenges for which the scale and scope of their national programmes alone may not be adequate. The EU Joint Programme - Neurodegenerative Disease Research (JPND) was the first Joint Programming Initiative to be launched and, as of today, 24 countries have come together to develop and implement this new approach.

Beyond the initial exchanges, essential to build trust and learn how to work together, the very first achievement of JPND has now been delivered. This common Research Strategy will guide research activity and investments in the field of neurodegenerative diseases over the coming decades in Europe. The fruit of a tremendous amount of work and enthusiasm, this holistic, multifactorial and multidisciplinary view is now a reality. This strategic approach will foster scientists' talents and unleash the creativity needed to accelerate the development of cures for neurodegenerative diseases, promoting European research and delivering medical and economic impact for its citizens.

Professor Philippe Amouyel,  
Chair of JPND Management Board

# Executive Summary

## 1. Background and Purpose of the Research Strategy

Neurodegenerative diseases (ND) are debilitating and largely untreatable conditions that are strongly linked with age. Amongst these disorders, the dementias are responsible for the greatest burden of disease, with Alzheimer's disease and related disorders affecting some 7 million people in Europe, and this figure is expected to double every 20 years as the population ages. It currently costs in the order of €130 billion per annum to care for people with dementia across Europe, highlighting age-related neurodegenerative disease as one of the leading medical and societal challenges faced by our society.

The EU Joint Programme - Neurodegenerative Disease Research (JPND) is an innovative, collaborative research initiative established to tackle the mounting challenges posed by ND. It aims to enhance the impact of research by aligning and building upon existing national programmes and identifying common goals that would benefit from joint action. This Research Strategy provides a framework for future investment and addresses how the European research effort can most effectively be harnessed to improve prevention, diagnosis, treatment and patient care for these debilitating conditions.

## 2. Scientific Priorities and Enabling Activities

### Scientific Priorities

To achieve impact there is a need to encourage novel as well as multidisciplinary approaches, and to strengthen and extend existing capabilities across the full spectrum of basic, clinical, health and social care, and translational research. A number of thematic priorities for future research have been identified:

- **The origins of neurodegenerative diseases (ND)**

Further knowledge is needed regarding the causes of specific ND, the factors that determine people's risk and resilience, and the triggering events leading to illness. The characterisation of 'at-risk' populations should ultimately inform preventive strategies, and this will necessitate research to uncover new genetic, epigenetic and environmental risk factors for ND, and assess their interplay. Alongside this, there is a need to better understand the normal ageing process and how this relates to the development and progression of ND. The identification of environmental and behavioural modulators of these processes will also provide insight into those factors that determine protection from, and resilience to, disease.

- **Disease mechanisms and models**

A more complete understanding of the underlying disease mechanisms is required to underpin the development of new diagnostic and therapeutic approaches, as well as to identify appropriate time-windows for intervention. Amongst the multiple approaches to be pursued, there is a need to establish novel cell-based and animal models that accurately represent key elements of the disease process, and that take into account factors such as the progressive nature of ND, comorbidities, gender and ageing. Effort will also be needed to elucidate the biological and environmental basis of behavioural and psychological symptoms in ND.

- **Disease definitions and diagnosis**

Standard clinical assessments fail to capture the presumed complexity of common ND, necessitating refinement and updating of the current diagnostic criteria. The various forms and subtypes of ND, including the stages before clinical symptoms emerge, require better definition, while new or improved diagnostic tools are needed to allow the earlier and more accurate detection of ND. New biomarkers are essential, and should seek to provide links between human and animal-based studies, as well as provide measures of disease progression, prognosis and treatment effects. Standardisation and harmonisation across such tools and assessments will be critical to ensure the comparability of results and support cross-centre studies.

- **Treatments and prevention**

Progress in identifying new targets and developing drugs against them will be enhanced by promoting bidirectional connectivity between studies in animal and cell models and patients, while procedures to improve the selection (or stratification) of subjects entering clinical trials might also provide a greater chance of showing clinical efficacy for new treatments. Studies should also be encouraged to further develop psychosocial interventions, paying attention to the promotion of social inclusion and carer involvement, while the establishment of cohorts of patients with preclinical ND would provide a platform for the future testing of interventions to either prevent or slow disease progression. Lastly, longer-term approaches should be pursued that promote regenerative strategies and that develop novel systems for the delivery and targeting of drugs and biologicals to specific sites in the brain and nervous system.

- **Healthcare and social care**

At present there is inefficient co-ordination between health and social care systems in individual countries, necessitating an evaluation of the equity of access to, and the effectiveness and cost-effectiveness of, pathways to diagnosis, treatment, care and support for ND across Europe. There is a need to identify the critical factors that impact upon disability and health-related quality of life in ND, including the effects of comorbidity, nutrition and frailty, and the interaction with family, carers, the environment, and health and social care systems. It is also necessary to address the fact that the current evidence base for therapeutic strategies is largely derived from intensive and short-term studies that do not readily translate into real-world settings, while improved outcome measures are required that better reflect patient and carer perspectives. Assisted living technologies may help address the needs of patients with ND and their carers in both early and moderate disease states, although greater emphasis should be placed on addressing the specific burden of ND as opposed to focussing on ageing in general. Further research should also be undertaken to inform palliative and end-of-life care, which along with other areas of ND research, should appropriately integrate research into the complex ethical issues relating to ND.

## Enabling Activities

A number of cross-cutting activities will be needed to progress the scientific themes outlined above:

- **Knowing our research capability**

National and European-level ND research activity has been mapped to identify both research gaps and those opportunities that can be addressed through improved co-ordination and investment. This forms the basis of a public database that will both showcase ongoing ND research across Europe and promote better use of resources and infrastructure.

- **Supportive infrastructure and platforms**

In seeking to create an enabling environment for ND research, there is a need to encourage integration and harmonisation of data and materials, and promote an open-access approach to their use. Standardised guidelines, methods and tools for data collection and analysis should be promoted, for example, to address the requirements of high-throughput technology platforms and biobanking, and to better exploit population cohorts. Policy frameworks should be reviewed to facilitate research across the full range of healthcare structures, including general hospitals and primary and community care.

- **Working in partnership with industry**

Many different commercial organisations engage with ND research, ranging from the pharmaceutical, diagnostic and biotechnology sectors to assisted living and healthcare providers, including the care home industry. Connection between and across the academic and commercial domains is essential to deliver new approaches to treatment and care. Data and resource exchange between industry and academia should also be encouraged.

- **Working with regulatory organisations**

The promotion of effective translation of research through to patient benefit requires engagement and co-operation with the key European and national regulatory agencies to ensure that regulation is easily understood by researchers and proportionate to risk. Regulatory support networks should be promoted to provide access to guidance that can inform study design and address potential bottlenecks at an early stage.

- **International partnership beyond Europe**

It is recognised that the unmet clinical need and societal impact of ND is a global issue, and that opportunities may emerge to link to worldwide research efforts in this area. Such co-operation should be strategically directed and offer clear added value to JPND's objectives.

- **Capacity building**

Certain areas of research lack capacity and need to be strengthened. Accordingly, networks should be established across and between disciplines and researchers, while particular effort is needed to promote clinical researchers and translational specialists, and increase the numbers of ND researchers with expertise in health economics, statistics, computational biology and bioinformatics. In order to ensure that excellence in the healthcare and social care field is established on a broader basis across Europe, methodological hubs might be created to support study development and the evaluation of interventions, service and care pathways.

- **Education and training**

The advice provided to patients with ND across the range of different health and social care professionals should be based upon a good understanding of the disorder, the patient needs characteristic of these conditions, and the available evidence-based options for treatment. Clinical and research education and training programmes should be tailored to promote this, and seek to embed a research culture across the full spectrum of health and social care. Alongside this, there is a need to promote public health messaging to help mitigate those risk factors for ND that are associated with an unhealthy lifestyle. Public health messaging must be supported by research into how best to effect behavioural change at the population level.

- **Connection to policy makers**

JPND will provide a framework through which to highlight important issues for national policy consideration, which should promote compatibility between the policy approaches of different countries. Two translational gaps in ND policy need to be addressed, firstly, in the implementation of new technologies or practices, for example, in the area of telemedicine, assisted living or in delivering services, and secondly to ensure that research outcomes are effectively implemented into public health policy.

- **Communication and outreach**

For effective translation into policy and practice, the research agenda must connect and engage with a wide range of sectors. JPND will ensure that all stakeholder communities are well informed about ongoing ND research and its outcomes, increasing awareness and support for ND research among decision makers, patients, patient and carer organisations and the public. This should also help to increase research participation and reduce the stigma attached to ND.

### 3. Delivery of the Research Strategy

The Research Strategy provides a framework of opportunities for countries involved in JPND and willing to participate in joint actions, which will be implemented through co-operative activities that realign or link national investments to achieve increased impact, and the provision of new funding. A guiding principle for its delivery will be that the research to be supported is of the highest scientific quality.

### 4. Summary

JPND is a pioneering example of 'Joint Programming', a new and flexible approach that has the capability to address a major societal challenge which cannot be resolved through national programmes alone. This document sets out the common vision of the 24 European countries involved, and provides a strategic approach to support world-class research that can exploit emerging scientific opportunities, confront barriers to progress, and provide new approaches to prevention, intervention and care. The recommendations outlined in the Research Strategy address the full spectrum of research and approaches that are required to achieve impact, and recognise the important role that other stakeholder groups have in delivering this agenda. The ultimate goal is to undertake research that can be translated into new interventions that improve the health and wellbeing of patients with ND and their families and carers, and that delivers economic and societal benefit throughout the European Union.

