



**European Cooperation
in the field of Scientific
and Technical Research
- COST -**

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COST 086/14

MEMORANDUM OF UNDERSTANDING

Subject : Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action BM1408: A collaborative European network of *C. elegans* early-stage researchers and young principal investigators (GENiE)

Delegations will find attached the Memorandum of Understanding for COST Action BM1408 as approved by the COST Committee of Senior Officials (CSO) at its 191th meeting on 12-13 November 2014.

MEMORANDUM OF UNDERSTANDING
For the implementation of a European Concerted Research Action designated as
COST Action BM1408
A COLLABORATIVE EUROPEAN NETWORK OF C. ELEGANS EARLY-STAGE
RESEARCHERS AND YOUNG PRINCIPAL INVESTIGATORS (GENiE)

The Parties to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the technical Annex to the Memorandum, have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 4114/13 “COST Action Management” and document 4112/13 “Rules for Participation in and Implementation of COST Activities”, or in any new document amending or replacing them, the contents of which the Parties are fully aware of.
2. The main objective of the Action is to promote and coordinate the use of the model system *C. elegans*, bridging fundamental research and therapeutic innovation. The Action is led by a collaborative interdisciplinary network of young Principal Investigators and ESRs in the ERA.
3. The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 76 million in 2014 prices.
4. The Memorandum of Understanding will take effect on being accepted by at least five Parties.
5. The Memorandum of Understanding will remain in force for a period of 4 years, calculated from the date of the first meeting of the Management Committee, unless the duration of the Action is modified according to the provisions of Section 2. *Changes to a COST Action* in the document COST 4114/13.

A. ABSTRACT AND KEYWORDS

The main objective of this Action is to promote the use of *C. elegans* for basic 'blue-skies' research and as a model for human disease, drug development and pre-clinical trials, through the establishment of a network of young *C. elegans* researchers acting as leading scientists and the creation of a centralised communications platform across Europe. The nematode *C. elegans* has been instrumental in the discovery of conserved principles of fundamental biological processes, leading to novel therapies for a broad range of human diseases. During the last decade, Europe has seen a dramatic increase in the number of laboratories using this model (80 new groups in 18 COST countries) but the community remains fragmented. This COST network is established to build capacity by uniting young European researchers working across three key fields essential to human health: organismal development, neurobiology and lifespan. GENiE (**Group of *C. elegans* New Investigators in Europe**) will enhance and speed up state-of-the art European research by promoting interactions and collaborations across Europe, and competitiveness with US labs. GENiE will position Europe at the centre of a scientific excellence network dedicated to the discovery of biological principles, the basis of therapeutic treatments of the future.

Keywords: *C. elegans* / human disease models / basic biological principles in developmental biology, neurobiology, ageing and immunity / young investigators / basis for innovative therapy

B. BACKGROUND

B.1 General background

Improving health and healthy-ageing are major societal challenges in Europe. More than 130 million Europeans are diagnosed each year with cancer or brain disorders, with the estimated annual cost reaching €1000 billion. Given Europe's ageing population, the number of people with these chronic or age-related diseases is expected to increase and the corresponding costs to rise.

Optimistic projections indicate that societal and economic costs could be controlled, provided that there are sufficient scientific and technological advances. Startlingly, patient counts have not improved in the last few years, suggesting that support for new approaches and new networks are needed.

Biomedical research takes two complementary approaches. Translational research aims at a rapid transition to medical therapies, but the types of experiments involved are often costly as they

involve rodent or primate models. In addition, the very low success rate of clinical trials is currently a bottleneck. More basic “blue-skies” research seeks to uncover fundamental biological principles at the molecular, cellular and mechanistic levels, providing the foundations of human disease diagnosis and potential new therapeutic targets for the future. The substantial molecular, morphological and functional similarities between invertebrate and vertebrate systems means that research in genetic model systems can significantly advance our understanding of key aspects of biology shared by all animals, including humans. Additionally, such *in vivo* models allow pretesting of drugs for toxicity, off-target effects and mechanisms of action.

One very successful model system is the nematode *Caenorhabditis elegans*. Despite the young age of this model (less than 40 years), nematode research has uncovered a number of basic principles ranging from programmed cell death (Nobel Prize 2002) to RNAi (Nobel Prize 2006), and it has pioneered technical advances now used widely, such as green fluorescent protein (Nobel Prize 2008). These discoveries have had a key impact in the conception of novel therapeutic approaches. Apoptosis inducing drugs targeting cancer cells are currently undergoing clinical trials, as well as RNAi-based therapeutic strategies for Huntington’s disease, HIV and cancer. In addition, more recent advances in understanding developmental potential and reprogramming have brought new prospects in regenerative medicine. However, the time it has traditionally taken to go from these fundamental discoveries to novel therapies is too long (>20 years!) and needs dramatic improvement. This is in part due to the slow appreciation of the power of this model, especially in Europe.

Although nematode research was initiated in Europe and benefited from tight personal connections, most groups are now located in the US and all support sites function there. Moreover, there is no support platform specifically aimed at young researchers. In recent years, the number of European *C. elegans* research groups has grown exponentially but the highly fragmented nature of the European worm community and the absence of any European exchange platform hamper the collective creation, diffusion and translational application of basic scientific knowledge. In order to discover and communicate the key fundamental biological principles that will allow us to address the human health issues outlined above more effectively, with **this Action a Network of *C. elegans* New Investigators in Europe (GENiE) is established. The Action creates a competence to facilitate scientific and technological exchange in three key areas of research** vital to fuel the personalised and combinatorial therapies of the future: **perturbations of cellular identity, neurobiology and ageing**. This Action pairs research-based funding from country-specific and European sources with a multi-disciplines network-based approach to promote *C. elegans* research in Europe and to foster the collaborations and dissemination of fundamental knowledge that is the

key driver of technological and medical advancement. A COST Action provides the perfect framework for GENiE to achieve its network objectives. GENiE's main goals, enhancing interdisciplinary collaboration, promoting technological innovation and European standards, enhancing translational efficacy, increasing mobility, disseminating novel discoveries and reducing duplication of funded research are perfectly suited to the COST framework of meetings, technology workshops and short-term scientific missions.

