Brussels, 13 April 2018

COST 032/18

DECISION

Subject: **Memorandum of Understanding for the implementation of the COST Action "Correlated Multimodal Imaging in Life Sciences" (COMULIS) CA17121**

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action Correlated Multimodal Imaging in Life Sciences approved by the Committee of Senior Officials through written procedure on 13 April 2018.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA17121
CORRELATED MULTIMODAL IMAGING IN LIFE SCIENCES (COMULIS)

The COST Member Countries and/or the COST Cooperating State, accepting the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action (the Action), referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any new document amending or replacing them:

a. "Rules for Participation in and Implementation of COST Activities" (COST 132/14 REV2);
b. "COST Action Proposal Submission, Evaluation, Selection and Approval" (COST 133/14 REV);
c. "COST Action Management, Monitoring and Final Assessment" (COST 134/14 REV2);
d. "COST International Cooperation and Specific Organisations Participation" (COST 135/14 REV).

The main aim and objective of the Action is to promote Correlated Multimodal Imaging (CMI) in biological and preclinical research. To achieve this inherently interdisciplinary goal, it is indispensable to establish a collaborative network of scientists across disciplines to foster and market CMI as a versatile tool in biomedical research.. This will be achieved through the specific objectives detailed in the Technical Annex.

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 96 million in 2017.

The MoU will enter into force once at least seven (7) COST Member Countries and/or COST Cooperating State have accepted it, and the corresponding Management Committee Members have been appointed, as described in the CSO Decision COST 134/14 REV2.

The COST Action will start from the date of the first Management Committee meeting and shall be implemented for a period of four (4) years, unless an extension is approved by the CSO following the procedure described in the CSO Decision COST 134/14 REV2.

OVERVIEW

Summary

The network aims at fueling urgently needed collaborations in the field of correlated multimodal imaging (CMI), promoting and disseminating its benefits through showcase pipelines, and paving the way for its technological advancement and implementation as a versatile tool in biological and preclinical research. CMI combines two or more imaging modalities to gather information about the same specimen. It creates a composite view of the sample with multidimensional information about its macro-, meso- and microscopic structure, dynamics, function and chemical composition. Since no single imaging technique can reveal all these details, CMI is the only way to understand biomedical processes and diseases mechanistically and holistically. CMI relies on the joint multidisciplinary expertise from biologists, physicists, chemists, clinicians and computer scientists, and depends on coordinated activities and knowledge transfer between academia and industry, and instrument developers and users. Due to its inherently multidisciplinary and cross-functional nature, an interdisciplinary network such as this Action is indispensable for the success of CMI. Nevertheless, there is currently no European network in the field. Existing scattered efforts focus on correlated light and electron microscopy or (pre)clinical hybrid imaging. This Action will consolidate these efforts, establish commonly-accepted protocols and quality standards for existing CMI approaches, identify and showcase novel CMI pipelines, bridge the gap between preclinical and biological imaging, and foster correlation software through networking, workshops and open databases. The network will raise awareness for CMI, train researchers in multimodal approaches, and work towards a scientific mindset that is enthusiastic about interdisciplinary imaging approaches in life sciences.

Areas of Expertise Relevant for the Action	**Keywords**
● Biological sciences: Morphology and functional imaging of cells ● Biological sciences: Biophysics ● Biological sciences: Molecular biology and interactions ● Biological sciences: Development, developmental genetics, pattern formation and embryology in animals ● Physical Sciences: Biophysics	● Correlated Multimodal Imaging ● Preclinical and Bioimaging ● Image Analysis ● CLEM ● Hybrid Imaging

Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

● Establish a European network of diverse expertise and provide a platform for knowledge transfer for Correlated Multimodal Imaging (CMI) in life sciences.
● Trigger the implementation and further development of CMI in life sciences by bringing together instrument users and developers, and by bridging biological and preclinical imaging.
● Evaluate and standardize existing approaches and assess their transferability to novel CMI pipelines.
● Trigger marketable products and facilitate technology transfer between Academia and Industry.
● Raise awareness of CMI and its numerous benefits in the life science community and general public.

Capacity Building

● Boost the use of CMI by setting up CMI communication channels and establishing a website and database for CMI approaches.
● Facilitate staff exchanges and collaborations through STSMs.
● Establish long-term collaborations among COMULIS participants.
● Facilitate knowledge transfer among CMI experts, ECIs and industry through conferences, meetings, training schools and STSMs.

1.S&T EXCELLENCE

1.1. CHALLENGE

1.1.1. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The main aim of this COST Action (COMULIS) is to **promote Correlated Multimodal Imaging (CMI) in biological and preclinical research**. To achieve this inherently interdisciplinary goal, it is indispensable to **establish a collaborative network of scientists across disciplines from both academia and industry** to foster and market CMI as a versatile tool in biomedical research.

CMI gathers information from a specimen with two or more modalities that – when combined – create a highly informative, composite view of the sample. It is a holistic approach that spans the entire resolution range from nano- to millimetres, and provides complementary information about structure, function, dynamics and molecular composition of the sample. CMI is the only way to understand cells, cellular networks, organisms and diseases mechanistically by deciphering their molecular mechanisms within their native context. So far, CMI strategies mainly focus on combining two modalities[1]. The two most prevalent examples are hardware-fused platforms in (Pre)clinical Hybrid Imaging (PHI) [2], or Correlated Light and Electron Microscopy (CLEM) in biological imaging [3]. Preclinical imaging refers to the visualization of living small animals and molecular processes *in vivo*; biological imaging (largely microscopy) to the *ex-vivo* visualization of molecular processes, cells, cellular networks or tissues. Currently, there is hardly any CMI approach bridging biological and preclinical imaging. Even though the merits of PHI and CLEM are well established, they still lack standardized protocols, terminologies and data handling, and leave room for optimization and the development of advanced implementations. Besides CLEM and PHI, there is a large variety of other CMI combinations, which can reveal priceless information when combined properly. The **1st challenge** of the Action is **to reveal this so far unexploited potential of CMI towards a practical use in biomedical research and thereby combine biological and preclinical imaging** – with synergetic benefits for medicine including increased diagnostic accuracy or precise monitoring of interventional procedures.

Progress in CMI requires optimizing and standardizing existing pipelines, and triggering the development of novel pipelines in showcase projects across a broad range of disciplines. In this challenge, PHI and CLEM will be optimized and used as starting points to boost further CMI pipelines including other or more than two modalities. It is difficult for a user to keep track and have access to the many existing sophisticated imaging modalities, which would be necessary before they can combine these techniques to answer specific research questions. Collaborations in CMI seem to be particularly rare since they require researchers of diverse scientific backgrounds, including structural, cell and developmental biologists, physicists, chemists, physicians, engineers and computer scientists. Besides, no single research group is likely to host several imaging platforms as necessary for CMI. The progress of CMI in biomedical research also depends on readily accessible commercial solutions, of which there are only few. These implementations need to focus on promising approaches as defined by user needs. The **2nd challenge** is consequently **to facilitate knowledge exchange across disciplines in academia** and **technology transfer from academia to industry.** Dedicated showcases studies, Short-Term Scientific Missions (STSMs) and round tables including business representatives will promote instrument development and optimization. This will foster novel biomedical research and trigger patents, marketable products and diagnostic applications.