Theme	Actions	Outcomes
<p><b>Understanding disease</b></p> <ul style="list-style-type: none"> <li>• Origins</li> <li>• Mechanisms</li> </ul>	<p><b>Establish Europe-wide, population-based and longitudinal studies</b></p> <ul style="list-style-type: none"> <li>• cohorts for rare and common ND, and for ‘at-risk’ and preclinical populations</li> <li>• biobanking for DNA and body tissues; promote data-sharing</li> </ul> <p><b>Develop improved animal and cell-based models</b></p> <ul style="list-style-type: none"> <li>• account for genetic variability, chronicity and ageing</li> </ul> <p><b>Understand the biological basis of behavioural and psychological symptoms</b></p> <p><b>Investigate the role of comorbidity in ND</b></p> <p><b>Understand ageing and its relationship to development of ND</b></p>	<p><b>Identify causes of disease</b></p> <p><b>Determine factors involved in risk and resilience</b></p> <p><b>Identify triggering events</b></p> <p><b>Identify new targets for drug development</b></p>
<p><b>Disease progression</b></p> <ul style="list-style-type: none"> <li>• Pathology</li> <li>• Diagnosis</li> </ul>	<p><b>Develop new diagnostic criteria and biomarkers of disease prediction, progression and treatment</b></p> <ul style="list-style-type: none"> <li>• develop common definitions and procedures across Europe</li> <li>• harmonise and standardise biomarkers, diagnostic tools and assessments</li> </ul> <p><b>Improve selection and stratification of patients for clinical trials</b></p>	<p><b>Diagnose disease earlier and more accurately</b></p> <p><b>Optimise therapeutic time window</b></p> <p><b>More effective drug development and trials</b></p>
<p><b>Interventions</b></p> <ul style="list-style-type: none"> <li>• Prevention</li> <li>• Treatment</li> <li>• Care/management</li> </ul>	<p><b>Support prevention and intervention studies</b></p> <ul style="list-style-type: none"> <li>• preventive approaches based on risk factors</li> <li>• both drug and non-pharmacological interventions, and combinatorial approaches</li> <li>• ensure clinical outcomes are patient-centred and factor in quality of life</li> <li>• partnership with industry</li> </ul> <p><b>Establish new cell-based screens for ND drug evaluation</b></p> <p><b>Promote assisted living technologies for ND</b></p> <p><b>Strengthen research into regenerative and other novel treatment approaches</b></p> <p><b>Assess health and social care pathways across Europe for patient access and cost-effectiveness</b></p> <p><b>Investigate how to manage challenging behaviour and support end-of-life care</b></p>	<p><b>New therapeutic approaches and preventive strategies for ND</b></p> <p><b>New delivery systems for drugs and biologics</b></p> <p><b>Positive impact on care and quality of life for patients and carers</b></p> <p><b>Relieve economic and social burden of disease</b></p>
<p><b>Society and policy</b></p> <ul style="list-style-type: none"> <li>• Education and training</li> <li>• Regulation</li> </ul>	<p><b>Build capacity, in particular for clinician and translational scientists</b></p> <p><b>Expand training of healthcare professionals and improve public health education</b></p> <p><b>Promote research in non-specialist settings (e.g. primary and community care)</b></p> <p><b>Encourage implementation into evidence-based policies and best practice</b></p> <p><b>Promote a supportive regulatory and ethical environment for ND research</b></p>	<p><b>Increased numbers of researchers</b></p> <p><b>Raised profile of ND research across all sectors</b></p> <p><b>Social acceptance of ND and increase in research participation of patients and carers</b></p>

# Glossary

**AAL** – Ambient and Assisted Living: Use of intelligent products and provision of remote services to allow people to live in their preferred environment by increasing their autonomy and assisting them, their carers and families in carrying out activities of daily living.

**Animal models** – Living, non-human animals that reproduce all or some aspects of a condition or part of a disease pathway and which are used during investigation into human disease. They are used both to test understanding of disease pathways and to provide the tools for developing and assessing therapeutics.

**Biomarker(s)** – Short for biological marker: A characteristic that is measured or evaluated as an indicator of a biological (or cognitive) state, e.g. to evaluate the presence or progression of disease or a response to treatment.

**Clinical trial** – A scientifically controlled study that is carried out in consenting human beings to evaluate the safety and effectiveness of a therapy.

**Comorbidity** – The presence of one or more disorders in addition to (in this case) neurodegenerative disease.

**Disability** – Following the World Health Organisation model, disability is an umbrella term for impairments, activity limitations and participation restrictions. It denotes the negative aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal).

**Disease register** – A collection of people with a particular disease who have indicated they would be willing to participate in medical research.

**ICT** – Information and Communications Technology.

**(Mechanistic) pathway** – The components involved in a physiological process, their relationship and interactions with each other.

**ND** – Neurodegenerative Diseases: An umbrella term for a range of conditions primarily involving neurodegeneration, which is the progressive loss of structure or function of neurons, including death of neurons. ND included in the JPND initiative are Alzheimer's disease and other dementias (AD), Parkinson's disease (PD) and PD-related disorders, prion disease, motor neurone diseases (MND), Huntington's disease (HD), spinocerebellar ataxia (SCA) and spinal muscular atrophy (SMA).

**Neuron or neurone** – A specialist cell found in the nervous system responsible for transmitting information by electrical and chemical signalling.

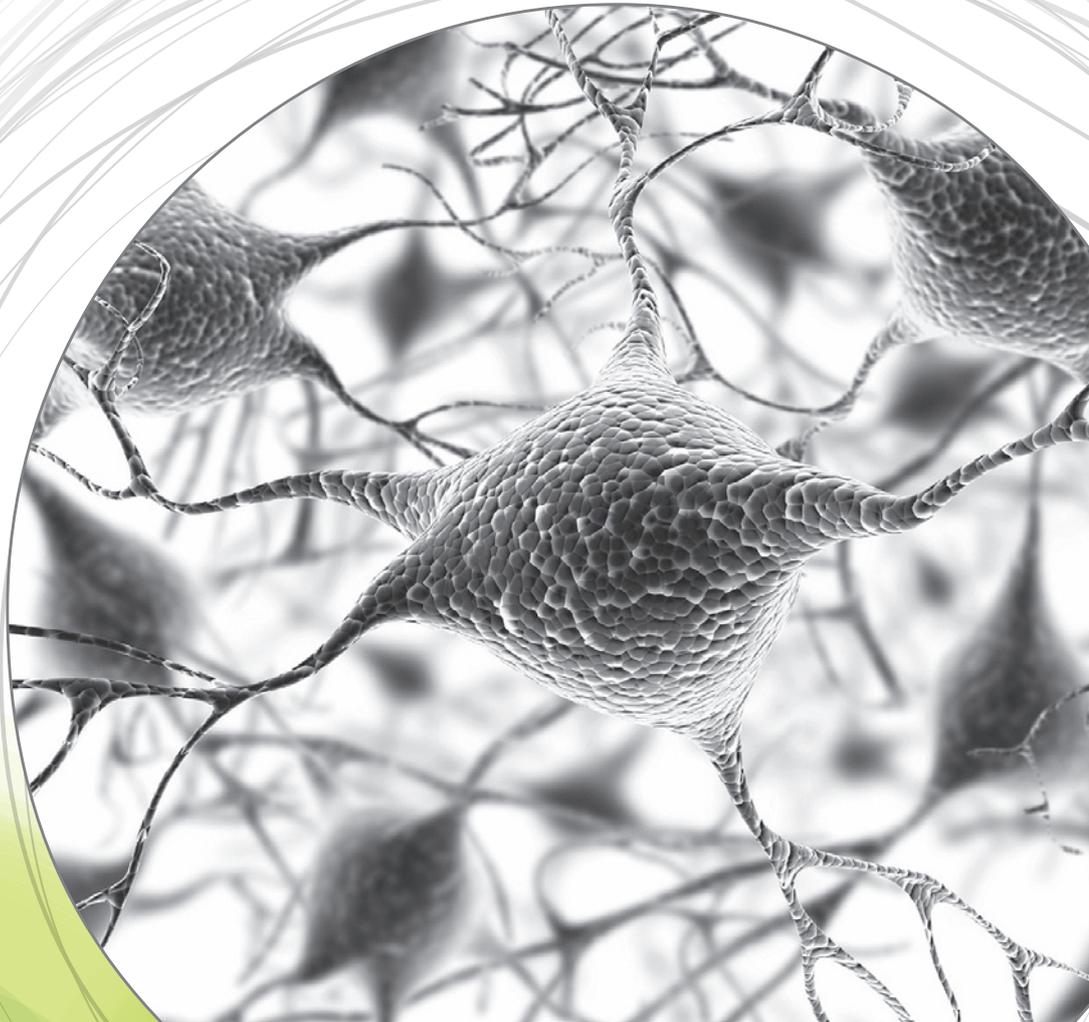
**Non-pharmacological interventions** – Prevention strategies and treatments that do not involve the use of chemical agents; for example, physical or behavioural therapy or initiatives that promotes meaningful activity or social interaction.

**QoL** – Quality of Life: An individual's total wellbeing including all emotional, social and physical aspects.

**Stratification** – The process of dividing patients into more specific classes or groups with the idea that their response to treatment will be more uniform (and so easier to assess).

**Translation** – The continuum of the process from scientific discovery through to its application; for example, to deliver new drugs or medical devices that can be used in the treatment of patients, or to ensure the implementation of scientific evidence into policy and practice.