B.2 Current state of knowledge

Originally chosen as a model system to study nervous system function and development, the nematode *C. elegans* has proven pivotal in the discovery of numerous fundamental biological mechanisms. Deregulation of these mechanisms is frequently the cause of human disease. The first ever microRNAs were discovered through genetic studies of developmental timing in the worm. Many components of conserved cell signalling pathways (Notch, TGF- β , Ras/MAPK) were characterized by studying body size or organ development and fundamental mechanisms of cell polarity, cell cycle and cell division were uncovered in the early worm embryo. Further characterisation of these pathways and the interactions between them has not only revealed how conserved these processes are across the animal kingdom but has also driven medical advances by providing new diagnostic tools and drug targets. Recently, *C. elegans* has been successfully used to characterize the genetic and epigenetic events that drive developmental plasticity at the molecular level. This has important implications for more translational studies aimed at generating certain cell types *in vitro* for cell regenerative therapies.

The stereotyped nature and complete description of the nervous system in *C. elegans* has allowed worm researchers to be at the forefront of developmental and functional neuroscience. A whole host of genes crucially required for the development of the nervous system in all animals were discovered via forward genetic screening in *C. elegans*, including for example, the netrin family of axon guidance molecules. Mutations in many of these genes are now being associated with a broad array of developmental neurological disorders in humans. Worm studies have revealed the transcriptional mechanisms by which neurotransmitter diversity is established in the nervous system. The same mechanisms are conserved in mammals, with major implications for diseases such as Parkinson's, which specifically affects dopaminergic neurons. Finally, *C. elegans* is the only animal for which the complete nervous system connectivity, the "connectome", is known. Combined with functional imaging and behavioural analysis, nematodes are therefore now pivotal in understanding how the nervous system integrates multiple external inputs with internal cues to

coordinate behavioural responses.

Fundamental mechanisms of ageing have also been uncovered using nematodes. Over 20 years ago, it was shown that lifespan in *C. elegans* is regulated by insulin signalling. The conservation of this mechanism in mammals ignited the era of molecular biology of ageing. Soon after, metabolic mediators were characterized as playing major roles in stress resistance, fecundity, metabolism, and ageing in *C. elegans* and later, in humans. Very recently new longevity pathways have been identified in *C. elegans* including germline signalling, mitochondrial metabolism, protein quality control and DNA-damage responses. Human progeroid (“premature ageing-like”) syndromes are increasingly being linked to underlying mutations in genome maintenance factors. DNA-damage can also induce innate immune responses that in addition to essential functions in host-defence, play a crucial role in sensing cellular stress. Studying immunity in worms has therefore not only provided crucial insights into host-pathogen responses but is beginning to shed light on how stress and neuroimmune communication can influence infection and ageing.

C. elegans is also consistently at the forefront of technological innovation, from the pioneering use of green fluorescent proteins, through reverse genetics or high-throughput screening approaches. *C. elegans* along with other model organisms, has embraced high-throughput sequencing techniques for the analysis of mutant genomes and cellular transcriptomes, pioneered advances in imaging of subcellular chromatin localisation and whole-brain neuronal dynamics and is leading CRISPR-based genome engineering methodologies.

Understanding the interplay between developmental, functional and ageing-related mechanisms using *C. elegans* will involve communication across all these disciplines and will be key to help understanding the molecular basis of complex human diseases.

B.3 Reasons for the Action

There is a strong need to develop more systems-based interdisciplinary approaches to address the most important fundamental biological questions, as well as to reduce the time between novel discoveries and novel therapies. Fundamental biological discoveries, when translated into modern therapies, can have enormous impact on society and the economy, improving health and healthy-ageing. One efficient way to enhance basic research is to unite the technical know-how and state-of-the-art research being performed by multiple young researchers across Europe. A large number of well-funded young group leaders working on *C. elegans* have recently established their laboratories in Europe, after successful postdoctoral periods elsewhere. There are currently over 80 young research groups spread across 19 European countries. However, only US-based support networks

exist. This Action establishes the GENiE competence network of young researchers. By helping the promotion of *C. elegans* as a model system in Europe and inter-discipline communication the Action facilitates the discovery of fundamental principles of cell identity, neurobiology and ageing. An innovative way this Action promotes translation and helps reduce the time to therapies is to directly involve industrial stakeholders and to establish translational collaborations. **GENiE's main aim is the strategic planning and advancement of basic *C. elegans* biological research and translation in Europe.** This will reduce the current fragmentation and high reliance on US-based networks and resources. Focusing specifically on Early Stage Researchers (ESRs) and young PIs, GENiE will enhance researcher mobility and technical training, providing support at a critical time of their career and create a pool of well-trained researchers for the future. GENiE will promote the fast dissemination of crucial results to medical institutions and will promote model-organism research to industrial partners and the broader public. GENiE researchers will benefit scientifically from closer integration that will establish and foster collaboration, raise their visibility and promote *C. elegans* as a model organism. Focusing efforts on three scientific areas as well as greater communication will decrease dispersal and maximise national research funding, which will benefit European research. Society will benefit, not only from increasing the pool of well-trained young researchers but also through the dissemination of basic biological research, the building block of therapies and treatments of the future.