To enable CMI's future development and further exploitation**, the Action's 3rd challenge** is defined **to raise awareness for the benefits of correlation and attract and educate the next generation of scientists in CMI approaches**, thus guiding the scientific mindset from isolated single-technique approaches towards integrative approaches and mechanistic analysis of diseases and organisms.

Importantly, both instrument developers and users will be trained and encouraged to develop a better understanding about specificities and limitations of imaging modalities.

1.1.2. RELEVANCE AND TIMELINESS

CMI integrates the best features of the combined techniques and overcomes limitations that would be faced when applying the single modalities independently. Any single imaging modality is not sufficient to comprehensively illustrate the inner working of a cell, cellular networks or organisms. CMI allows biological processes to be studied within their overall spatio-temporal context, and pathologies and diseases can be targeted down to an individual cell and underlying molecular events. Additionally, the application of combined techniques to the same region of interest allows conclusions from a single modality to be validated since each technique can provide unique information based on fundamentally different contrast mechanisms. Imaging with single modalities comes with three main limitations: (1) Either the sample is imaged at high resolution which visualizes the details of the cell while losing contextual information, or a large field-of-view is analysed at low magnification which provides an overview and tissue context, but restricts localization. (2) High lateral resolution usually comes at the expense of penetration depths in the third dimension and hence restricts 3D in-vivo imaging. (3) A single modality usually provides either structural (anatomical) or functional (metabolic) information. All this can be overcome by CMI: PHI and CLEM, for example, provide both functional and structural information. CLEM gathers spatial and temporal information about a specific molecule within its ultrastructural context and can achieve near-atomic resolution within a broad field-of-view.

While the benefits of CLEM are increasingly being recognized in the life science community, there are further correlative combinations that will broaden the accessible biomedical information significantly. Identifying and fostering existing and novel CMI pipelines, including requirements concerning sample preparation, probes, software and hardware relocation procedures and visualization tools, will have a huge impact on data generation and analysis in life sciences. A collaborative interdisciplinary network to foster these developments is hence very much needed and to great advantage to the biomedical community with applications in basic and (pre)clinical research.

COMULIS is in line with major changes occurring in the imaging sector. It complements recent developments whilst paving the way for a powerful novel field of imaging and analysis. The emergence of novel microscopy techniques and ancillary tools has given imaging technology a major boost: Super-resolution allows biological processes to be observed well below the diffraction limit (Nobel Prize in Chemistry in 2014), new camera technology enables unprecedented resolution in EM, and novel imaging techniques, such as Brillouin Microscopy, are being translated into the field of life sciences. Various European initiatives are promoting the use of imaging techniques, such as Euro-BioImaging (EuBI) or NEUBIAS. Nevertheless, the appearance of increasingly sophisticated imaging instruments makes it complicated for the user to decide which imaging technique is best suited to answer his or her question since emerging modalities are highly specialized and cover only specific niches in the life science sector. This is the right time to leverage CMI through a multidisciplinary dialogue and combine these highly specialized technologies into readily accessible imaging pipelines to tackle biomedical questions holistically. To the knowledge of the network, there is currently no dedicated community or platform to advance CMI, which is why this COST Action is necessary.

1.2. OBJECTIVES

1.2.1. RESEARCH COORDINATION OBJECTIVES

The main objective of this COST Action is to foster CMI by creating synergies between the inherently diverse scientific expertise that is needed for its advancement in the life sciences. In the following, global objectives of the Action are defined accordingly – and go in hand with the specific, continuously reviewed objectives for the individual Working Groups (WGs):

(1) Establish a European network of diverse expertise and provide a platform for knowledge transfer in life sciences. The network will be used by the active CMI research community both for exchange of information and test samples. This is crucial since particularly physics- or engineering-trained instrument developers lack accessibility to relevant biomedical samples or even biomedical research questions. Exchange will be facilitated via the COMULIS website. The network will also serve as a first contact point for all researchers from any background interested in CMI. **(2) Trigger the implementation and further development of CMI in life sciences by bringing together instrument**

users and developers, and by bridging biological and preclinical imaging. This aims at identifying and showcasing new CMI imaging pipelines to address unanswered biomedical research questions and promote their benefits. **(3) Evaluate and standardize existing approaches** and assess their transferability to novel CMI pipelines. Implementations will be assessed in terms of versatility and compatibility. Correlative approaches may vary in their implementation and are often based on custom-developed preparation, acquisition and analysis protocols, aspects of which might not be optimal for the specific research question. Establishing representative protocols and quality standards will encourage scientists interested in CMI to optimize their experiments. A CMI database will be set up to describe CMI implementations and recommended protocols, correlative probes, correlation software and contact details of experts. **(4) Trigger marketable products and facilitate technology transfer between Academia and Industry**. Potential industrial implementations rely on constant dialogue and knowledge exchange between users and instrument developers from both academia and industry, and between physical and life scientists. Prerequisite for such commercial solutions is the recognition of CMI as a versatile tool by life scientists. Implementations might include hybrid imaging systems, similar to PET/CT (Positron-Emission-Tomography/Computed Tomography), ancillary tools to facilitate compatible sample preparation or sample relocation between imaging modalities, or software solutions to identify the same region of interest across imaging platforms and to visualize the data. **(5) Raise awareness of CMI** and its numerous benefits in the life science community and general public according to the dissemination & exploitation plan.

1.2.2. CAPACITY-BUILDING OBJECTIVES

Extending CMI towards new applications in biomedical research will boost European research competitiveness in the field of imaging technologies. Bringing together scientists of diverse disciplines to establish a CMI community will be a crucial step to exploit the immense potential of this promising technology and work on its further development. Capacity building objectives therefore aim at unifying scattered attempts at CMI development, building up collaborations, fostering exchange of knowledge and best practices, and facilitating education and exchange of personnel for joint projects across various disciplines:
(1) Boost the use of CMI by setting up CMI communication channels and establishing a website and database for CMI approaches. This database will include a synopsis of successfully implemented CMI showcases, used correlative probes, detailed sample preparation protocols and available correlation software. Contact names and CMI laboratories will be listed, and further links will provide open access to custom-developed correlation software. The website will allow the coordination of STSMs and sample exchange. There will be an online forum to discuss technical problems and provide advice from scientists from different disciplines about the feasibility of planned CMI developments. The website will also be used to inform interested scientists about CMI and the limits and opportunities of accessible imaging techniques. **(2) Facilitate staff exchanges through STSMs**. Due to the fast-evolving imaging field and highly advanced imaging setups that take several months or even years to master, researchers tend to be highly skilled only at one imaging technique. For a holistic approach, imaging techniques need to be interconnected and their range of application need to be better understood. STSMs will specifically target Early Career Investigators (ECI) to provide them with the necessary skill set to judge feasibility and practical implementation of CMI approaches beyond their technical imaging knowledge. **(3) Establish long-term collaborations among COMULIS participants.** These collaborations will be integral to the advancement of CMI since no research group alone can meet all the technical and cross-disciplinary challenges in the development of CMI setups. Specifically, these collaborations should bring together instrument developers with technical or computational skills and users with thrilling biomedical research questions which are best tackled with CMI. **(4) Facilitate knowledge transfer among CMI experts, ECIs and industry through conferences, meetings, training schools and STSMs.** These activities will involve hands-on experiences and information exchange on novel CMI strategies and the optimization of current approaches. Conferences will also host pre-courses about the basics of specific imaging techniques, image processing or biomedical research, that are specifically designed to give an overview to researchers from diverse disciplines.