**Reverse translation** – The use of human/clinical data to inform and refine laboratory or animal-based research.



# 1. Introduction

Neurodegenerative diseases (ND) are debilitating and largely untreatable conditions that are strongly linked with age and lead to disability and reduced quality of life (QoL). In Europe there are estimated to be between 6.3 and 7.3 million people<sup>1,2</sup> with Alzheimer's disease and related disorders, the most frequent class of ND, and this figure is expected to double every 20 years as the European population ages.<sup>3</sup> In addition to the heavy burden put on the patients, relatives and carers, the total direct and informal care costs of Alzheimer's and related disorders is in the range of €105–160 billion<sup>2,4</sup> across the EU27, highlighting age-related ND as one of the leading medical and societal challenges for the next 15 years.

To tackle the societal problems posed by ND as effectively as possible and accelerate progress in the search for solutions, 24 European countries have established an innovative collaborative research initiative: EU Joint Programme - Neurodegenerative Disease Research (JPND). The objectives of JPND are to align and build upon national programmes to increase the impact and effectiveness of research undertaken within the participating countries, and to identify common goals that would benefit from joint actions between these countries and the European Commission. Ultimately, JPND seeks to improve the scientific understanding of ND, provide new approaches for their prevention, diagnosis and treatment, and ensure effective provision of healthcare, social care and support so that individuals receive optimum care and optimised QoL at all stages of their illness.

The development of a Strategic Research Agenda (SRA) is central to the JPND initiative, establishing a platform for future Europe-wide activity and a reference point for developing national and organisational strategic plans. The SRA forms the basis for this Research Strategy, which provides a framework for future investment and addresses how the European research effort can most effectively be harnessed to improve prevention, diagnosis, treatment and patient care for these debilitating conditions. The SRA is based on scientific recommendations made by the JPND Scientific Advisory Board (SAB), reflecting the outputs obtained through a series of thematic workshops involving research opinion leaders. Consideration of stakeholder priorities was obtained through a mixture of meetings and individual contacts with key groups, including industry, organisations representing people with ND and their carers, healthcare and social care professionals, and healthcare providers. This process provided a holistic view of the research landscape and a roadmap for future research activity, with key recommendations validated via a public consultation exercise, prior to consideration of feasibility and prioritisation by the SAB and JPND Management Board (MB).<sup>5</sup>

1. [http://ec.europa.eu/health/ph\\_information/dissemination/echi/docs/dementia2\\_en.pdf](http://ec.europa.eu/health/ph_information/dissemination/echi/docs/dementia2_en.pdf).

2. Gustavsson A et al. (2011) Cost of disorders of the brain in Europe 2010. *Eur. Neuropsychopharmacol.* Oct;21(10):718–779.

3. Alzheimer's Disease: Scientific, medical and societal implications. *INSERM Collective Expert Report* (2007).

4. Wimo A et al. (2010) The economic impact of dementia in Europe in 2008: cost estimates from the Eurocode project. *Int. J. Geriatr. Psychiatry* Oct;28(26):825–832.

5. Further information on the development of the SRA and the governance of JPND can be found in the Annexes and on the JPND website: [www.neurodegenerationresearch.eu](http://www.neurodegenerationresearch.eu).

# 2. Current Research Landscape

## Science

The number of neurodegenerative diseases for which treatments are available is very limited at present and those that do exist only treat the symptoms and not the cause. Furthermore, standard clinical diagnoses are based on relatively advanced signs of disease and often do not take into account underlying biological diversity, meaning that treatments are generally initiated at too late a stage to have significant impact and that the different aetiologic factors cannot be targeted directly. There is also a gap in our understanding of the environmental exposure risks in early life, as most current evidence is derived from patients born in the first half of the last century, meaning that further research must be conducted if the risks associated with modern lifestyles, which are increasingly sedentary and isolated from family, are to be identified.

The complexity of brain structure and function provides a significant challenge for fully understanding the molecular and biological basis of neurodegeneration, and, as a consequence, the appropriate clinical and therapeutic tools to limit the incidence and spread of ND are still lacking. However, in the last two decades the combined application of novel research methods (such as molecular genetics, cell engineering, animal modelling and *in vivo* imaging) has provided significant progress, enabling us to identify markers of pathology and to begin to generate innovative therapeutic strategies to limit the progression of these diseases. The strength of cohort and population studies in Europe has contributed much to the understanding of risk factors associated with ND, and through the increasing integration of genetic, cellular, brain imaging and population data it is increasingly recognised that a number of mechanistic pathways are common to several ND. This in turn provides the hope that advances in fundamental research can accelerate the translation of such findings into early detection and effective therapies.

## Current Activity

To date, large investments in research have been made to address the impact of age-linked diseases, such as cancer and cardiovascular disease, resulting in major improvements in treatment and patient outcomes. In contrast, neurodegenerative and other brain diseases have not received the same level of support; for example, while brain disorders collectively constitute around 35% of the total (direct) cost burden of all diseases in Europe, a far smaller proportion of the healthcare (~15%) and research budgets are allocated to this area.<sup>6</sup>

As outlined further in Section 3.2, a mapping exercise of the national and European research landscape relevant to ND has provided an objective view of current research activity across Europe. A snap-shot of research programmes or grants<sup>7</sup> 'live' as of 1st January 2011 positively identified nearly €1620 million of investment in research directly relevant to ND, with the majority of this investment (82%) in major programmes or grants.<sup>8</sup> A breakdown of the total and per year costs captured during the mapping exercise is presented below.

6. Andlin-Sobocki et al. (2005). Costs of disorders of the brain in Europe. *Eur. J. Neurol.* 12(Suppl 1):1–27.

7. This figure excludes spend on training or career-development posts (PhDs, fellowships, etc.), and resources or infrastructure.

8. Individual programmes or grants of >€500,000 in the basic and clinical research domains or >€200,000 in the health and social care domain.

	Number of projects	Full value (€ millions)	%	Per year (€ millions)	%
<b>Total</b>	2,244	1,620	-	370	-
<b>Major investment<sup>8</sup></b>	357	1,329	82	273	73.8
<b>Smaller projects</b>	1,887	291	18	97	26.2
<b>By research category<sup>9</sup></b>					
Basic	1,538	1,361	84	301	81.2
Clinical	515	183	11.3	47	12.8
Health and social care	919	76	4.7	22	6
<b>By disease (major)<sup>10</sup></b>					
AD	192	346	26	86	31.4
MND	18	37	2.8	8	3
Prion	28	57	4.3	14	5
PD	80	171	12.9	39	14.3
HD	19	41	3.1	10	3.7
SCA	3	2	0.2	0.6	0.2
SMA	4	9	0.7	2	0.7
ND in general	89	665	50	114	41.7

As might be expected in an area with so few available treatments, only 11.3% of research (12.8% annualised) is carried out in patients or a patient population (i.e. clinical research, as strictly defined here).

While figures for investment by the industry sector are not available, commercial investment in research and development is critical for the development of drug- or biologic-based therapies, diagnostics and devices, and assisted living technologies for ND. However, it is a concern that in recent years a number of major companies within the biopharmaceutical sector have either withdrawn or reduced their activity in neurodegeneration research due to the pressure of the economic down-turn, coupled with a perceived lack of tractability of the research questions and a relatively large number of failures of new drugs during early-stage clinical trials.

9. For the definitions of basic, clinical, and health and social care research used here, see Annex 2 and the linked Mapping Analysis paper.

10. Major investments only; see Annex 2. Figure 3.

In many European countries, some of the key research infrastructures and technologies are available in the academic sector. For example, established DNA collections, brain biobanks, clinical and population cohorts, statistical resources, and patient/health registers ensure that researchers have access to pertinent patient information, samples and cohorts, including valuable cohorts of patients with rare ND and rare genetic variants of common ND. The organisation of healthcare in Europe allows the linkage of research subjects to medical records, thereby facilitating a longitudinal approach and the provision of rich datasets. From a population perspective, cultural diversity provides opportunity for studies of gene–environment interaction, though this highlights the need to consider varied diagnostic approaches.

Collectively, these resources provide a solid foundation to progress research into ND. However, it is clear that there are numerous gaps compared with what is needed and that problems exist relating to resource quality and access, which are currently limiting what can be achieved both individually and collectively. Specific issues are highlighted, and recommendations for action proposed, in Section 3.



# 3. JPND Scientific Priorities and Enabling Activities

The strategic agenda aims to accelerate progress in research into the causes, prevention and treatment of neurodegenerative diseases and the care and quality of life for patients with ND, and to facilitate its translation into practice and policy. This section outlines the key scientific areas for action and the enabling steps that have been identified.

## 3.1 Scientific Priorities

The JPND Research Strategy sets out a number of research priorities that take account of scientific, health and social importance and tractability. To achieve impact there is a need to encourage novel and multidisciplinary approaches, and to strengthen and extend existing capabilities across the full spectrum of basic, clinical, health and social care and translational research. Progress will be dependent upon the promotion of bottom-up approaches, supported by more top-down strategic activities. Since new scientific discoveries often emerge from unexpected sources, novel thinking will need to be encouraged and recognised if new and effective therapies are to be developed in this area.

Below, specific scientific themes and, within these themes, priorities for future research are identified.