B.4 Complementarity with other research programmes

This Action will complement similar recent COST Actions such as EUFishBioMed and will work very closely with other model organism networks that currently exist, such as Junior European Drosophila Investigators (JEDI) with whom preliminary contacts have been established. In addition, this Action will synergise with the only other FP7-funded Action focusing on *C. elegans*, "Si elegans", which aims at providing a neuromimetic computational platform for *C. elegans* scientists studying behaviour and brain-like architectures. Platform technology aspects of the GENiE network will be integrated with currently running FP7 programmes including EuroBioImaging and LaserLab-Europe, which are aiming to provide European-wide networks of high-level imaging and laser facilities respectively.

C. OBJECTIVES AND BENEFITS

C.1 Aim

The main objective of the Action is to promote and co-ordinate the use of *C. elegans* for basic 'blue-skies' research as a model for human disease and bridge the gap between fundamental research and therapeutic innovation. The Action establishes a network of young *C. elegans* researchers (GENiE) and promotes collaborative interdisciplinary approaches through the creation of a centralised communications platform across Europe. As the current European *C. elegans* community is fragmented and lacks opportunities to interact, this Action, led by and focusing on young Principal Investigators (PIs) and ESRs, will foster high-quality collaborative research and build research capacity by pooling expertise. Target audiences include *C. elegans* researchers and the wider biomedical research community, the general public, policy makers and industry members.

C.2 Objectives

1. Defragment the European *C. elegans* community in biomedical research through the **creation of a reference network of laboratories (GENiE) led by young Principal Investigators**, a new resource world-wide.
2. Promote a novel approach to “blue-skies” *C. elegans* research by **creating interdisciplinary subgroups of researchers across three key scientific areas** (control of cellular identity, neurobiology and ageing).
3. Promote the development and spread of **novel cutting-edge technology** across Europe.
4. Reduce the time between novel discoveries and novel therapies through the **promotion of translational research and communication with industry stakeholders**.
4. Increase scientific quality via the establishment of **gold standards and centralised databases** of methodologies, resources and reagents.
5. Increase attractiveness of the European *C. elegans* community and **train the next generation of European *C. elegans* ESRs**.
6. Raise awareness and interest in the use of *C. elegans* as a **model for basic biological research related to human disease** and disseminate the most recent scientific findings to medical researchers, industry partners, and the general public.

C.3 How networking within the Action will yield the objectives?

GENiE will implement the following activities and facilities (see timetable of deliverables I.F):

1. A **website**, serving the whole European *C. elegans* community and beyond offering a centralized,

searchable repository of research interests/expertise, contact information, maps of ERA key technology platforms, protocols, general public information and ebooks and discussion forums [Deliverables 1: website creation, database creation, web traffic, number of protocols, comments and updates, public involvement].

2. Biennial **Conference** and **annual WG meetings** [Deliverables 2: participation number, collaborations and co-authored papers/patents, evolution into a reference European Worm Meeting].

3. Focused **Workshops** and **Training Schools** to train researchers in specific technologies and areas [Deliverables 3: career progress, newly established groups].

4. **STSMs** for joint funding grant preparations, for ESRs for specific training in another lab and to promote lectures by PIs to ESRs [Deliverables 4: joint funding application, adoption of cutting-edge techniques, exchange/recruitment inside the network].

5. **Coordinated access to technology platforms** (advanced light and electron microscopy, worm sorting, genome editing, Y2H mapping, calcium imaging, 4D-lineaging, laser photodestruction) [Deliverables 5: map of infrastructures, facility usage]

6. **Open communication channels with industry stakeholders**, using both the personal and institutional connections of GENiE members and via direct contact [Deliverables 6: participation of industry stakeholder to the Action meetings, establishment of partnerships, potential patents]

C.4 Potential impact of the Action

Through this inclusive Action, GENiE will improve ERA research capacity by enhancing the speed and scope of breakthrough discoveries, will introduce the worm as a powerful model for drug and clinical trial pre-screening and will improve translation to industrial partners. This Action will **defragment** the European *C. elegans* research community. Providing a regular discussion platform to researchers is one of the key goals of the Action and is expected to continue well beyond the duration of the Action. By **maximising European interactions** and collaborations, the Action will **avoid duplication of research efforts**, therefore saving tax-payer money whilst increase the overall European research output and visibility. In addition, by **consolidating groups at a critical step** in their existence, this Action will maximise the use of the starting-up funds invested in these teams. By nature, the network is **interdisciplinary** and integrates various subfields and partners, fostering scientific and technical collaborations between researchers of complementary backgrounds and expertise that otherwise would not have met. This will allow them to accomplish research goals that cannot be addressed by any single laboratory and build up a critical mass in research areas that will have the most impact on quality of life, health-related costs and future novel therapies. Providing

databases of experts, platform technologies and results will improve research quality and **facilitate the development of new technologies and limit under-use of specialised high-end equipment**.

This Action is expected to have a long lasting impact in addition to the immediate impact on the European science and laboratories, for example by creating meetings that will become the **reference biannual rendezvous** of the European *C. elegans* community.

Broader awareness of the excellent European research performed with *C. elegans* will **attract high-quality ESRs to the European Research Area (ERA)** and will place Europe at the centre of an excellence network, ensuring Europe's competitiveness, especially in relation to the US. The Action will also **enhance the opportunities for young researchers** to develop independent careers, promoting the emergence of the next generation of talented researchers. The network focuses on young researchers, who often do not have **access to European networks** and therefore do not benefit from framework programmes. The Action offers a platform for these young researchers to build other (non-COST supported) European networks. In particular, the Action will **support researchers in COST member states or neighbouring countries with few or even no *C. elegans* laboratories**, who want to start nematode research. Worms have low usage cost and are therefore well suited in countries with a lower budget for scientific research.