1.3. PROGRESS BEYOND THE STATE-OF-THE-ART AND INNOVATION POTENTIAL

1.3.1. DESCRIPTION OF THE STATE-OF-THE-ART

CMI's use of two or more imaging techniques to gain structural/anatomical, functional/molecular, dynamical and chemical knowledge from the same sample across multiple scales makes it particularly well suited to tackle the intricate questions arising in modern biological and biomedical research. COMULIS specifically focuses on CMI for preclinical and biological research. There are two prominent examples within each of these areas: PHI and CLEM. In PHI, two complementary imaging modalities are fused within a single setup. For example, PET/CT or PET/MRI (Magnetic Resonance Imaging) enable co-registered functional (from PET) and structural information (from CT or MRI) within a single study. PHI serves as a valuable diagnostic tool and research platform that can reveal molecular processes and biochemical pathways in living animals noninvasively within the structural context, providing *in-vivo* insights into cancer biology or angiogenesis [4]. CLEM describes the combination of light microscopy (LM) and electron microscopy (EM) and also combines functional with structural information from a singular biological event. In CLEM, LM is also used to identify areas of interest for subsequent ultrastructural analysis with EM. It has become the method of choice to target rare and specific processes within tissues or cell lines, and has been used to study cell division, signalling, viral infections or membrane trafficking [5]. Both PHI and CLEM lack standardized procedures, protocols and data handling, although PHI has several commercial implementations (e.g. PET/CT or PET/MRI) and CLEM is becoming accessible with first commercial tools and software to assist with sample relocation between microscopes or image correlation. Recent major developments in both EM and LM will lead to further beneficial combinations of both modalities, but have only started to appear in scattered proof-of-concept studies.

Recently, other combinations of microscopy techniques have been described in the research literature. Examples of these prototypes include the correlation of Atomic Force Microscopy (AFM) with LM to study the dynamics in macrophages, combinations of super-resolution microscopy with AFM, and X-ray tomography with LM to localize specific proteins within their native ultrastructural context [6,7,8]. CMI pipelines with more than two modalities are in their infancy due to lack of access and the broad expertise required to oversee several modalities. One recent example combines intravital microscopy, CT and EM to study single tumour cells in the cerebral vasculature [9].

1.3.2. PROGRESS BEYOND THE STATE-OF-THE-ART

Although some CMI approaches have been established (CLEM and PHI) or are being developed, there is great need for further standardization, optimization and automation of existing approaches and the identification and development of novel imaging pipelines and applications. COMULIS will lead to substantial progress beyond the state-of-the-art since it brings together all relevant multidisciplinary stakeholders and establishes a concerted effort between them, which will boost method development and enthusiasm about CMI. Methodologies and protocols for PHI and CLEM will be optimized, providing reference points, from which novel CMI combinations that bridge biological and preclinical imaging will be identified and initiated. Novel CMI implementations will be assessed against feasibility, benefits and application range. CMI pipelines will need to identify, optimize, trigger and evaluate (1) sample preparation procedures that are compatible with various imaging modalities without compromising data quality, (2) correlative probes and fiducial markers that can be visualized in different imaging technologies, (3) hardware and software solutions to find the same region after relocation between imaging platforms, (4) software solutions to co-align data from different modalities, and (5) concepts for data handling and storage.

The identification and showcasing of novel CMI pipelines broadens the range of accessible research in life sciences and contributes to significant biomedical and social advancements. Newly identified pipelines will allow novel applications and studies to address fundamental biological questions, cancer biology, or drug development and eventually will lead to improved disease diagnostics and monitoring. CMI pipelines will specifically target multimodal approaches that span the resolution range from small animals down to cellular or molecular structures.

Showcasing novel pipelines and optimizing existing approaches will raise the interest of companies as an integral part of this Action. This network will foster commercialization of promising CMI setups. The developments will streamline CMI by triggering integrated setups that do not require relocation of the specimen between imaging platforms. This will greatly increase the practical availability of CMI since

research groups would not need to go through tedious and time-consuming method optimizations, but could directly address their research question with readily available CMI setups.

COMULIS will also trigger computational advancements and big data strategies to correlate and handle volumetric image data from different modalities. The development of approaches for automated feature segmentation, visualization and exploration of complex, time-varying, multiscale, multimodal data volumes can only be successfully achieved by involving computer scientists in the network and establishing an efficient dialogue between them and life scientists. The Action will also introduce data standards and ontologies to facilitate the merging of different imaging modalities. The increase in CMI pipelines will drive a rise in the development of computational tools to zoom in from single cells (or even whole organisms) to individual cellular structures.

In summary, this Action will help to transform CMI from a niche technique to a versatile tool with great benefits and a multitude of applications in life sciences and biomedical research.

1.3.3. INNOVATION IN TACKLING THE CHALLENGE

The challenge is tackled innovatively by opening novel communication channels and development tracks towards novel imaging technology and prototypes – based on collaborative efforts of various disciplines: **(1)** Technological progress will be driven by user needs and challenges posed by biological and biomedical research questions. Developments will be kept up in track by constant user feedback by life scientists during conferences and other meetings within the Action. **(2)** Based on identified WGs, progress is triggered in several areas in parallel (CLEM, PHI, correlation across biological and preclinical imaging, correlation software) while they are interconnected through overlapping tasks and ongoing communication. **(3)** Developments will be sparked bidirectionally: From academia to industry via technology transfer, expertise exchange and showcase projects; from industry to academia via translational collaborations and prototype testing. **(4)** Fertile and unique contacts between life scientists, imaging scientists and instrument manufacturers will be established throughout the development cycle to ensure its best possible implementation. Feedback will be given already at an early stage, and showcase projects will be evaluated after their completion.

The processes of conceptualization of CMI technologies triggered by this network are unprecedented. The main pillars of these developments are: transnational interdisciplinary showcase projects, sharing of imaging platforms, and annual WG meetings to identify and evaluate these proof-of-concept studies. Open databases and repositories provide the necessary framework to judge the innovation potential of envisioned pipelines and associated prototypes.

Further innovation originates from the training schemes that will be applied during educational events (CMI conferences and training schools), including pre-courses about the basics of specific imaging techniques, image processing or hot topics in life sciences. These pre-courses will be specifically designed for non-specialists from diverse scientific disciplines, give an overview of the chosen topic, and will be essential for a better mutual scientific understanding during the conference.