### **Theme One: The origins of neurodegenerative diseases**

One major issue is that not enough is known about the fundamental causes of specific ND, the factors that determine people's risk and resilience, and the triggering events leading to illness. Priorities are to:

- Uncover new genetic, epigenetic and environmental (including social) risk factors for ND and identify 'at-risk' populations. The relationships between risk factors and their relative importance will also need to be established if those that can be modified to delay or prevent disease are to be identified. More specifically there is a need to:
  - > Systematically identify the genetic variability underlying ND, using state-of-the-art technologies, such as exome and genome sequencing.
  - > Undertake regional and temporal mapping of the transcriptome, proteome and epigenome of the human brain in both healthy individuals and people with ND.
  - > Explain phenotypic variability and determine, for example, the role gender plays in ND and the reasons for, and the impact of, variable age of onset.
  - > Better understand the interplay between genetic and environmental factors. This will necessitate the development of new tools and approaches to identify and quantify environmental risk for ND, and the effective integration of new genetic and molecular assessments within existing and new cohort studies.
  - > Establish large Europe-wide, population-based and longitudinal studies of populations incorporating integrated and in-depth phenotyping that link clinical and lifestyle data to biological and behavioural measures associated with ND. This could be achieved by sustaining and building upon existing cohorts (including validated control subjects) and, where they can provide insight or cover novel aspects, creating new cohorts. Studies

should include those with recruitment in middle-age or earlier to help identify risk factors and inform preventive strategies.

- > Promote the creation of cohorts of patients with both rare (e.g. SCA, HD, Mendelian forms of common diseases) and more common ND. In-depth phenotyping should be standardised across studies, including, but not limited to, the collection and use of biomaterials (cerebrospinal fluid [CSF], blood, fibroblasts, etc.), imaging and cognitive assessment data. Increased availability of post-mortem analyses could be achieved by fostering brain donation and brain banking.
- Conduct research into understanding ageing and how this relates to the development of and resilience to ND. To achieve this there is a need to:
    - > Develop cohorts of centenarians that include clinical evaluation, exposure and lifestyle history, neuroimaging, and sample collection for use in comparative studies.
    - > Promote research into the molecular mechanisms of ageing in model systems.
    - > Define the phenotype of the 'physiological' ageing process at the cellular, synaptic, system, cognitive, functional and social levels.
    - > Identify environmental and behavioural modulators of ageing and ND with the ultimate aim of determining protective and resilience factors.

## Theme Two: Disease mechanisms and models

In order to develop new diagnostic and therapeutic approaches, and identify the appropriate time windows for intervention, as well as establish predictive disease models, a more complete understanding of the biological basis underlying disease mechanisms and the evolution of ND is needed. This will require, in parallel with further assessment of current ideas, the development and testing of new hypotheses on novel disease pathways. Integral to this process will be the use of improved animal and cellular models of disease. These should not be expected to capture the full extent of the human conditions but should provide important insights into the mechanistic pathways underlying ND. Accordingly, priorities are to:

- Develop novel animal models that are relevant to ND and take into account factors such as the progressive nature of ND, comorbidities and ageing. Consideration must also be given to:
  - > Genetic background, generational aspects and other influences on phenotype.
  - > Development of new tools and methodologies to provide models with more physiologically relevant levels of target gene expression.
  - > Standardisation of testing and the development of reporter (e.g. optogenetic) technologies that allow real-time monitoring of the progression of disease pathology.
  - > Increasing accessibility to validated models, for example, through repositories.

- Establish cell-based disease models utilising innovative approaches to create patient-specific cell lines that represent ND more accurately than current methods. For example, these may be established using embryonic<sup>11</sup>, induced pluripotent stem (iPS) cell or trans-differentiation technologies.
- Utilise animal- and cell-based models to focus on rare genetic variants that will inform studies of sporadic ND.
- Investigate traits and pathways that are either common to, or specific for, different ND, spanning molecular-, cellular-, and systems-level approaches.
- Investigate ND mechanisms, such as physiological versus maladaptive plasticity, non-cell-autonomous mechanisms and inflammatory processes, in addition to the well-studied areas of protein aggregation, neuronal dysfunction and death. Further research is also needed to elucidate to what extent non-coding regulatory RNA contributes to ND and disease progression.
- Elucidate the biological and environmental basis of behavioural and psychological symptoms in ND via the development of cognitive test batteries in humans that can be reverse-translated to relevant animal models.
- Investigate the role of comorbidities (e.g. vascular, infection) in the establishment and progression of ND.

### Theme Three: Disease definitions and diagnosis

Standard clinical assessments lack sufficient accuracy to capture the presumed complexity of common ND, necessitating refinement and updating of the current diagnostic criteria. The various forms and subtypes of ND, including presymptomatic stages, require better definition, while new or improved diagnostic techniques and methods, supported by new biomarkers, are needed to enable the earlier and more accurate detection of ND and to monitor disease progression. Further classification of disease and stratification of patient cohorts will in turn be assisted by the development of these new diagnostic techniques; for example, new imaging methodologies, genomic, proteomic and metabolomic technologies and telemedicine. In particular, effort is needed to:

- Standardise cross-cultural disease definitions, diagnostic criteria, assessment tests and procedures for ND, developing and validating new ones where required.
- Develop and validate new diagnostic criteria and procedures in a way that supports their implementation from the population level through to primary care and specialised clinical settings.
- Harmonise and standardise existing biomarkers and develop, validate and standardise new biomarkers (molecular, imaging, functional, cognitive), where required. Biomarkers are needed for ND that:

<sup>11</sup> The regulations concerning research using human embryonic stem cells vary across JPND member countries, and the participation in related JPND activity will respect all relevant national frameworks.

- > Help predict conversion from a presymptomatic to symptomatic phase.
- > Link to disease mechanisms as well as functional endpoints, including disease-related QoL, thereby promoting bidirectional translation between human-and animal-based studies.
- > Provide surrogates for progression, prognosis and treatment effects.

## **Theme Four: Developing therapies, preventive strategies and interventions**

Close working with industry is essential for the successful translation of basic findings through to clinical therapies (see Enabling Activities, Theme 3). Existing preclinical drug-development programmes have been significantly hampered by a lack of suitable biomarkers and models of disease. Accordingly, new therapeutic strategies should be promoted; for example, using approaches that are immunology-based, or combinatorial in nature, or which seek to modify or slow disease progression. Progress will also be accelerated through the adoption of a more systematic approach that promotes bidirectional translation between animal and cell models and patient cohorts. Potentially, the establishment of cohorts of patients with preclinical ND would allow the future testing of interventions to prevent or slow disease progression; however, the ethical and regulatory implications of treating someone at risk of developing, but not certain to develop, disease would need to be considered and resolved. To make progress in this area there is a need to:

- Adapt or develop disease models for use in drug development and toxicity testing encompassing both cell-based approaches and model organisms. For the former, iPS cell-based approaches offer the promise of establishing high-throughput neuronal cell screens representative of specific genotypic backgrounds.
- Strengthen investigation of compensatory mechanisms for disease, including neuronal plasticity, as a basis for novel treatment approaches.
- Improve selection and stratification of patients to ‘enrich’ clinical studies and provide a greater chance of showing clinical efficacy. Stratification could, for example, be based upon biomarkers, genetic or environmental risk profiles, endophenotypes and/or functional endpoints.
- Better understand the most beneficial time window to assess treatment efficacy, an issue that may have contributed to the high failure rate of early-phase clinical trials in the pharmaceutical sector.
- Support the development of studies investigating intervention and prevention strategies based on an understanding of known and novel risk or protective factors. Specifically, studies targeting both biological and psychosocial factors should be encouraged to identify how best to effect changes in behaviour at the population level (at the early and mid-life stages) in order to lessen the risk of developing ND.

- Encourage theoretical and empirical research and education regarding the use of non-pharmacological interventions, and aim to better understand their mechanisms of action, how best to measure their outcomes and their interaction with pharmacological interventions.
- Encourage the development of psychosocial interventions, paying attention to the promotion of social inclusion and carer involvement. These should consider the different stages of disease and avoid negative side-effects that reduce people's abilities to retain dignity and make positive contributions to society. Improved methodologies are also required to assess such interventions.
- Ensure that clinical outcomes and endpoints are patient-centred and factor in QoL. For this and other related areas, success will require the involvement of patient and carer organisations in study planning.
- Promote regenerative strategies, whether based upon stem cell transplantation or the stimulation of endogenous repair mechanisms, for disorders such as Parkinson's, Huntington's and motor neurone disease where specific neuronal deficits are implicated.
- Develop novel systems for delivery and targeting of drugs and biologicals to sites in the brain and other parts of the nervous system. Delivery systems could, for example, utilise nanoparticles, peptides, cells, viruses and pumps. Coupled to this, the problem of getting medications across the blood–brain barrier will need to be addressed.
- Encourage socio-economic studies that investigate the hurdles for the development of novel drugs for ND; for example, how clinical studies can be undertaken in 'at-risk' or presymptomatic individuals, and the limitations of the current patent model in relation to therapeutic development in chronic illnesses, such as ND. In this area, clinical trials need to be both large and lengthy to establish drug efficacy, which increases costs while reducing the length of time a drug can be marketed before patent protection expires. Potential alternatives to the current patent model as applied to ND should be explored so that pharmaceutical companies remain motivated to take the long-term risks needed to develop therapies in this area.