Through publicly accessible dissemination activities, the Action will **provide its expertise** to the scientific community as well as policy makers and the general public. Journals, foundations, panel chairs and industry leaders can **find the experts** they need and other academics and industry leaders can establish the collaborations they require. The Action will improve European biomedical research by **educating medical researchers and potential industry partners about *C. elegans* use in early and pre-clinical phases of drug development**. In particular, how *C. elegans* can speed up research (*e.g.* miRNAs, discovered in nematodes and currently in clinical phases for Alzheimer's or cancer) or supplement existing medical research tools (*e.g.* to minimize costly experimentation on vertebrates). In the longer term, this Action will **accelerate translation of knowledge from *C. elegans* into clinically relevant applications**.

C.5 Target groups/end users

The network intends to reach a broad group of stakeholders and end users. They include young European researchers already working with *C. elegans*, ESRs and researchers wishing to enter *C. elegans* research (especially from countries with no established *C. elegans* groups), biomedical researchers working in related fields or involved in the design of clinical trials, and the general public through dedicated website sections. In addition preliminary contacts have indicated that the

Action is of high interest to many potential industry partners (drug screening: Boehringer Ingelheim/M. Pearson, Bayer CropScience, Novartis Syngenta, Roche/M. Hoener; pest control: Novartis AH, GSK, e-nema, NEB/T. Carlow, Bayer; technological development/valorisation: Zeiss, Sigma, Source Bioscience, Addgene, ZPD, Definiens)

D. SCIENTIFIC PROGRAMME

D.1 Scientific focus

Personalized medical treatments require the understanding of how genotype shapes phenotype. This Action will take advantage of the conservation of fundamental principles across organisms and the power of the genetic and cellular tools in *C. elegans* to address key basic scientific questions essential to human disease, healthy ageing (WG1-3) and sustainable agriculture (WG5).

Importantly, discoveries in the worm have come from an unexpectedly wide range of different fields. Indeed, >60% of our genes and all fundamental biological processes are conserved between worms and humans. Results obtained in the worm have been shown to be predictive of outcomes in higher eukaryotes. This Action will furthermore foster the development and implementation of novel, innovative technologies and ensure all network researchers have access to and are familiar with the latest advancements (WG4). In addition to focusing on the basic research and the technological advancements required to improve human health, this Action will also promote translational approaches across the entire network and facilitate communication with industry stakeholders (WG5).

Basic Science Aims

Mechanisms that perturb cell identity and their consequences: The specific questions to be addressed are (A.i) how cell fates are established, maintained and reprogrammed; (A.ii) how the dynamics of spatial genome organisation in the nucleus affect transcriptional states; (A.iii) how key cell biological process, such as cell polarity and cell cycle regulate cell identity or lead to cancer.

From molecules and genes to actions – neurobiology and behaviour: Research will focus on (B.i) the specification and maintenance of neural subtypes; (B.ii) advanced live-imaging to monitor single-cell, neural circuits and whole brain neuronal activity ('ethome'); (B.iii) high-throughput quantification of behavioural phenotypes ('functional connectomics'); (B.iv) modelling neurodegeneration.

Influence of metabolic fluxes, immunity and stress on lifespan: Research will focus on (C.i) characterising additional novel genetic programs that regulate lifespan (ie mitochondria, protein

quality control and lipid metabolism); (C.ii) the identification of new biomarkers of ageing; (C.iii) understanding how immunity, stress responses and neuroimmune communication impact upon lifespan.

Working Groups

Because the basic scientific questions outlined above are complex and require the examination of different tissues and their interactions at the genetic, cellular and biophysical levels, a multi-group interdisciplinary approach is necessary. Thus each scientific WG will integrate researchers working on different fields. WG1-3 will be organised around one of three specific human health related themes. WG4 will focus on technology development and innovation. WG5 will promote translation. Indeed, an innovative aspect of this Action is the integration of multi-faceted (genetics to high-end imaging to biophysics), multi-scale (microscopic to mesoscopic) and multi-level (molecules to single cells to cellular circuits) approaches. This Action will therefore foster state-of-the-art research through an innovative collaborative effort between experts that do not normally mix.

WG1 *Genetics of human congenital disease and regenerative medicine.* Understanding the genetic mechanisms controlling cell identity will lead to a better diagnosis of congenital human diseases and their underlying genetic causes, will facilitate the development of innovative therapeutic strategies and will advance cellular replacement in regenerative medicine. WG1 will integrate researchers working on aims A.i-iii and B.i-ii above.

WG2 *Neurological and behavioural disorders.* Many human neurological disorders have their origin in the misspecification, malfunction or degeneration of the nervous system due to genetic alterations allowing the basic mechanisms to be addressed in genetic model organisms. To understand the effects that single genes have upon neuronal function, information flow around higher order neuronal circuits and how this can modify behaviour this WG2 will integrate researchers working on aims A.i, B.i-iv and C.iii.

WG3 *Metabolism and healthy ageing.* Longevity mutants were first identified in *C. elegans* and research using worms has identified several conserved pathways that regulate lifespan in humans, including insulin signalling and caloric restriction. WG3 will integrate researchers working on aims B.iii-iv and C.i-iii. Basic research in these areas will reveal novel drug targets that could potentially extend human longevity, treat metabolic disease and pathogen infection and increase the wellness of an ageing European population.