1.4. ADDED VALUE OF NETWORKING

1.4.1. IN RELATION TO THE CHALLENGE

COMULIS aims to promote CMI as a versatile approach in life sciences by bringing together the diverse scientific community. This aim can only be achieved through networking and knowledge exchange. Concerted efforts and networking become indispensable to combine and integrate the requisite CMI knowledge from all relevant disciplines, such as optics, engineering, physics, chemistry, biology, medicine and computer science.

Research groups applying CMI usually rely on custom-developed implementations and protocols that need optimization and standardization. Networking and open exchange will trigger information exchange of optimal implementations and help to establish best practices and quality standards. Open exchange and training schools will promote knowledge about the strengths and weaknesses of each imaging technique. In this context, a valuable knowledge base and web platform compiling and explaining accessible imaging techniques and feasible correlative studies will be set up for the interested scientific community.

To increase CMI availability, this network will integrate the efforts of leading imaging companies and raising start-ups. By involving all relevant stakeholders, this network will allow knowledge transfer from academia to industry (and vice versa) and trigger marketable CMI products or pipelines.

1.4.2. IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

Imaging in life sciences is currently experiencing a real boom. This is driven by major technological progress, such as the advent of super-resolution microscopy, and by joint collaborative efforts to promote imaging in Europe. In this context, EuBI constitutes an important initiative to provide open access, service and training for European scientists to state-of-the-art imaging technologies. EuBI triggered the foundation of national BioImaging initiatives in most of the European countries which aim at promoting their national imaging research infrastructure. The need for consolidating imaging activities at EU level is also evidenced by the support given by the European Commission in Horizon 2020 with the call 'Fostering co-innovation for future detection and imaging technologies'. Despite these concerted efforts, there is currently no European network that focuses specifically on CMI. Establishing such a CMI network, seeing current imaging developments in a broader context independent of scientific background, and correlating imaging approaches to form a novel, more versatile technique is hence crucial to reach the next level of truly holistic analysis.

COMULIS will organize international meetings and training schools with the sole focus on CMI and complement existing workshops (mainly on CLEM) or sessions within imaging conferences. Satellite meetings will be organized in the framework of international conferences (such as European Light Microscopy Initiative Meetings, European Molecular Imaging Meetings, European Microscopy Congress, or Biophysical Society Annual Meetings).

COMULIS will collaborate closely with other COST Actions that aim at promoting bioimage analysis (NEUBIAS) or at using imaging technologies to advance specific research fields, such as cellular structural networks (EuroCellNet) or forensic science (MULTI-FORESEE). The mentioned activities strive to promote imaging for the benefits of life sciences, but none specifically targets CMI and aims at correlative method development and novel imaging methodologies.

2. IMPACT

2.1. EXPECTED IMPACT

2.1.1. SHORT-TERM AND LONG-TERM SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS

The outstanding feature of this Action is its extensive multidisciplinarity that brings together experts from different scientific disciplines. This fact itself increases COMULIS' impact significantly as the Action will bring innovation and new impulses into many fields of science and businesses:

Short-term scientific and technological impact: **(1)** The Action will allow all participating researchers to better understand the requirements and potential of their CMI methodologies and protocols, and foster a common approach to practical expectations of CMI. **(2)** Networking will minimize ineffective experimental duplications and time losses. Development of standardized ontologies and best practices for CMI will be beneficial both for future users and for instrument developers including private manufacturers, and speed up their efforts. **(3)** Coordinated efforts will yield accelerated development of CMI instrumentation and applications. Networking between instrument developers and scientists across disciplines is crucial to identify showcase projects and key applications which will become the focus of further grant applications. **(4)** Coordinating distributed and parallel studies between different labs helps to validate novel and existing CMI pipelines. **(5)** The implementation and optimization of CMI provides answers to intricate biomedical research questions with unprecedented information content. **(6)** Positions for undergraduates, PhDs and postdocs will be generated via joint grant applications stimulated by COMULIS, which will introduce CMI to ECIs and encourage the infusion of fresh ideas.

Short-term socio-economic impact: Although the impact is primarily on exchanging ideas and good practices and advancing novel CMI implementations, the short-term impacts will include **(1)** enabling a new generation of scientists to come together and receive training in CMI and corresponding career development, and **(2)** creating a platform where all relevant stakeholders are directly involved, generating opportunities for growth through identified CMI pipelines and stimulating further grant

proposals to support validation and novel implementations. **(3)** A platform giving industrial partners access to scientific discoveries will lead to expedited development of marketable products and filing of patent applications.

Long-term scientific and technological impact: (1) Bringing together all the players in CMI will help introduce international standards and norms, and stimulate its long-term evolution towards a readily accessible, reliable and routine tool in biological and biomedical research. **(2)** Introducing this novel methodology will increase biomedical knowledge and research output in life sciences. **(3)** The Action will have an overall impact on the European scientific community by becoming the main source of knowledge on CMI. It will improve visibility of the involved parties worldwide. **(4)** Support of ECIs will yield the next generation of CMI experts who will continue working on the development of CMI for life sciences and clinical applications. **(5)** Long-term collaborations among involved players will be generated, maximizing the coordinated development of CMI and paving the way for leveraging European funds in joint European research and development projects.

Long-term socio-economic impact: **(1)** In the future, development of CMI towards clinical use beyond biological and preclinical research will have a general impact on improving public health through novel diagnostics and treatments of diverse medical conditions. CMI has a variety of potential applications in basic research, drug development, cancer, neurodegenerative diseases and aging. **(2)** Applying CMI in clinical diagnostics will introduce a novel methodology that will foster cross-disciplinary and cross-departmental exchange between clinicians and scientists and provide improved diagnostic approaches. **(3)** The Action has potential to create spin-off companies for the development of research- and diagnostic-grade CMI instrumentation and software, as well as service-orientated companies offering biomedical analysis. **(4)** European countries will be involved in COMULIS on a pathway to mutual development and concerted growth. **(5)** Knowledge transfer among top European imaging laboratories and Inclusiveness Target Countries (ITC) countries will help to decrease disparities between European countries in the field of imaging technologies.

2.2. MEASURES TO MAXIMISE IMPACT

2.2.1. PLAN FOR INVOLVING THE MOST RELEVANT STAKEHOLDERS

The relevant stakeholders are instrumentation developers, instrumentation users, industry, students and ECIs and general public:

(1) End Users & Life science Experts: Life scientists will be the driving force behind CMI method development and novel applications. They include biologists and clinicians that are active across the fields of biological and biomedical research. Method development will be driven by their user needs. They will identify showcase projects in joint round tables of current relevance to biomedical research and assess the significance and real-world feasibility of CMI methodologies. Beyond the scope of the current Action, in the long term, clinicians will also benefit from novel CMI implementations for improved disease diagnostics and treatments. **(2) Instrument Developers & Experts**: Imaging experts will provide input for CMI method development and the implementation of showcase projects in close collaboration with life scientists. They comprise physicists, medical and software engineers, and computer scientists, and experts in microscopy and preclinical imaging techniques. Importantly, this also includes computer scientists for data correlation and handling. Beside this network, an Action website will be published with an interactive platform for ideas exchange, troubleshooting, and experience sharing. Dedicated events as described in the Dissemination plan will attract scientists to get the newest knowledge on CMI developments and its applications. **(3) Industry**: Several instrumentation manufacturers and software start-ups interested in novel CMI pipelines and data handling, which will be used for conceptualization of marketable CMI solutions will be involved in the Action. Besides, round tables with selected industry representatives will be held with the goal to make them aware of these new market opportunities. Companies are expected to benefit most significantly in the medium and long term. **(4) Students and ECIs**: The clear short-term benefits for this group will be the opportunity to participate in various events organized by COMULIS including STSMs, which will enable them to work at the most prestigious European laboratories and get unique expertise in an emerging scientific field across various imaging setups. In the long term, a positive impact on their careers through knowledge gain and work in multicultural research teams is envisaged. They are expected to be the new generation of CMI developers with the best prerequisites to promote CMI in the future.