## **Theme Five: Healthcare and social care**

The nature, availability and quality of health and social care for individuals with ND vary considerably across Europe; however, it can generally be said that there is inefficient and inequitable co-ordination between health and social care systems in individual countries. Accordingly, an evaluation of the strengths and weaknesses of formal and informal care approaches and infrastructures should be considered as a prelude to implementing new, evidence-based, systems. When considering this evaluation it is of fundamental importance that researchers seek to understand the factors within these systems that contribute to social inclusion, civic participation, dignity and QoL for individuals with ND and their families, and take into account comorbid conditions that often impact upon the delivery of treatment and care. If the incidence of disease is to be reduced, it will also be necessary to identify and overcome barriers to the adoption of evidence-based health and wellbeing promotion strategies. Sufficient consideration of cross-cultural issues and diversity, particularly when developing instruments and implementing intervention strategies, must be ensured across all research efforts. Key priorities are to:

- Chart current healthcare and social care pathways relevant to ND and evaluate the equity of access to, and the effectiveness and cost-effectiveness of, pathways to diagnosis, treatment, care and support across Europe. This will also require investment in the key evaluative tools, particularly the development of robust outcome and cost measures. Mixed-method approaches should be employed.
- Investigate the interplay of biological, environmental, social, economic and other factors in the determination of cognitive decline and behavioural and psychological symptoms. Research should also investigate the management of such symptoms in relation to addressing challenging behaviour and improving QoL.
- Determine the critical factors that affect disability and health-related QoL in ND, including the effects of comorbidity, nutrition and frailty, the interaction with family, carers, the environment, and health and social care systems; develop improved outcome measures, including functional assessments and tools that would allow the measurement of the quality-adjusted life year (QALY) impacts of interventions for ND.
- Evaluate approaches both to the better recognition of carer needs and preferences, and to the support of carers, particularly through carer-centred and carer-mediated interventions.
- Investigate the most effective and cost-effective ways of implementing efficacious therapeutic strategies on a broad basis, addressing the fact that the current evidence base is largely derived from intensive and short-term studies that do not readily translate to real-world settings.
- Promote research into end-of-life and palliative care. This should include an assessment of the transferability of current hospice care models into social care situations, the ethical issues involved, and the core criteria of effectiveness, cost-effectiveness and equity.
- Investigate the ability of assisted living technologies to address the needs of patients with ND and their carers, in both early and moderate disease states, and target and integrate their use. For example, this might include information and communications technology (ICT) approaches, providing alerts to alleviate memory loss and improve adherence to medication, the development of new digital technologies for monitoring symptoms and to provide remote support, and the design of smart homes and the wider environment to improve QoL and prolong independent living.
- Ensure the integration of research into ethical issues relating to ND; for example, the provision of consent in relation to people with mental incapacity, an assessment of how the level of disease risk is defined to allow intervention in preclinical populations, and how dignity might be preserved in patients with ND.

## 3.2 Enabling Activities

The specific requirements to progress the scientific themes outlined in Section 3.1 are identified below.

### **Theme One: Knowing our research capability**

To underpin development of the SRA, a mapping exercise of the national and European research landscape relevant to ND was conducted to give an objective view of the level and strength of research activity across Europe and to identify gaps and opportunities. Data were collected on national and Europe-wide programmes and initiatives, infrastructure such as research networks, and on bio-resources such as DNA collections, tissue (bio)banks, animal models, and data banks for gene/protein expression. This information will help identify opportunities for improved co-ordination and alignment, at both European and national levels. This asset map will also assist decision making for the implementation of the Research Strategy, and it is planned that this information will be suitably updated as the initiative progresses to ensure the information is current and to help monitor the impact of JPND.

The baseline information collected through the mapping exercise will be made available to the wider community with the aim that it will aid connectivity between research groups both within and beyond Europe. To this end, a publicly accessible database has been established to showcase ongoing ND-relevant research across Europe and to promote better use of resources and infrastructure. Further information is provided in Annex 2.

### **Theme Two: Supportive infrastructure and platforms**

An overarching goal is to create an enabling environment for research in key areas. There are opportunities to harmonise many aspects of ND research across Europe and to develop an integrative approach that spans the dimensions of basic, clinical, healthcare and social science. In this regard, JPND will seek to explore synergies with existing platforms/infrastructure with relevance to this area, such as ELIXIR,<sup>12</sup> BBMRI<sup>13</sup> and ECRIN.<sup>14</sup> Accordingly, JPND should seek to:

- Encourage integration and harmonisation of data and materials and promote an open-access approach to sharing data and materials.
- Establish standardised methods, platforms and tools for data collection and analysis, with particular attention to neuroimaging and clinical/cognitive/functional assessment, including QoL (test batteries/scales). In certain areas, such as cognitive assessment, standardised guidelines could be developed through an expert board or specialised forum.
- Support the development of multimodal imaging platforms to utilise complementary information from different neuroimaging technologies, with a view to integrating preclinical and clinical research to better define brain structure–function relationships and underlying disease mechanisms.

12. European life science infrastructure for biological information: <http://www.elixir-europe.org/>

13. Biobanking and Biomolecular Resources Research Infrastructure: <http://www.bbmri.eu/>

14. European Clinical Research Infrastructures Network: <http://www.ecrin.org/>

- Provide coherence to the Europe-wide investment in cutting-edge but high-cost areas, such as genome sequencing, proteomics and computational biology, in order to establish centres or networks at the national or European level that can provide broad access to a critical mass of expertise.
- Ensure there is wide access to high-quality biomaterials (e.g. brain tissue, CSF and cells from both patients with ND and controls) provided through biobanks operating to standardised procedures and promoting best-practice in sample collection, curation and handling.
- Link and better exploit existing cohorts, patient registers and sample/data collections. This will require the development and implementation of new software and technologies to improve the capture and sharing of information, and should encourage external research groups to undertake secondary analyses of population data.
- Establish Europe-wide registers of people with both common and rare forms of ND.
- Establish registers of patients with cognitive impairment, with minimum requirements for entry to reflect real-world situations; most current cohorts are drawn from specialised populations and are not fully representative.
- Consider new and existing policy frameworks to enable research to be conducted across the full range of healthcare structures, for example, research in primary care, general hospitals, care homes and specialised centres.



### **Theme Three: Working in partnership with industry**

Many different commercial organisations engage with ND research, ranging from the pharmaceutical, diagnostic and biotechnology sectors to assisted living and healthcare providers, including the care home industry. Connection between and across the academic and commercial domains is essential to deliver new approaches to treatment and care. This will require improved awareness of the respective capabilities and needs of each sector, as well as legal and organisational frameworks that promote and incentivise the formation of long-term partnerships.

While scientific opportunity is emerging in the biomedical domain, the limited understanding of mechanisms and lack of validated drug targets, as well as the challenges of undertaking clinical trials in people with ND poses a risk to continued industry investment in this area. Effort is therefore needed to:

- Foster partnership with and between the industry sectors, taking advantage of the changing landscape for commercial R&D where many companies are now looking to outsource some of their capability to the academic sector.
- Promote collaborative system-level approaches to the development and testing of new pharmaceuticals, such that multiple components of the relevant mechanistic pathway are targeted rather than the current emphasis on individual drug targets.
- Encourage data and resource exchange between industry and academia, for example, by:
  - > Facilitating academic access to compounds and toxicity/safety data from stalled or terminated drug-development programmes.
  - > Addressing barriers to allow wider use of clinical data, animal models and biomaterials (including post-mortem material) by bioindustry.
- Reconsider funding mechanisms to promote joint academic-industry research, specifically in the areas of private-public clinical trials and precompetitive research.

Regarding ambient and assisted living (AAL) and ICT approaches, a number of Europe-wide initiatives are already in place to promote the development of AAL technologies. However, greater emphasis should be placed on addressing the specific burden of ND, and dementia in particular, as opposed to focussing on ageing in general. Research that provides an evaluation of the economic dimension of the digital/ICT solutions available should also be encouraged, particularly where it might help to identify new business models that offer sustainability for SMEs in this area, for example, by taking a holistic view of costs to account for the potential savings to be made through prolonging care provision at home.

#### **Theme Four: Working with regulatory organisations**

The promotion of effective translation of research through to patient benefit requires engagement and co-operation with the key European and national regulatory agencies to ensure that regulation is easily understood by researchers and is proportionate to risk. Accordingly, JPND needs to:

- Facilitate better interaction between researchers and regulatory organisations to ensure there is access to guidance that can inform study design and address potential bottlenecks at an early stage.
- Provide regulatory support networks, portals or hubs to help disseminate best practice and lessen the delays in commencing experimental medicine or intervention studies.
- Re-examine research governance and regulation in relation to the unique aspects of ND, for example, concerning studies in presymptomatic individuals and those with mental incapacity.
- Reconsider the patenting framework in relation to the challenges of developing new drugs for ND; the current length of trials needed to establish clinical benefit makes this a high-risk research area for the biopharmaceutical sector.

#### **Theme Five: International partnership beyond Europe**

While attention will naturally be focussed on addressing research at national and European levels, it is recognised that the unmet clinical need and societal impact of ND is a global issue, and that opportunities exist to link to worldwide research efforts in this area. Such co-operation should be strategically directed and offer clear benefit to JPND's objectives. This might operate at different levels, for example, to:

- Utilise resources and infrastructures outside Europe; for example, through linking to large-scale initiatives that provide access for European researchers to major genetic or epidemiological samples, datasets or emerging technologies.
- Exploit opportunities that might arise through studying specific populations where unique genetic predispositions or novel environmental exposures might contribute to risk or resilience in ND.
- Widen our understanding of how cultural differences affect the management of health delivery and social care.

## **Theme Six: Capacity building**

Certain areas of research lack capacity and need to be strengthened to ensure future opportunities can be realised. Approaches to capacity building that have already been utilised within JPND countries or at the European-level should be shared, with a view to identifying approaches that might be adapted to the specific needs identified below. Accordingly, JPND needs to:

- Encourage research networks and better networking across and between disciplines and researchers, both within individual countries and across Europe. There should be promotion of effective models and approaches where these exist already, and consideration of novel approaches to incentivise, promote and reward fruitful collaboration.
- Improve the training of clinical researchers, and translational specialists and ensure their role is recognised and sustained.
- Increase the numbers of neurodegeneration researchers especially those with expertise in health economics, statistics, computational biology and bioinformatics. In the biomedical field, opportunities should be sought to attract those with a background in conjoint disciplines, such as neurophysiology and developmental neurobiology.
- Promote Europe-wide research forums to encourage innovative thinking and interdisciplinarity.
- Ensure that excellence in the healthcare and social care field is established on a broader basis across Europe. For example, methodological hubs could be used to support study development and promote the use of new modelling techniques and integration of health economics in the evaluation of interventions, service and care pathways.