WG4 *Technology and Innovation:* Work in *C. elegans* has consistently been at the forefront of technological advancement. From the use of green fluorescent protein through to the latest genome-editing and whole brain imaging techniques. As the innovative science outlined above requires state-of-the-art techniques, this transversal WG will bring together researchers from across the

network (WG1-3) whose work is at the forefront of technological advancements in order to promote technology development and ensure dissemination of the latest technologies and methodologies.

WG5 Translation: To allow innovative new therapies to be developed requires not only an improved basic understanding of fundamental processes to provide novel drug targets but also the development of human disease models, the testing of new drugs to improve clinical trial rates (for toxicity and to identify modes of action) and dedicated routes of rapid communication to industry stakeholders. WG5 will bring together those researchers from across the network (WG1-3) whose work is translationally focused (eg modeling of human disease genes) together with industry stakeholders. In addition, it will promote the use of *C. elegans* as a fast, cost-effective, ethically justifiable model for first pass *in vivo* drug testing and drug target identification and toxicity, a current roadblock underlying the very low clinical trials success rate; and make use of the non-conserved mechanisms uncovered to open new directions in parasitic nematode (cattle and crops) targeting, in conjunction with industry stakeholders.

WG6: Networking and public awareness of basic research: This workgroup is not scientifically focused and is discussed in more detail below.

D.2 Scientific work plan methods and means

To focus, enhance and achieve the scientific goals described above, nine main network-based tasks to be performed by this Action have been identified:

Task 1 Action website. Produce and maintain a **highly interactive GENiE website** that will serve as the main platform for scientific exchange between researchers. This centralised platform will improve the dissemination of knowledge to scientific, medical and business leaders and promote a greater understanding of model organism based research to the general public. It will be the main mechanism for disseminating information related to the following tasks. The GENiE website will be established by WG6 (see section E)

The website will include (but will not be limited to): (i) a front page displaying latest blog posts, COST Action documents and Action events, an interactive European map displaying the location of each GENiE member and the location of specific technology platforms; (ii) a searchable profile for each GENiE member indicating skills/resources, technical and lay research summaries; (iii) a blog accessible to GENiE members, students, postdocs and industry stakeholders organised by searchable #hashtags (e.g. #joblisting, #newpublication); (iv) a password-protected GENiE blog to facilitate more specific communications on Action confidential information; (v) public engagement pages – with an ‘ask the expert’ section; (vi) a repository of protocols and databases ; (vii) meeting

and workshop listings; (viii) network funding opportunities (mobility, training etc).

Task 2 Define and establish European standards and databases. WG1-3 (for detail see section E) will each be tasked with drafting European experimental standards (specific assay design and also relating to phenotypic characterisation). These documents will be circulated amongst experts in each of the three key scientific areas for comments and refinement. During the course of the Action certain “gold standards” will be determined in this manner. WG1-3 will also determine, establish and maintain interactive databases of phenotype information relevant for their research areas. One member of each WG will be elected to work in coordination with WG6 to ensure interactive dissemination of these databases via the GENiE website.

Task 3 Technology platforms. Establish and **coordinate platform technologies** (whole-genome sequencers, high-throughput imaging platforms, genome-engineering facilities, worm sorters, 4D-lineaging systems). WG4 will be specifically focused on promoting the development, dissemination and provision of these latest technologies throughout the network. As part of this it will coordinate a database of platform technologies (and associated experts) available for shared use across Europe. This database will provide listings of available equipment, usage requirements and personal contacts, the lack of which is currently a brake. **Establish** a limited amount of funding for specific STSMs and travel for GENiE members to utilise technology platforms in other countries if there is no other option (overseen by WG5 and the MC).

Task 4 Protocols database. Establish and maintain a **repository of state-of-the-art protocols and innovative new methods**. A specific emphasis will be placed on the latest technologies. WG6 will establish an interactive (*i.e.* easy to upload to and download from) database of techniques. WG1-3 will curate this database to ensure they are the most up-to-date and of high quality. WG4 will ensure a focus on state-of-the-art new techniques.

Task 5 Virtual stock centre. Establish a **coordinated nematode strain list** across European laboratories to facilitate speedy transfer of new mutants, new transgenic lines and new tools across the European community. WG6 will seek, with the help of one or two part-time staff, to integrate GENiE member laboratory strain databases into a unified European strain database that will allow the creation of a ‘virtual stock centre’. This will reduce costs and the increasing difficulties of importing strains from US-based resources

Task 6 Enhance scientific collaboration, technological innovation and translation. Organisation of both **general and targeted meetings and workshops**. This will include but will not be limited to annual WG meetings and a general biennial meeting. WG1-3 will be responsible for the organisation of interdisciplinary topic-specific meetings and proposing topic-specific workshops related to the specific scientific questions outlined earlier (see section B). Discussions between

WG1-3 and the MC will determine which workshops are brought to fruition. Small grants will be made available upon application for Short-Term Scientific Missions (STSMs) to enhance collaborations. An STSM committee appointed by the MC will seek suitable peer-reviewers from among GENiE members to assess STSM usefulness. WG5 will organise technology-based workshops in addition to co-ordinating technology platforms. Promoting translation will be the sole purpose of WG5. This WG will co-ordinate, via specific meetings and workshops, researchers working on more translational aspects from across our three areas of scientific focus (WG1-3). WG6 will also be responsible for promoting the use of *C. elegans* for drug testing and ensuring bi-directional communication with the more translational members of WG1-3 and current and future industry stakeholders.

Task 7 Mobility and training. Enhance the training, education and mobility, particularly of ESRs, through the provision of **STSMs, Training Schools and career advice workshops**. A number of STSMs specifically aimed at ESRs, to get training in GENiE laboratories and disseminate their findings, and to prepare them to seek job opportunities across Europe, will be provided by the Action to each of WG1-3. They will be allocated on the basis of application and determined by the WGs.