2.2.2. DISSEMINATION AND/OR EXPLOITATION PLAN

Dissemination is an essential part of the Action. To ensure that all activities will be carried out in a timely and effective manner, one of the Management Committee (MC) members will be appointed as **Dissemination Coordinator**. The first task will be to set up a dissemination plan with a set of guidelines where duties of the Action participants are listed:

Action identity: An Action design (logo, presentation, poster, and report templates) will be established by the Dissemination Coordinator. **Action website**: The page will be crucial and will offer open-access to databases and correlation software, a discussion platform and a porthole for organizing joint projects and staff exchanges. It will also compile information about CMI projects and details of imaging techniques. To keep the website updated and to avoid doubled information, one of the MC members will be voted as **Website coordinator** at the first MC meeting of the Action. His/her role will be the creation and regular update of the website. S/he will be responsible for a constant collection of input from all Action members and for communication with other stakeholders which will happen via the website. Target group: Scientific community, industry, students, ECIs, general public. **Scientific publications**: Each WG will produce 1 – 2 scientific publications and/or reviews, targeting imaging experts, computer scientists and/or the life science community. They will be published either in open-access peer-reviewed journals or green open-access will be secured. All scientific publications will be published also on the Action website. No of publications: ~10. **Annual CMI conferences** (2-3 days): All WGs will meet and assess their achievements against the defined work plan. Planning of further activities, mutual discussion and personal meetings will be essential parts of the conferences. A part of the conference will be devoted to the talks of invited speakers – top experts in various fields of life sciences, imaging and CMI. The conferences will be connected to the meetings of MC, pre-courses and round tables with industrial partners to effectively leverage travel costs. Target group: Scientific community, industry, students, ECIs. No of conferences: 4. **Round tables**: To foster synergies and mutually beneficial, constructive interactions with the imaging industry, annual round tables (starting in the 2nd year of the Action) will be organized to conceptualize exploitable technology based on identified promising pipelines and running showcase projects. Based on this round-table discussion, joint development of prototypes will be initiated. Target group: Scientific community, industry. No of round tables: 3. **Press releases**: At least two press releases in the course of the Action will be published. Target group: General public. **Open days**: Four open days at different locations will be organized in the course of the Action. These events will be aimed at students with diverse backgrounds and end users. Open days will be organized in connection to other Action networking events to leverage funds in the most effective way. Target group: Students, end users. **Social media**: Regular contributions to social media (min. 2x monthly) will be done by the Dissemination Coordinator. Target group: Scientific community, general public. **Publication of popular-science articles aimed at lay audiences**: There will be at least two in the Action course. Target group: General public.

2.3. POTENTIAL FOR INNOVATION VERSUS RISK LEVEL

2.3.1. POTENTIAL FOR SCIENTIFIC, TECHNOLOGICAL AND/OR SOCIOECONOMIC INNOVATION BREAKTHROUGHS

COMULIS will deliver several technological breakthroughs that will directly increase scientific output in biomedical research. The Action will establish gold standards in CLEM and PHI, avoid redundancies, and trigger novel CMI pipelines, prototypes and intellectual property in close collaborations with industrial partners. Risks for industrial partners will be minimized by agreeing strategies for protecting intellectual property arising from showcase projects to fuel a fruitful and trusting dialogue between academia and industry. Showcase projects are stimulated and risks are minimized by including instrument developers and users from diverse scientific disciplines. Exploitable concepts are expected to include hybrid systems with two or more hardware-fused imaging modalities, ancillary equipment to facilitate sample relocation or preparation, correlative probes, correlation software, as well as recommendations for best practice for users. These technological advancements will directly impact life sciences in all European countries: **(1)** The developments will encourage a progressive mindset that boosts integrative and holistic approaches. It will establish a fruitful dialogue and communication channels across diverse scientific disciplines and help to bridge the gap between biological and preclinical imaging. **(2)** Implementing CMI will expand the available spectrum of relevant methodologies in life sciences, transforming the study of biomedical processes by providing unprecedented information content. **(3)** Holistic approaches help researchers to discover molecular interdependencies over a wide

range of temporal and spatial scales and foster the study of cellular and molecular processes within their native context. This will significantly increase the understanding of biological and biomedical processes.

Progress in biomedical methodologies and research provides benefits for the European society by improving our understanding of organisms and diseases, yielding better diagnostics and treatments. Marketable prototypes will be beneficial for European imaging and software companies. Industries will gain valuable insights into state-of-the-art knowledge and user needs. This allows them to develop their portfolio and increase competitiveness, which boosts European economy and fosters its technological excellence in innovative imaging technologies.

3.IMPLEMENTATION

3.1. DESCRIPTION OF THE WORK PLAN

3.1.1. DESCRIPTION OF WORKING GROUPS

The Working Groups (WGs) are organized as outlined below: Establishing standards and optimizing CMI approaches in biological and preclinical imaging with a focus on CLEM and PHI as the best-established technologies in each area, and using these implementations as demonstrator technologies to showcase the wider benefits of CMI to the life science community **(WG1 & 2)**; Triggering novel CMI implementations of modalities that have not been correlated before, thereby bridging the gap between biological and preclinical imaging **(WG3)**; Involving all relevant scientific disciplines including software developers for input on image data handling and analysis **(WG4)**; Fostering recognition of CMI and promote its benefits in life sciences via dissemination, training and networking **(WG5)**.

Approaches to achieving the objectives defined for WGs 1- 4 follow the same principles: **(1)** Current knowledge and successfully established CMI pipelines will be compiled in **repositories and databases** in close collaboration with WG5 to help standardize and optimize CMI approaches, and to identify promising novel implementations. Repositories will include specifics about involved imaging technologies, sample preparation, acquisition protocols, and tackled research questions. **(2) Proof-of-principle studies and showcase projects** will be triggered to assess the feasibility and application range of novel CMI pipelines. These collaborations will be driven by biomedical research questions of participating life scientists and implemented via STSMs and available internal funding. Projects will be selected and evaluated in annual WG meetings based on the joint efforts of instrument developers and users. During these meetings, additional financing strategies and grant applications will be identified. **(3)** Marketable CMI technology, correlation software and ancillary tools will be identified and triggered. **Annual round-tables between industrial representatives and academia** will be organized to conceptualize exploitable technology based on identified promising pipelines and running showcase projects. Based on these round-table discussions, joint development of prototypes will be initiated. These prototypes can be the implementation of novel CMI imaging systems, ancillary tools or software solutions for data visualization and correlation.