## **Theme Seven: Education and training**

During the progression of their illness, patients will meet a range of different health and social care professionals. At present, there exists considerable heterogeneity in awareness amongst healthcare professionals and related stakeholder groups about the particular ways in which ND cause distress and loss of normal functioning. While it is a recognised problem, there is little consensus on how best to improve the overall situation.

There is already a considerable body of knowledge available that could benefit the healthcare field, yet this is not effectively translated into practice. It is clearly important that healthcare professionals have a good understanding of ND and awareness of the available evidence-based care to ensure that the patients seeking their professional advice are treated in the most effective and acceptable way. This requires tailoring mainstream clinical education and training programmes to ensure that the relevant professions (nurses, physiotherapists, doctors, social workers, etc.) are provided with the necessary background and specialist training in ND, across the full range of relevant disciplines, including ethics and sociology.

Clinical and research education and training should also include a broad appreciation of research needs and the benefits of research participation. This will help to foster a culture that is receptive to research studies that aim to improve diagnosis, treatment and care in future patients. There is also a need to better understand why individuals do or do not choose to take part in research relevant to ND, and the factors that encourage or discourage participation.

For longer-term societal benefit, there should also be investment in educating younger generations about ND. This strategy will help to reduce stigma and misunderstanding that surround these conditions and may, for example, lead to greater involvement in care.

An evidence-led educational approach should be adopted to help embed a research culture across the full spectrum of health and social care, promote public health messaging, and address stigma. Specific recommendations for education and training in relation to ND are to:

- Expand the clinical education and training of health and social care professionals who interact with patients with ND with respect to the patient needs that are characteristic of these conditions and the available evidence-based options for treatment.
- Promote appreciation amongst health and social care professionals of the benefits of research participation, both to improve recruitment to longitudinal and clinical studies and to increase donation of human tissue for research.
- Investigate methods of ensuring an adequate, effective and positive work force is available to care for people with ND.
- Undertake research to improve and implement effective health education to promote broader awareness about ND in younger generations.
- Understand more clearly how to create changes in behaviour in the population (at the early- and mid-life stages) through strategies aimed at mitigating risk factors associated with an unhealthy lifestyle and lessening the chance of developing ND.

## **Theme Eight: Connection to policy makers**

JPND provides a new, single European framework through which to highlight important current and emerging issues for national policy consideration. The initiative aims to promote compatibility between the policy approaches of different countries. Effective evidence- and analysis-based policies that are informed by people with ND and their carers should be the benchmark.

Historical, political, regional and cultural considerations have resulted in different policy approaches across Europe, for example, healthcare provision may be organised privately or be government-provided or both. Few European countries have specific national or regional policy frameworks for ND, which means that evolution of policy for this area falls into different, and sometimes disconnected, health and social care policy arenas. There is a clear need to undertake research that assesses the effectiveness of different health and social care models and approaches throughout Europe, and determine if an integrated public health framework is the best national option. Reducing segmentation of the care sector and evaluating alternative strategies for long-term care are two priorities that could improve service, cost-effectiveness and efficiency.

Two key translational gaps in ND-related policy are apparent where national policy makers can act to improve the impact of research for patients, carers and their families. First, better links with technology developers are needed to implement new technologies or practices; for example, in the areas of telemedicine, assisted living or delivery of services. Second, there is a need for national policy frameworks to ensure that research outcomes – for example, evidence to indicate the best pathway of care for a particular stage of a particular ND – lead to effective implementation in public health policy.

The attention of policy makers should be drawn to the special considerations that arise from issues of consent and data disclosure in the context of diminished mental capacity in ND. The following activities are required to help address these issues:

- Promote good communication between researchers and policy makers.
- Adopt and harmonise evidence-based policies and best practice across Europe.
- Increase awareness and understanding of the ethical and legal issues associated with ND, including mental incapacity, with corresponding steps taken to address them.

## Theme Nine: Communication and outreach

For effective translation into policy and practice, the research agenda for ND must connect and engage with a wide range of sectors. It is crucial that individuals with ND and their carers are well informed about ongoing ND research and its outcomes, and that they are appropriately involved in the planning of clinical, health and social care research to ensure relevant study endpoints and QoL perspectives.

The promotion of effective communication between patients, carers, and health and social care practitioners (alongside education and training; see Theme 6) can be expected to increase research participation. Additionally, wider knowledge and awareness can help to reduce the stigma that society may attach to neurodegenerative conditions and to encourage, for example, the adoption of assisted living techniques.

The JPND website will serve as a focal point for communication and dissemination to a wide range of sectors and provide a searchable database of European ND research capability. Regular news-feeds already reach a large number of stakeholders who have expressed an interest in the initiative, and this will continue throughout JPND's life-span.

To promote communication and outreach with the wide range of sectors, JPND will:

- Disseminate ND research outcomes to all stakeholder communities in an effective and balanced manner to assist successful translation into policy and practice.
- Increase awareness and support for ND research amongst decision makers in participating countries.
- Encourage JPND-funded researchers to engage in dissemination and outreach activities as appropriate, thereby increasing awareness and support for ND research among patients, patient organisations and the public.
- Promote the development of innovative tools to facilitate communication between individuals with ND, their families and carers, healthcare professionals, and care service providers, as a means to increase social inclusion and reduce the stigma associated with dementia.
- Continue to support dialogue with stakeholder communities on a national and international level.

# 4. Delivery of the Research Strategy

## Timeframe and Framework for Delivery

The Research Strategy establishes a framework of opportunities for countries involved in JPND and which are willing to participate in joint actions. Starting from recommendations made within the strategy, working groups and taskforces will establish short-, medium- and long-term priorities and specify what actions, instruments and resources are required for implementation. JPND will seek to implement its SRA in the most effective manner, whether through co-operative activities that realign or link national investments to achieve increased impact, or through the provision of new funding. This may involve either the use/adaptation of existing instruments and initiatives or the launch of new activities, such as data sharing to increase interdisciplinary or cross-sector research.

A guiding principle for delivering the objectives identified within the Research Strategy will be that research investment is provided in a competitive environment that supports research of the highest scientific quality. In this way, public funding will be used efficiently to ensure the best outcomes for patients and families affected by ND.

## Stakeholder Engagement

A key indicator of the success of JPND will be direct communication and engagement with all stakeholders, including patient organisations, industry representatives and policy makers. Supporting key stakeholders with appropriate information at relevant times will maximise both the support for JPND and the involvement of participating member states in the collaboration. As an integral part of JPND, a broad, multi-national stakeholder community will be created to encourage stakeholder engagement and address unmet needs. Stakeholder engagement will enable co-operation, interaction, communication, dissemination, knowledge transfer, networking, and consultation on plans and initiatives.

JPND has identified its stakeholder groups as key influencers (politicians, decision makers); scientific researchers (public and commercial); research funding organisations; health policy makers; patient interest groups; regulators; healthcare professionals; the media; and the public.

# 5. Impact

Over the coming decade, JPND aims to achieve the following:

- A positive influence on treatment, care and quality of life for patients with ND and their carers.
- A raised profile and de-stigmatisation of ND.
- Increased visibility at a political level of the burden of ND and the benefits of research.
- Catalysis for the development of national and organisational strategic plans in JPND countries.
- Increased investment in European R&D for ND, across the academic and commercial sectors.
- Increased capacity in neurodegeneration research, through linkage both to conjoint disciplines and to other international activities.
- The development of new therapeutic approaches and interventions for ND, including preventive strategies for at-risk individuals, which could also lead to new business and commercial opportunities.
- Research elements relevant to ND to be embedded more routinely in health service and care infrastructures.
- The delivery of evidence-based policy relevant to ND with efficient uptake of research outputs.



## 6. Evaluation

To assess the JPND initiative regarding its direct outputs, early effects and long-term impacts, a monitoring and evaluation framework will be constructed that will serve as the basis for the development of a set of key performance indicators. This framework will be built in close consultation and collaboration with JPND stakeholders and will align JPND's objectives (on both scientific and policy levels) with the scientific priorities and enabling activities presented in the Research Strategy.

Monitoring and evaluation of the initiative will occur at different, but interrelated, levels with the approach focussing on the initiative's process and progress on its aims, such as delivery of the scientific objectives and interaction between the scientific community and wider society.



# 7. Conclusion

JPND is a pioneering example of 'Joint Programming', a new and flexible approach that has the capability to address a major societal challenge that cannot be resolved through national programmes alone. This document sets out the common vision of the 24 European countries<sup>15</sup> involved, and provides a strategic approach to support world-class research that can exploit emerging scientific opportunities, confront barriers to progress, and provide new approaches to prevention, intervention and care. The recommendations outlined in the Research Strategy address the full spectrum of research and approaches that are required to achieve impact, and recognise the important role that other stakeholder groups have in delivering this agenda. The ultimate goal is to undertake research that can be translated into new interventions that not only improve the health and wellbeing of patients with ND and their families and carers, but also deliver economic and societal benefit throughout the European Union.

15. At 22nd November 2011: Albania, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxemburg, Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.

# Annex 1

## Development of the Strategic Research Agenda

The Strategic Research Agenda (SRA) addresses the full spectrum of research activity that is required to address the growing burden of neurodegenerative diseases (ND), and is based upon the scientific recommendations of the JPND Scientific Advisory Board (SAB). During its development a series of workshops, meetings and consultations were held to ensure a comprehensive assessment was undertaken of the scientific landscape and future research possibilities in this area, taking into account a broad range of relevant viewpoints and opinions.