Task 8 Specialist community visibility. Provide a continually updated **searchable list of the skills**, expertise and key research findings of GENiE members. This will increase visibility of *C. elegans* to key specialist communities, a target audience. It will allow funding bodies and journals to find expert peer reviewers. Similarly, it will provide business and industry leaders with potential research partners. WG6 in collaboration with other WGs will be tasked with ensuring that one very prominent feature of the website is the ability to easily identify GENiE members interests, skills and expertise.

Task 9 Public awareness. Raise the profile and understanding of basic biological model organism research amongst the general public via **dedicated programmes designed to engage and encourage bi-directional communication with the public**. Members of WG6 will be identified, through discussions, to work in collaboration with the web designer and oversee the creation of the dedicated public-awareness sections of the website. Web docs and interviews of GENiE members aiming at explaining their research and relevance will be posted on the GENiE website. Aided possibly by a part-time staff member they will coordinate the ‘ask an expert’ section. This will involve moderating and coordinating responses to these questions via a network of GENiE volunteer experts.

E. ORGANISATION

E.1 Coordination and organisation

The 80 research teams that will participate in this Action all have national funding for their own research programmes, and 20 of them also hold European funding as part of the FP7 framework (ERC and Marie Curie), while 16 are ESRs. Thus, the requested funding is necessary to co-ordinate all these individual efforts in an interdisciplinary collaborative network capable of accomplishing the goals presented above. This will be co-ordinated as follows:

Management Committee (MC). The MC will be formed and will function according to the Rules and Procedures described in document COST 4112/13. The MC will meet twice a year to oversee all activities carried out under this Action (some of these meetings may be held by teleconference to minimize the travelling burden). The MC will set up rules that the Working Groups will follow to carry out these activities and allocate the funds for each one of them. In addition, the MC, in conjunction with the Domain Committee (DC) expert, will evaluate the progress on each of the Objectives of the Action. It will do so based on the described Deliverables for each Objective, and also based on annual reports from the different Working Groups and from the Scientific Advisory Board. During the first MC meeting the Leaders and Task Team members to manage each Working Group will be nominated, and sub-committees with specific focuses will be formed: STSM, Platform technology, Outreach to the wider research community and non-COST countries, Gender balance and ESRs.

Working Groups (WGs). Each WG, composed of GENiE laboratories, platforms, industry stakeholders will be organised by two Leaders who will identify additional Task Teams to carry out the different activities (website, workshops, meetings, public outreach). The Leaders will oversee the organisation of these activities and will liaise with the Management Committee and sub-committees. In addition they will be responsible for submitting an annual report to the MC for progress evaluation. The WG Leaders, as well as some of the Task Team members, if necessary, will meet once a year, and will hold an additional teleconference to ensure a productive coordinated action.

Scientific Advisory Board (SAB). An external group of experienced, international scientists will advise and evaluate the performance of the Action and submit an annual report to the Management Committee. In addition, this SAB will facilitate coordination with other European and global networks. To further promote relations with industrial partners, one of the SAB members will come from the pharmaceutical industry.

E.2 Working Groups

Working Groups 1-3 have a scientific focus, each one an interdisciplinary association of groups from different fields and expertise, nucleated around the basic science aims and human health questions addressed in this Action: WG1 is focused on genetic mechanisms of disease and regenerative medicine, WG2 on neurological and behavioural disorders and WG3 on metabolism and healthy ageing. The two leaders for each WG and their Task Teams will propose and organise the topic-specific technological workshops and summer schools relevant to each area.

Working Group 4 is a transversal group specifically focused on technology. The two leaders for this WG and their Task Teams will coordinate the technology platform resource, liaising with WG6 who will maintain the website listings. They will also organise topic-specific technological workshops and summer schools. This group will also be tasked with outreaching to the wider research community to disseminate the advances generated by the Action.

Working Group 5 is specifically focused on translation. The two leaders for this WG and their Task Teams will coordinate a specific sub-group of researchers from across WG1-3 who take more translational approaches. Along with their task team they will maintain and promote active bi-directional communication and collaboration between these researchers and industry stakeholders.

Working Group 6 is focused on networking and public outreach and, as such, will act as a bridge between WGs 1-5, with external researchers and to the general public. It will professionally develop and maintain the website and organize public outreach activities (e.g. “ask an expert” see part H for more details). A young web designer with experience in public outreach is part of this Working Group and will further be commissioned to produce webdocs, ebooks and interviews of GENiE teams on their research and activities that are intended for the lay public, and find avenues for reaching the general public (national radio and newspapers, links to high schools and universities). It will also organise the biennial general Conferences for group leaders and ESRs, which will be open to the scientific community, and the annual Working Group meetings. These meetings will place a particular emphasis, in addition to science, on discussions related to EU funding, career development, women in science and team management. In addition, through an appointed STSM committee, this subgroup will implement and oversee the exchange between research teams and institutes (i.e. the short-term scientific missions (STSMs)).

E.3 Liaison and interaction with other research programmes

Interaction with the rest of the community and other global research programmes (as in I.B.4) will

by actively promoted in several ways: 1) by holding an open-access Conference biennially; 2) by inviting leading scientists external to the network to WG meetings; 3) through the website; 4) through the more senior and connected members of the SAB. In addition, appropriate links will be generated to and from our website and other resources website, such as Flybase, FlyJedi, ZFin, Wormbase (the american major resource for *C. elegans* researchers). The activities of this Action will also be advertised and promoted at the International meetings attended by GENiE members, including the International Worm Meeting in Los Angeles, USA, opening communication with American research programmes.