WG 1: CLEM

Objectives: Develop CLEM as a CMI case study, set up CLEM standards, and trigger novel CLEM approaches through best practices. These standards and developments will foster the recognition of CLEM in life sciences and serve as reference points for other CMI approaches.

Tasks (T) & Deliverables (D): T1.1: Identify gold standards and best practices for CLEM, and pinpoint other successful biological CMI approaches. **D1.1**: Repository and database for CLEM and other biological CMI approaches (Month 6). **T1.2**: Optimize CLEM procedures concerning sample preparation, relocation between imaging platforms, and correlative probes. The Action will identify bottlenecks in all three steps based on compiled databases in annual WG meetings, and set up collaborative projects to overcome these bottlenecks, exchanging tools, probes and samples where needed. **D1.2**: Platform for exchange of samples and correlative probes to test their CLEM viability in different settings (M9). **D1.3**: Criteria to assess CLEM optimizations (M9,22). **D1.4**: Report on selected small collaborative projects to overcome CLEM bottlenecks (M20,37). These projects will be selected in annual WG meetings and implemented via STSMs. **D1.5**: Scientific publications (M48). **T1.3**: Trigger novel approaches in CLEM showcase projects. **D1.6:** List of joint research question to be tackled using novel CLEM approaches arising from the compiled repository (M7). **D1.7**: Criteria for evaluation of obtained results (M9,22). **D1.8**: Report on implemented proof-of-principle experiments and showcase projects (M20,37). **D1.9**: Scientific publications (M48). **T1.4**: Identify available correlation software for CLEM and other biological CMI

approaches. **D1.10**: Compiled database with existing CMI software in biological imaging and its working principles in close collaboration with WG4 (M6). **T1.5**: Promote CLEM in life sciences and train next-generation scientists. **D1.11**: Report on CLEM training schools (4) and STSMs with focus on established approaches (M22, 45). **T1.6**: Trigger marketable CLEM technology in round tables. **D1.12**: Minutes of round tables (M25,37,48). **D1.13**: Report on initiated prototype development (M48).

Milestones (M): M1.1: Annual WG meetings (4) to coordinate implementation strategies and monitor progress on deliverables and CLEM advancements. **M1.2**: Repository of current and novel CLEM workflows and protocols in online database. **M1.4**: STSMs (several per year) specifically between EM and LM laboratories and particularly for ECIs and PIs. **M1.5:** Round-tables (3) between industrial representatives and academia on marketable CLEM concepts and tools.

WG 2: PHI

Objectives: Standardize existing and trigger novel PHI approaches through best practices; promote PHI and its benefits as a reference point for other CMI approaches.

T2.1: Identify gold standards and bottlenecks (specifically for data handling) in current PHI implementations. **D2.1**: Repository and database for PHI and other preclinical CMI approaches (M6). **T2.2**: Trigger novel PHI approaches in showcase projects. **D2.2:** List of joint research question to be tackled (M7). **D2.3**: Criteria for evaluation of obtained results (M9,22). **D2.4**: Report on implemented proof-of-principle experiments and showcase projects (M20,37). **D2.5**: Scientific publications (M48). **T2.3**: Identify existing correlation & visualization software for preclinical imaging. **D2.6**: Compiled database with existing open-access and commercial correlation software and working principles in close collaboration with WG4 (M6). **T2.4**: Promote PHI approaches specifically among biologists and train next-generation scientists. 2 PHI training schools will be organized along with several STSMs. **D2.7**: Report on preclinical CMI training schools (2) and STSMs with focus on established approaches (M22, 45). **T2.5**: Trigger marketable PHI technology in round tables. **D2.8**: Minutes of round tables (M25,37,48). **D2.9**: Report on initiated prototype development (M48).

M2.1: Annual WG meetings (4) to coordinate implementation strategies and monitor progress on deliverables and advancements in PHI. **M2.2**: Repository of current and novel PHI workflows, technologies and protocols in preclinical imaging. **M2.4**: STSMs (several per year) specifically in preclinical imaging laboratories and particularly for ECIs and PIs. **M2.5:** Round-tables (3) between industrial representatives and academia on marketable PHI concepts and tools.

WG 3: Novel CMI Pipelines

Objectives: Trigger novel CMI approaches beyond CLEM and PHI, and bridge biological and preclinical imaging. The WG aims at working towards the recognition of CMI as a versatile tool in biomedical research.

T3.1: Identify existing CMI approaches that specifically combine biological and preclinical imaging. **D3.1**: Repository and database for current CMI approaches with both microscopy and preclinical imaging technologies (M6). **T3.2**: Trigger novel approaches in showcase projects for biological or preclinical CMI modalities that have not been correlated before in life sciences in close collaboration with WG1 & 2. **D3.2:** List of joint research question to be tackled using novel CMI combinations (M7). **D3.3**: Criteria for evaluation of obtained results (M9,22) **D3.4**: Report on implemented showcase projects, assessing feasibility, informational content and accuracy (M20,37). **D3.5**: Scientific publications (M48). **T3.3**: Combine and bridge specifically biological and preclinical imaging in showcase projects. **D3.6**: List of selected joint projects to be implemented through STSMs (M7). **D3.7**: Report on implementation and results of joint projects (M20,37). **D3.8**: Scientific publications (M48). **T3.4**: Identify correlation software for CMI pipelines combining biological and preclinical imaging in close collaboration with WG4. **D3.9**: Compiled database of existing software and working principles (M6). **T3.5**: Promote CMI and raise awareness for its benefits among life scientists. The novel CMI developments will be presented at conferences (4) and training schools (2). **D3.10**: Proceedings of the CMI conference (M13,25,37,48). **D3.11**: Report on 2 training schools and STSMs (M22, 45). **D3.12**: Scientific publications (M48). **T3.6**: Trigger marketable novel CMI technology for both preclinical and biological imaging (and their combination) beyond CLEM and PHI. **D3.13**: Minutes of round tables (M25,37,48). **D3.14**: Report on initiated prototype development (M48).

M3.1: Annual WG meetings (4) to coordinate implementation strategies and monitor progress on deliverables and developments in CMI beyond CLEM and PHI. **M3.2**: Repository of current and novel CMI workflows and protocols that bridge biological and preclinical imaging. **M3.2:** CMI conferences (4). **M2.4**: STSMs (several per year) particularly for ECIs and PIs. **M3.7:** Round-tables (3) between industrial representatives and academia on marketable CMI concepts beyond CLEM and PHI.

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WG 4: Correlation Software

Objectives: Improve and develop concerted software solutions for image correlation and visualization of multimodal data sets. The WG will work closely together with WG1-3 which will compile existing software solutions for their specific field of application.