To identify the key research priorities, an initial horizon-scanning exercise involving the SAB and academic opinion leaders from across Europe was conducted through three thematic workshops (for which detailed reports are available, see Annex 4):

- Basic Research: Madrid, 22nd March 2011
- Clinical Research: Paris, 4th March 2011
- Healthcare Research: London, 31st March 2011

The aim of these workshops was to identify research opportunities and gaps relevant to ND, with attendees asked to highlight the research areas that would benefit most from European co-operation and indicate short- and long-term priorities for action. Outputs from these workshops provided a preliminary idea of what was required and a framework around which the opinions of other groups could be sought. To determine the viewpoints of two of the key stakeholder categories, dedicated meetings covering similar themes were held with opinion leaders from the biopharmaceutical industry (Milan, 16th May 2011) and patient and carer organisations (Brussels, 26th May 2011). Both meetings provided valuable insight into the requirements of these two groups as well as their opinions on the initial set of priorities.

To integrate these various perspectives and provide a more holistic view of the research landscape, a Final SRA Workshop was held in Rome (20th June 2011) attended by selected participants from the previous workshops/meetings along with individuals from organisations representing healthcare professionals and providers. Through a series of focussed brainstorming sessions and group discussions, a set of priorities and needs were produced that formed the basis for much of the SRA.

To ensure this set of potential actions was in line with the viewpoints of the wider community, a public consultation exercise was conducted on the outputs of the Final SRA Workshop. Over 350 responses were received, mostly from academic researchers, patients/carers and healthcare professionals. The vast majority of the responses and opinions expressed by respondents were supportive of the initiative and positive in terms of the priorities and recommendations that had emerged from the strategic workshops.

Lastly, to ensure that the priorities and needs identified by the activities outlined above factored in the existing research and funding landscape, a meeting was held between the SAB and representatives of European funding organisations. Workshop outputs were considered in light of the mapping data (see Annex 2) and in terms of potential mechanisms and means of delivery.

Reports summarising the workshops, stakeholder interactions and consultation exercises outlined above can be found via the hyperlinks or on the JPND website (see Annex 4).

## Annex 2

### Mapping exercise

An in-depth and objective analysis of current research activity and resources relevant to ND has been performed to underpin the development of the SRA.

A brief outline of the methods used and data collected during the mapping exercise can be found below; more extensive information and analysis can be found in the **'Report of the Mapping Exercise'** available on the JPND website.

#### **1. Data collected**

The primary goal of this activity was to ensure that recommendations made in the SRA paid due consideration to the existing research landscape. The information collected during the exercise had two distinct aspects:

- i. Details of research funding in individual JPND member countries, collected via funding organisations, as well as relevant EC-funded programmes.
- ii. Details as to the nature and accessibility of relevant resources/infrastructures that support research into ND, collected via the principle investigator or director of the resource.

#### **2. A resource for the research community**

The secondary aim of the mapping exercise was to turn the data collected into a usable and useful resource for the research community. The availability of a freely accessible and searchable web-based database, containing detailed information on funded research, resources and infrastructures, should encourage networking, collaboration and resource sharing. It also has the potential to help bring new researchers to the field. This information is also likely to be valuable for anyone interested in finding out about ongoing research relevant to ND, a need highlighted during the stakeholder consultation exercise, where patients, carers and their representatives indicated that they would like details of research projects to be made more widely available.

This resource is available through the JPND website at:  
[www.neurodegenerationresearch.eu/search-our-database](http://www.neurodegenerationresearch.eu/search-our-database).

### 3. Overview of mapping results

#### 3.1 Methodology

The mapping exercise captured investments according to the following criteria:

- Projects relating specifically to research activity on or relating to ND as included under the JPND initiative: Alzheimer's disease and other dementias (AD), Parkinson's disease (PD) and PD-related disorders, prion disease, motor neurone diseases (MND), Huntington's disease (HD), spinocerebellar ataxia (SCA) and spinal muscular atrophy (SMA).
- All research programmes and grants included were active on 1st January 2011.
- Projects were categorised as a major investment if either i. exceeding a total investment of €500,000 as basic or clinical research or ii. exceeding €200,000 if classified as health and social care research. For such awards, information was collected on each regarding the title, principal investigator(s), project abstract and disease relevance (up to three diseases).
- For smaller investments, individual detail was not collected. Instead, projects were classified by research type, with detail on the gross investment total and number of projects provided by each funding organisation.

#### Key exclusions were:

- Funding attributed to buildings, resources or infrastructure.
- Investment in training or career development posts (PhDs, fellowships, etc.).
- Research that was not specifically, or for the most part, focused on ND (e.g. research into broader areas of neuroscience). As such it should be noted that in addition to the totals included here, there is much supporting research that may be of value to the ND research effort.

Research classification was based on a set of criteria drawn up in conjunction with the SAB. The full set of criteria are laid out in the report of the mapping exercise, but can be summarised as follows:

- **Basic:** Aetiological and underpinning research and research relating to detection, screening, diagnosis or development of treatments and therapeutic interventions carried out in model systems or preclinical settings (i.e. not in human patients).
- **Clinical:** Research relating to detection, screening, diagnosis, prevention or treatment of disease or promotion of patient wellbeing, conducted in/on (live) humans, and patient-oriented at some level.
- **Health and social care:** Research relating to care or management of disease, provision and delivery of health and social care services (including health economics, health policy, research governance, etc.) and the social or societal impact of disease.

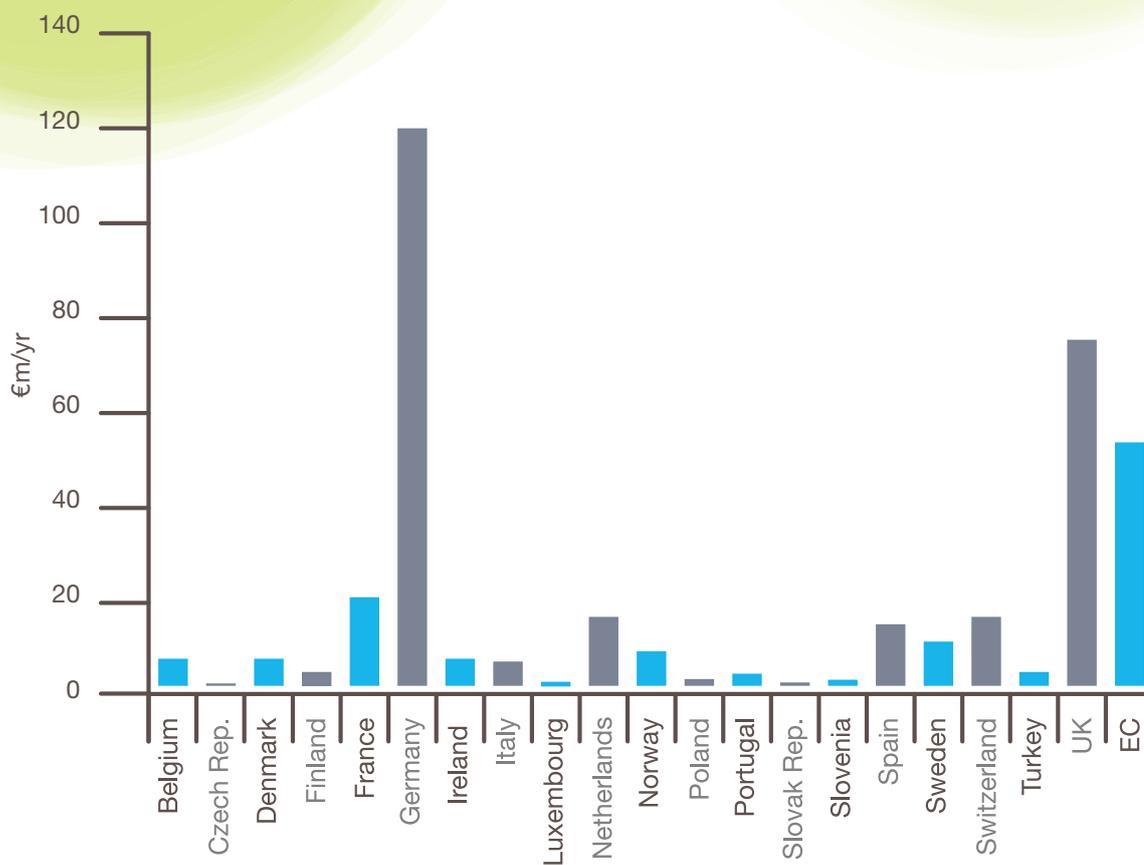
More comprehensive details of the methodology and research classification can be found in the report of the mapping exercise.