E.4 Gender balance and involvement of early-stage researchers

This COST Action will respect an appropriate gender balance in all its activities and the Management Committee will place this as a standard item on all its MC agendas. The Action will also be committed to ensuring the involvement of early-stage researchers. This item will also be placed as a standard item on all MC agendas.

Measures to promote gender balance

This Action has been initiated by a female scientist. All female *C. elegans* researchers in Europe who started their labs in the last ten years have registered their interest and will take part in this Action. To further promote participation of female scientists and the inclusion of young women in science in general, this Action will:

1. Organize and support workshops for women in science. A workshop for female group leaders as well as students and postdocs is planned during the Action Main Meeting that will take place every other year. A workshop for female group leaders will be organized, again appended to the annual WG meeting.
2. Ensure that meetings are not held at critical times during the school year.
3. Facilitate the arrangement of on-site childcare during the Main Conference and the Working Groups meetings according to the “COST family friendly policies” described in doc. COST 295/09.
4. Promote mentoring between women in the network through the interactions established during the workshops.

Measures to promote and integrate early-stage researchers (ESRs)

An innovative aspect of this Action is a particular focus on ESRs, and the coordination of research teams where the Team Leader has had a laboratory for less than 8 years. In particular, all *C. elegans* groups started within the last two years that registered an interest (16) are included in this Action. In addition, many of the activities that this Action will carry out are aimed at the education/training of

Ph.D. students and postdoctoral scientists and their integration into the international research community. Specifically, this Action will:

1. Organize annual summer schools where students and postdocs can learn from experts in the different research areas and flex their networking skills.
2. Organize technological workshops where ESRs can acquire hands-on experience on specific techniques.
3. Provide additional experience in scientific communication by supporting ESRs to travel to other GENiE institutes and give seminars to new audiences. ESRs usually have limited opportunities to present their work outside of their institutes and allowing them to visit other institutions within the network would boost visibility, experience and confidence.
4. Provide training in scientific communication via group leader networking visits to other institutes to give seminars and lectures to ESRs.
5. Provide Short-Term Scientific Missions (STSM) in participant laboratories to get specific technological training for ESRs as they develop new avenues of their research.
6. Involve ESRs in the outreach activities towards the lay public, in particular by having them draft the answers to the "ask an expert" interaction feature.

F. TIMETABLE

The duration of the Action is four years. The proposed timetable may be reformulated if this appears to be necessary during the running of the Action.

	Deliverables (I.C.3)	Year 1	Year 2	Year 3	Year 4
1 st MC meeting		x			
Website	DL1	x			
MC meeting		x x	x x	x x	x x
Open-access conference	DL2		x		x
Action Main Meetings		x	x	x	x
WP 1 meeting	DL3	x x x	x x x	x x x	x x x
WP 2 meeting		x x x	x x x	x x x	x x x
WP 3 meeting		x x x	x x x	x x x	x x x
WP 4 meeting		x x x	x x x	x x x	x x x
WP 5 meeting		x x x	x x x	x x x	x x x
WP 6 meeting		x x x	x x x	x x x	x x x
Technological workshops	DL3	x	x	x	x
Summer schools		x	x	x	x
STSM	DL4	15/year	15/year	15/year	15/year

Coordinated tech. platforms	DL5	x			
Final meeting					x

When possible, MC and WG meetings will be held immediately before or after the main Action meetings. Some meetings might be held by teleconference.

Annual Training Schools and Technological Workshops. These will be organized by WG1-3, focused on specific topics relevant to these WG. They will be designed to provide an opportunity for interested junior scientists to interact with senior participants, and to help foster the emergence of a strong community of young scientists.

Short-Term Scientific Missions. Throughout the Action, Short-Term Scientific Missions for stays of up to three months will be set-up whenever possible and relevant, both within and between WGs. This aspect of the Action is viewed as critical for its success. These missions will be proposed to WGs by participants on an ad-hoc basis, and will be ensured to involve primarily young scientists.

G. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest: AT, BE, CH, CZ, DE, DK, EL, ES, FI, FR, HU, IL, IT, NL, NO, PT, SE, TR, UK. On the basis of national estimates, the economic dimension of the activities to be carried out under the Action has been estimated at 76 Million € for the total duration of the Action. This estimate is valid under the assumption that all the countries mentioned above but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.

H. DISSEMINATION PLAN

H.1 Who?

Activities, knowledge, good-practice standards and results will be publicly shared with a wide audience:

- The **stakeholders** of the GENiE network will share knowledge, expertise and resources and will be provided with opportunities to setup better and more efficient

collaborations, which will increase the productivity, quality, translation and impact of results.

- **Researchers** outside the network, in particular those working on *C. elegans* biology or those working on related topics in other model systems, will be informed and stimulated to share knowledge and expertise with the GENiE network. **Non-*C. elegans* researchers** that wish to utilise *C. elegans* will be informed on how to work with *C. elegans* and which collaborations would be possible to initiate such research.
- **Industry, journals, policy makers and funding bodies** that look for information on the GENiE network, its members or *C. elegans* research. More specifically, **enterprises** that look for fruitful collaborations.
- **Early stage researchers** (ESR) looking for career opportunities or know-how transfer opportunities, for instance by means of short term visits or internships in foreign laboratories. Indeed defragmentation actions, such as the development of a centralised website presenting a map of participants and their latest advances, will enhance the European scientific community and visibility in many ways.
- The **general public** will be addressed by dedicated sections of the website informing them about the research conducted in the framework of the Action, focusing on the major discoveries made using model organisms and the current application of these results for biomedical research.

H.2 What?