T4.1: Exchange and update compilations of correlation software with WG1-3. Joint software meetings with WG1-3 will be organized in the first year to exchange information and databases about available correlation software. They will be classified into 3 categories: (1) visualization of multimodal data sets, (2) automated segmentation, and (3) registration of multimodal data sets**. D4.1**: Minutes of the joint software meeting (M9). **D4.2**: Publication of review (M48). **T4.2**: Trigger correlation software development in all three categories via showcase projects implemented through STSMs. Main players in each category will be identified. Most powerful correlation software for each category will be selected. Multimodal data sets from showcase projects from WG1-3 will be available through open access and correlated with identified correlation software. **D4.3**: Report on strategy meeting with the identified main players (M22). **D4.4**: Criteria list for evaluation of obtained results (M22). **D4.5**: Report on results obtained by the selected software and proposed improvements (M29,44). **D4.6**: Scientific publications (M48). **T4.3**: Identify solutions to share large multimodal image data sets. **D4.7**: List of minimum requirements for sharing platforms (M9). **D4.8**: Compilation of existing solutions and identification of best suited implementations (M12). **T4.4**: Trigger marketable software solutions. **D4.9**: Minutes of the round tables (M25,37,48). **D4.10**: Report on initiated solutions (M48).

M4.1: Annual WG meetings (4) to coordinate implementation strategies and monitor progress on deliverables and software developments. **M4.2**: Joint software meeting between this WG and WG1-3 for exchange of available correlation software and sharing platforms. **M4.3**: Strategy meeting between main players in multimodal data visualization, segmentation and correlation. **M4.4**: STSMs (several per year) particularly for ECIs and PIs. **M4.5:** Round-tables (3) between industrial representatives and academia on marketable CMI software concepts.

WG 5: Outreach, Dissemination & Partnerships

Objectives: Foster the recognition of CMI in life sciences as a versatile tool for holistic analyses. Recognition of CMI by all stakeholders is indispensable for its further development, use and boost of European competitiveness in the field of imaging technologies. Synergies between CMI and existing imaging-related communities will be created, including other COST Actions (e.g. NEUBIAS), ESFRI research infrastructures (Euro-BioImaging, ELIXIR, INSTRUCT), and imaging meetings and societies (ELMI, EMIM, Biophysical Society). Dissemination of scientific results will be achieved through peer-reviewed publications whose publication is a part of each WG.

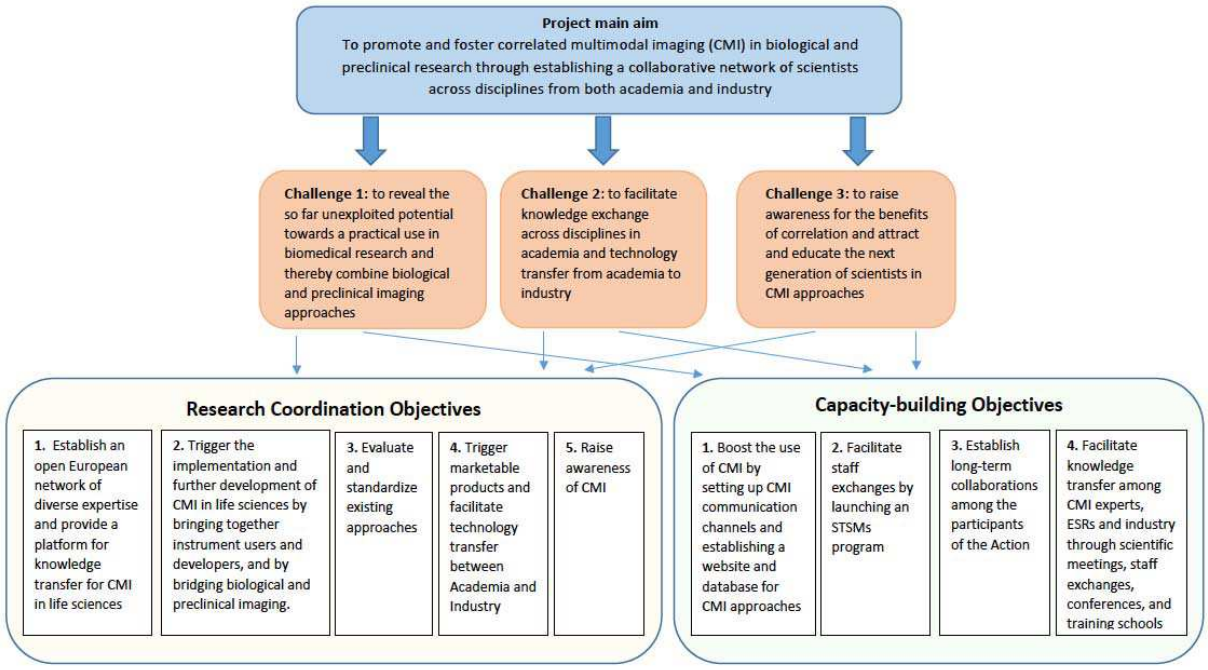
T5.1: Set up the COST Action webpage. This will be crucial to the Action and will offer open-access to repositories, databases and correlation software, a discussion platform and a porthole for organizing joint projects, staff and sample exchange. It will also feature information about CMI. **D5.1:** Website publication (M3). **D5.2** regular website updates (M48). **T5.2**: Compile a compendium of represented imaging technologies in the network and their application range, specificities and limitations, and publish it on the CMI webpage. **D5.3**: Publication of compendium (M36). **T5.3**: Set up training activities specifically for ECIs and life scientists as users of CMI technology. **T5.4**: Disseminate benefits and advances of CMI. **D5.4**: Scientific reviews about the state-of-the-art in CMI (M24,48). **D5.5:** Press releases (2) to reach general public (M24,48). **T5.5**: Harness synergies and define a joint agenda with above imaging-related communities. **D5.6**: List of contact persons for identified partner communities (M9).

M5.1: Annual WG meetings to coordinate implementation strategies and monitor progress on deliverables and dissemination. **M5.2**: Annual CMI conference with pre-courses.

3.1.2. GANTT DIAGRAM

GANTT CHART		Duration
WG1	**CLEM**	48 months
T1.1	Identify standards for CLEM	
T1.2	Optimize CLEM procedures	
T1.3	Novel approaches in CLEM showcase projects	
T1.4	Identify correlation software for CLEM and other biological CMI	
T1.5	Promote CLEM in life sciences	
T1.6	Trigger marketable CLEM technology	
WG2	**PHI**	48 months
T2.1	Identify standards and bottlenecks in current PHI	
T2.2	Novel PHI approaches in showcase projects	
T2.3	Identify correlation and visualization software for preclinical imaging	
T2.4	Promote PHI approaches among biologists	
T2.5	Trigger marketable PHI technology	
WG3	**Novel CMI Pipelines**	48 months
T3.1	Identify approaches combining biological & preclinical imaging wth	
T3.2	Novel approaches in showcase projects	
T3.3	Bridge preclinical and biological imaging in showcase projects	
T3.4	Identify correlation software for CMI pipelines	
T3.5	Promote CMI and raise awareness	
T3.6	Trigger marketable novel CMI technology	
WG4	**Correlation Software**	42 months
T4.1	Exchange and update compilations of correlation software with WG1-3	
T4.2	Trigger correlation software development via showcase projects	
T4.3	Identify solutions to share large image data sets	
T4.4	Trigger marketable software solutions	
WG5	**Outreach, Dissemination & Partnerships**	46 months
T5.1	Website	
T5.2	Compendium	
T5.3	Set up training activities	
T5.4	Scientific publications (~10)	
	Press releases, social media	
T5.5	Harness synergies	
	Management & Coordination	48 months
	Kick-off meeting & Final conference	
	WG meeting	
	MC meeting	
	Round tables	
	Activities	42 months
	Training schools (4)	
	Call for STSMs	
	STSMs	
	Annual CMI conferences & Pre-courses (4)	