## 3.2 Research funding

### 3.2.1 Funding for programmes and projects

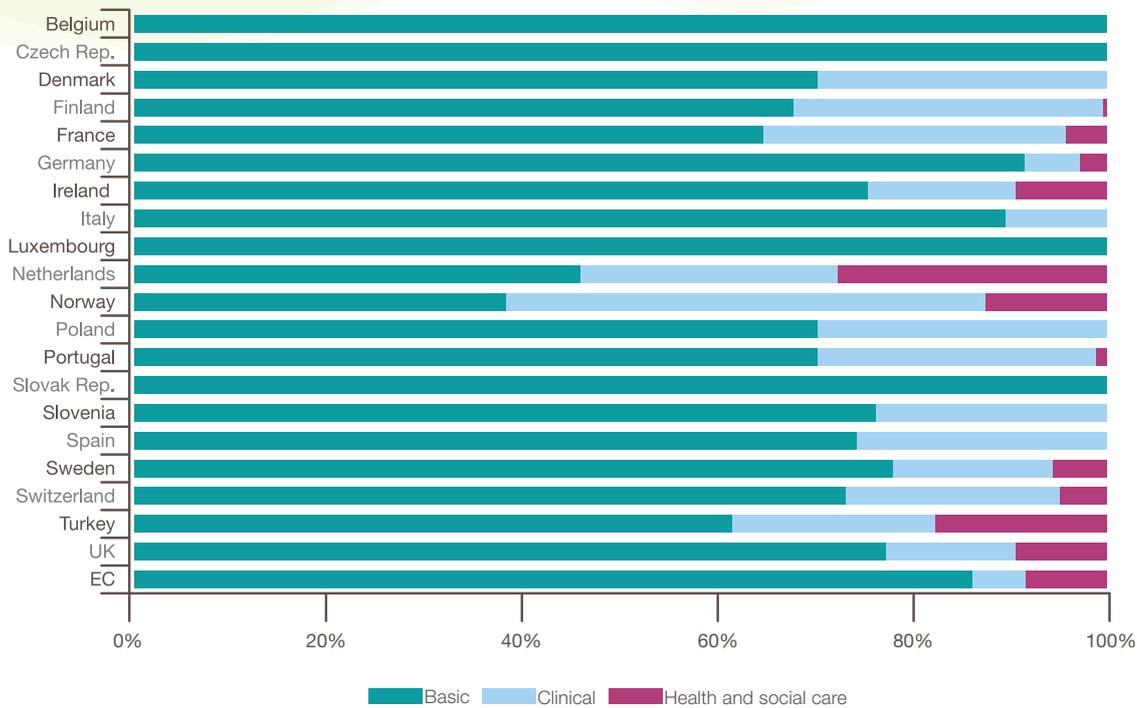
	Number of projects	Full value (€ millions)	%	Per year (€ millions)	%
<b>Total</b>	2,244	1,620	-	370	-
<b>Major investment</b>	357	1,329	82	273	73.8
<b>Smaller projects</b>	1,887	291	18	97	26.2
<b>By research category</b>					
<b>Basic</b>	1,538	1,361	84	301	81.2
<b>Clinical</b>	515	183	11.3	47	12.8
<b>Health and social care</b>	919	76	4.7	22	6

**Table 1: Total investment in programmes and projects:** Combined gross and annualised (full award ÷ length) totals for investment in major programmes/grants and smaller research projects identified across the participating JPND countries/organisations and the EC (FP7). A break-down of these totals according to research category is also shown. Totals have been rounded to the nearest million euros.



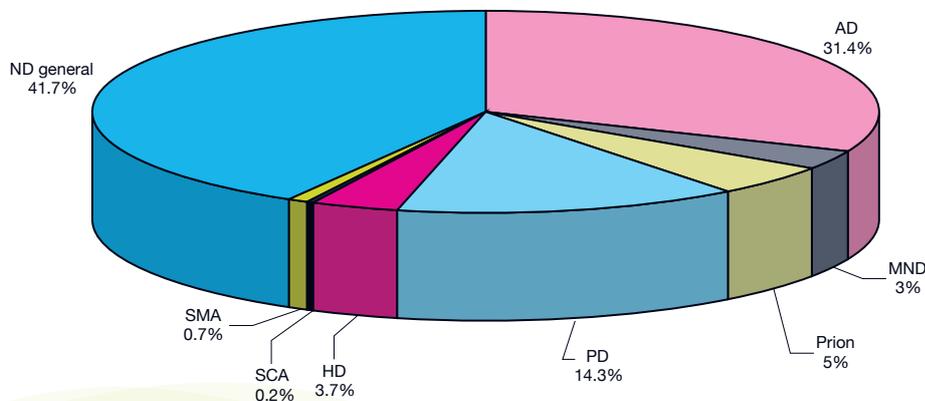
**Figure 1: Investment by country:** Annual investment (€ millions per year) identified through the mapping exercise according to JPND member country and the EC (FP7).

As reflected in the figures presented in Table 1, the vast majority of research investment identified across JPND member countries and the EC can be classified as basic (and preclinical) research, with a relatively minor proportion attributed to health and social care research. Within individual countries the percentage investment captured across the three research domains does vary (see Figure 2, below).



**Figure 2: Investment by research domain by country:** Percentage annualised investment identified in basic, clinical or health and social care research for JPND countries and the EC (FP7).

Across JPND, the highest percentage of identified investment was in research that was either relevant to ND in general or in projects that encompassed more than three ND. In terms of individual diseases, the majority of investment was directed towards projects relevant to AD (31.4%) or PD (14.3%).



**Figure 3: Investment by disease area:** Major investment in research projects identified through the mapping exercise for the ND covered by JPND.

### 3.2.2 Research infrastructure

The following resources and infrastructures were recorded during the mapping exercise, with details captured regarding the characteristics and accessibility of the relevant resource or data:

Resources	Disease relevance								
	No.	AD	MND	Prion	PD	HD	SCA	SMA	ND gen
Research networks	34	17	8	3	14	6	3	4	17
Population cohorts	81	53	3	3	25	0	2	1	50
Case control studies	22	18	1	1	3	1	0	0	8
Disease registers	21	11	5	3	7	3	3	1	6
Biobanks	87	57	28	17	32	16	16	11	50
Animal model repositories	12	5	2	1	7	5	3	1	4
Bio/neuroinformatic infrastructures	24	8	1	1	2	1	1	1	9

**Table 2: Types of resources/research infrastructures:** Total numbers captured during the mapping exercise with break-down according to individual diseases also indicated (note: some are relevant to more than one disease).

Brief descriptors of the resource categories and their characteristics are provided below:

- **Research networks:** Broadly defined as infrastructures and/or co-ordination activities to support research at the national level.
- **Population cohorts:** Large, long-term studies which collect data from a population rather than a (specific) group of patients. Only population cohorts of greater than 1000 participants were collected in the mapping exercise, with the following range of participants enrolled:

1,000–5,000 participants:	48
5,001–10,000 participants:	8
10,001–15,000 participants:	4
> 15,000 participants:	2

- **Case control studies:** Studies are designed to collect data (and often samples) from an extensively defined (phenotyped) group of patients (cases). Studies with the following numbers of participants were captured in the exercise:

1–1,000 participants:	19
1,001–5,000 participants:	2
5,001–10,000 participants:	1

- **Disease registers:** Registers of patients who either participate in or have offered to participate in research studies (on ND). Registers with the following number of clinical cases were captured in the exercise:

0–500 clinical cases:	7
501–1,000 clinical cases:	1
1,001–5,000 clinical cases:	10
5,001–10,000 clinical cases:	2
> 10,000 clinical cases:	1

- **Biobanks:** Collections of (human) biological material for use in research studies. The following number of repositories held the specified types of biological material:

DNA samples 67; tissue samples (brain, muscle, CSF, etc.) 57; cell lines 28.

- **Animal model repositories:** Sites holding and maintaining animal models of ND which act as access and distribution centres for groups of external researchers. Repositories related to disease models primarily in rodents (29), but with one recorded in each of the following:

Non-human primate; *Drosophila* (fly) and *C.elegans* (worm).

All 12 repositories held (live) animals, with four of them also holding frozen embryos and genetic material, and three holding frozen sperm (all from animals).

- **Bio/neuroinformatic infrastructures:** Databases, networks or infrastructures to share/distribute data relevant to ND (medical images, prescribing data, etc.) or to develop/provide computational or analytical tools to acquire, store, organise, archive, analyse or visualise such data.

## Annex 3

### Governance of JPND

The management structure of the JPND initiative comprises a Management Board (MB), an Executive Board (EB), a Scientific Advisory Board (SAB) and a Secretariat.

- **Management Board**

The MB is the decision making body of JPND. Established in June 2009, it works within the terms of reference adopted by all participating countries. It is composed of a (non-voting) Chair and Vice-Chair and a maximum of two representatives of each country participating in JPND.

- **Executive Board**

The EB supports the MB in all aspects concerning the preparation and implementation of decisions. Its membership comprises the Chair and Vice-Chair of the MB plus three other MB members.

- **Scientific Advisory Board**

The SAB is an independent advisory body consisting of 15 internationally recognised experts, spanning the domains of basic, clinical, and social and health services research. Its primary role is to offer advice to the MB regarding the SRA and other scientific issues.

- **Secretariat**

The Secretariat organises the day-to-day management of JPND and implements those tasks assigned to it by the MB and EB. The Secretariat and specific Work Packages tasked to develop, implement, communicate and evaluate the SRA and JPND have been funded through a co-ordinating action grant from the European Commission, known by the acronym JUMPAHEAD.

More details on the management structure and governance of JPND, JUMPAHEAD and the various work packages can be found at [www.neurodegenerationresearch.eu/about](http://www.neurodegenerationresearch.eu/about).

# Annex 4

## Supporting Documents

### Workshop Reports

#### 1. Basic Research Workshop

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/basic-research/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/basic-research/)

#### 2. Clinical Research Workshop

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/clinical-research/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/clinical-research/)

#### 3. Healthcare Research Workshop

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/healthcare/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/healthcare/)

#### 4. Final SRA Workshop

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/final/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/workshops/final/)

### Consultation Reports

#### 1. (Biopharmaceutical) Industry Meeting

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/industry/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/industry/)

#### 2. Patient and Carer Meeting

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/patientcarer/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/patientcarer/)

#### 3. Public Consultation

[www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/online-consultation/](http://www.neurodegenerationresearch.eu/initiatives/strategic-research-agenda/consultations/online-consultation/)

### Mapping Exercise

#### Report and Analysis

[www.neurodegenerationresearch.eu/for-researchers/about-the-mapping-exercise/](http://www.neurodegenerationresearch.eu/for-researchers/about-the-mapping-exercise/)