A public, interactive website dedicated to the activities of this COST Action will be central to the dissemination of knowledge and results. For the scientific community, this website will provide information on the network itself, its members, good practice guidelines, technical and scientific **discussion forums, protocols, a virtual strain repository** and other **databases**. By integrating modern communication tools and social media, for instance Twitter, the website will aim to form an active online community that will facilitate real-time networking between COST Members. The website will directly link to participating laboratories, each with their expertise and facilities, to boost efficient and productive collaborations. This information will also help to stimulate and

initiate collaborations with non-*C. elegans* researchers that wish to incorporate *C. elegans* studies into their research. These collaborations will have a major impact on future (cross-European) funding applications. Furthermore, this information will provide students, post-docs and possibly future PIs looking for career opportunities with the necessary information on other labs, contact details, and job offers. To inform policy makers, industry and the general public, a dedicated web interface will provide **information and documentation**, in nontechnical language, on ongoing research, achievements and impact of the COST Action. Industry leaders will be invited to meetings to encourage usage of nematode as a biomedical research model and/or facilitate translational research for nematode pests.

To **educate European citizens, an interface targeting the lay public will be set up**. This interface will aim at explaining the relevance and importance of the scientific questions addressed by this COST Action, highlight the scientific approaches and technological developments used, and formulate the results obtained and their impact in accessible terms. These will be presented in the form of web documentaries or an ebook and interviews of the participants on their research. In addition, through an interactive webpage, there will be the opportunity for the general public or interested parties to **ask experts in the field**. ESR will be encouraged to participate in these activities.

In addition to the website, **scientific knowledge, results and techniques** will be transferred between GENiE members in the form of workshops, STSMs and summer schools. They will also be shared with the scientific community at national and international meetings. Furthermore, **results and techniques will be published in peer-reviewed scientific journals** and via online video tutorials. Whenever possible, this COST Action will encourage open access publications, to achieve a maximum outreach and accessibility of results. As a result of the collaboration between the participants in this COST Action, **video-tutorials of different techniques** in which the participating laboratories are expert, will be published. The diffusion of these tutorials will provide a huge benefit to the scientific community in order to establish new techniques in their respective laboratories. Furthermore, it will be the first option for students or new *C. elegans* laboratories looking for technical know-how. In addition, it will serve as a way to directly contact an expert in the field to answer questions related to the experiment. The impact of this activity is not restricted to the scientific community alone but will be of general interest for universities and even schools to set up practical courses in different fields like microscopy, genetics, apoptosis, transgenic generation, etc...

If applicable and desirable, participating researchers will issue **press releases** of cooperative efforts and results via the associated institutes, which will help to communicate scientific knowledge to the

general public through the use of nontechnical publications. All media coverage of activities will be shared via the website of this COST Action and associated social media (e.g Twitter, etc).

To arouse the interest of the public, students and potential undergraduate applicants, this COST Action will generate a **digital information package on *C. elegans* biology and research (including teaching slides etc.) that can be used in biology curricula** at universities and schools. Also, this information package will provide several **protocols for easy ‘do-it-yourself’ scientific experiments** and links to online video-tutorials. This COST Action and *C. elegans* research will also be promoted by providing contact details of individual COST members per country that can be invited to give a guest-lecture on *C. elegans* biology and research at universities or high schools.

H.3 How?

An **easy accessible and interactive website** that conforms to these aims will be maintained professionally. In addition, a web designer is associated with this COST Action that specialises in producing scientific ebooks and webdocs for the lay public and will be commissioned to design a dedicated web interface for the lay public.

Regular **Workshops**, at least once a year, will be organized by this COST Action, to promote the transfer of expertise among participants. As this Action focuses on ESR and young PIs, in addition to Workshops, **Training Schools** dedicated to the training of the young researchers in participating laboratories will be organised annually. These events will furthermore provide young researchers with invaluable networking opportunities.

As most collaborations start with informal contacts, at the commencement of this COST Action a **Working Group meeting** will be organized to bring together all participating PIs. This will enable each participant to introduce his/her research and lab and provide opportunities to raise new ideas, to reflect on current research developments and possibilities and to initiate or strengthen collaborations. In addition, by incorporating dedicated workshops that will disseminate cutting-edge technical information, a particular focus of the meetings will be to bring together diverse technical and scientific experts to generate cross-cutting collaborations and stimulate future funding.

There will be an annual **Action Main Meeting** to promote the exchange of ideas and results and to provide a platform for networking. Experts (external to network) will be invited to WG meetings to increase dissemination in a more global European community. Furthermore, industrial partners will be invited to meetings to encourage links with industry and facilitate translational research with high impact.

The stakeholders will convene in an **open-access general Conference** that will be organised every

other year, in alternate years to the biennial International Worm Meeting held in the US. This meeting will lay the foundation for a European *C. elegans* meeting that will bring together the European *C. elegans* community, and in the end, transcend and persist beyond this COST Action. Workshops and conferences will be **announced on the website**, promoted via social media but also via other means within the world-wide *C. elegans* community (e.g. via the Wormbase database, www.wormbase.org) to attract scientists from outside this Action as well.

Attention to workshops and conferences will be drawn via the **publication of proceedings** on the website and in peer-reviewed journals. Furthermore, to increase impact of this COST Action, a yearly review and action plan on achievements, which is generated and evaluated at the yearly main Action meeting, will be publicly provided.

Finally, the recent advances taught during technologically-oriented workshops and in individual GENiE labs will be submitted as **video-tutorials** to the Journal of Visualized Experiments (<http://www.jove.com/>). This on-line journal publishes scientific videos, is indexed in PubMed and can be cited and referenced. COST support will be acknowledged in the Action publications. When possible, the video-tutorials will be directly accessible through a link on the GENiE Action web page.

Press releases will be used to inform and draw attention from the general public, policy makers and the industry.