3.1.3. PERT CHART



3.1.4. RISK AND CONTINGENCY PLANS

WG	Risks	Contingency plan
General	Multidisciplinarity: • Non-efficient communication within the scientifically very diverse COMULIS network	Promote interdisciplinary discussions & scientific exchange; Elect representatives for each discipline to communicate difficulties in technical communication; Pre-courses to give an overview about basics of selected topics
WG1-4	Showcase Projects: • Insufficient funding to achieve the target number • Technically difficult implementation • Research questions provided by life scientists cannot be matched with best suited technologies	Exploit STSMs; Design reasonable studies with minimal financial involvement based on available resources; Identify potential additional funding & grant applications; Recruit more participants; Market CMI & showcase projects at conferences and via partnering initiatives & networks
WG1-4	Involvement of Companies: • Difficulties in involving industries in show-case projects & prototype design due to IP	Establish trusting communication outlining jointly-agreed strategies for IP & provisions for IP ownership
WG1-4	Standardization & optimization: • Disagreement on standards/figures of merit for assessing feasibility, best performance & reliability	Open discussions to draft a consensus on technical standards early on in Action; Referring to this document when disagreements arise; Exchange with partner initiatives (e.g. EuBI) on best practices
WG3	Showcase projects: • Access to both microscopy & preclinical imaging infrastructure needed	Careful coordination at WG meetings to identify & schedule showcase studies; Promote interdisciplinary discussions between biological & preclinical imaging scientists
WG4	Standardization & optimization: • Software for showcases only commercially available	Identify potential additional funding; Focus on freeware
WG5	• Delays in publishing reports & reviews • Limited attendance at training schools & STSMs • Access to several biological & preclinical modalities needed during single workshop	Closely follow the agreed work plan; Promote meetings & projects through journals, conference websites; Preferably select (neighbouring) institutions with access to both biological & preclinical imaging

3.2. MANAGEMENT STRUCTURES AND PROCEDURES

COMULIS management will follow the COST Action Management rules, as specified in the 'Rules for Participating in and Implementation of COST Actions' and 'COST Action Management, Monitoring and Final Assessment' and will work in agreement with the Action Science Officer.

COMULIS will be initiated by the 1st **MC Meeting**; this date will represent the official start of the Action**.** MC meetings will take place annually and back-to-back with annual CMI conferences to minimize travel costs. From the 2nd year of the Action, round tables with industry will be attached to the annual CMI conferences. All Action decisions are taken by the MC; the Chair with the support of the **Core Group (CG)** will propose decisions that may then be taken by the MC. Scientific goals of each WG will be discussed and assessed annually. Throughout the course of the Action, 2- to 3-days CMI conferences jointly with MC meetings will take place at different locations, reflecting the geographical distribution of the Action members. The Action will establish a CG as an operative body to facilitate the day-to-day management, communication and decision-making. The CG will be composed of **Chair, Vice Chair, Web Coordinator, Grant Holder, Dissemination Coordinator, STSM Coordinator** and the **WG Leaders**, and serves to ensure overall effective implementation of management, monitoring and networking procedures. The composition of the CG and its mandate will be decided during the 1st MC

meeting. Key tasks with approval of the MC will include to **(1)** ensure transparent and efficient Action management; **(2)** organize and coordinate all networking activities; **(3)** maintain the Action website, database and published repositories; **(4)** monitor, evaluate and mitigate potential risks that might arise in accordance with the risk management plan. Deliverables will include: **(1)** 1st MC meeting minutes (Month 1); **(2)** dissemination plan (M2); **(3)** website publication (M3); **(4)** documenting minutes of MC meetings (M1, 13, 25, 37, 47); **(5)** progress reports (M12, 24, 48). Milestones will include **(1)** 1st MC meeting (M1); **(2)** realization of first STSMs (M13); **(3)** CMI conferences (M4, 13, 25, 37), attached pre-courses and round tables. CG meetings, held monthly via Skype, will discuss the coordination of the next steps in the Action plan.

Beside Chair, Vice Chair and Grant Holder, a Web, Dissemination and STSM Coordinator will be appointed. The Web Coordinator (a currently employed IT specialist of one of the participating organizations) will be responsible for the creation of the Action website, maintenance of the repositories and regular updates. The Dissemination Coordinator (a voted MC member) will be responsible for the Dissemination Plan and its proper implementation. The MC will appoint amongst its members an STSM Coordinator and a STSM Committee that will be responsible for defining transparent criteria for the evaluation of STSMs in accordance with identified CMI showcase projects, and will report to the MC. A **COST Action Website** (e.g. www.comulis.eu) along with a mailing list will keep Action members up-to-date with current events and developments related to the Action. Delays resulting from disagreements between participants or coordination problems will be solved by initiating open discussions among involved parties and closely following the work plan and deliverables agreed upon.

Training schools (~4 days) will be organized 4 times during the Action at different participating institutions with infrastructure for both biological and preclinical imaging. Shorter open-days will be organized twice during the Action (3rd and 4th year) and focus on attracting undergraduate and PhD students from life and physical sciences. Pre-courses about the basics of imaging or hot topics in life sciences will be attached to CMI conferences and specifically designed for non-specialists.

A number of STSMs will be financed each year for exchange of knowledge and training between participants in different member states and to facilitate showcase projects. STSMs will be organized via the Action website where a call for STSMs will be regularly published. After each call, the STSM Committee will evaluate the applications and give recommendations to the CG which to finance. The final decision will be approved by the MC, who bears the right to override the CG's decision. The CG will favour mobility and training of ECIs and promote gender balance.

3.3. NETWORK AS A WHOLE

COMULIS brings numerous benefits and synergy effects for life sciences, medicine, computer sciences and the European industrial landscape. Although there is a strong need for joint efforts between stakeholders across various disciplines from academia and industry to promote CMI, there is currently no dedicated network for CMI. Lack of communication across disciplines has slowed down advancements in CMI and restricted its recognition in biomedical research.

To boost CMI as a versatile approach in biomedical research, COMULIS will integrate a diverse set of expertise including biologists, chemists, clinicians, engineers, computer scientists and physicists with strong expertise in biophysics or optics. For the development of marketable products, the network will also integrate industrial members of imaging or image processing technologies from leading companies and start-ups. Scientists will hold diverse positions at all stages of their careers and include managers of imaging facilities or researchers at companies. The network will comprise leading scientists in the field of imaging, image analysis and big data, and leading life scientists interested in applying imaging technologies to answer their biomedical research questions. The participation of ITCs is particularly welcome and involvement of ITC stakeholders in individual Action activities will be emphasized. The network will continuously strive to involve new academic and industry members to include arising developments and ensure their impact.

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