EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Brussels, 24 March 2020

COST 008/20

DECISION

Subject: **Memorandum of Understanding for the implementation of the COST Action "Pan-European Network in Lipidomics and EpiLipidomics" (EpiLipidNET) CA19105**

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action Pan-European Network in Lipidomics and EpiLipidomics approved by the Committee of Senior Officials through written procedure on 24 March 2020.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA19105
PAN-EUROPEAN NETWORK IN LIPIDOMICS AND EPILIPIDOMICS (EpiLipidNET)

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 build and maintain a pan-European expert centre for integrative (epi)lipidomics, facilitate multidisciplinary networking, knowledge building, technology development, and training with a focus on standardization of (epi)lipidomics workflows, understanding significance of (epi)lipid signalling and assessing its potential for clinical translation. 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 92 million in 2019.

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

Lipids represent a wide variety of molecules that play different biological roles such as energy resources, structural components or signaling molecules that regulate metabolic homeostasis. Most notably, lipids and oxidatively modified lipids have been found to be involved in regulating important mechanisms mediating tissue injury, inflammation, and related non-communicable diseases, which are responsible for near 70% of all deaths in developed countries.

Lipidomics and Epilipidomics are the most promising strategies for the progress in the knowledge of lipids, aiming at biomarker discovery for the prevention, early diagnosis, monitoring, evaluation of diseases therapeutics. These approaches involve the use of complex protocols, different instrumentation and processing huge amounts of data. Effectiveness, while reducing the high costs associated with these technologies, requires a harmonized multidisciplinary approach involving coordinated actions from pan-European centres of lipidomics investigation. This will avoid unnecessary redundancy, improving reproducibility and ensuring efficient and productive research.

EpiLipidNET aims to build and maintain a multidisciplinary pan-European network of researchers, clinicians and enterprises working in the field of lipidomics and epilipidomics to boost a hub of research excellence, advanced knowledge and technology transfer, to promote high level of training for young researches and facilitate clinical translation. EpiLipidNet will include five interactive Working Groups covering analytical methods and computational approaches in (epi)Lipidomics, clinical significance and applications, lipid signaling and mechanisms of action, dissemination and outreach.

Areas of Expertise Relevant for the Action	**Keywords**
● Chemical sciences: Analytical chemistry	● Lipids
● Biological sciences: Metabolomics	● Mass spectrometry
● Biological sciences: Biochemistry	● Omics
● Basic medicine: Metabolomics	● Lipids in health and disease
● Clinical medicine: Non-communicable diseases	● Clinical translation

Specific Objectives

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

Research Coordination

● To provide (via publication and Action website) lipidomics guidelines for biological samples analysis for blood plasma lipidome and other samples (e. g. cells, tissues), based on lipidomics and quality control standards already available for analysis in and beyond the EpiLipidNET network;

● To evaluate lipid quantification strategies using different analytical workflows and types of standardization, calibration and data normalization and to provide corresponding guidelines (via publication and Action website; one for absolute and one semi-absolute quantification);

● To establish and share pre-analytical, analytical and post-analytical workflows for the identification and quantification of modified lipids with an emphasis on oxidized phospholipids, cholesterol esters and triglycerides;

● To initiate integration, curation and quality control of structural databases of modified lipids detected experimentally and provide access to the collected data (via publication and Action website);

● To initiate integration and annotation of available data for lipidomes of different origins (human biofluids, tissues, cell lines, model organisms) and provide access to the collected data (via publication and Action

website);
● To improve software tools for high throughput identification of native and modified lipids;
● To showcase at least one new integrated inter-laboratory workflow for the detection, identification and quantification of lipids and their modified forms based on the implemented guidelines, improved bioinformatics tools and validation of proposed mechanisms of action.
● Materials exchange – biological samples, cell culture and animal models materials, chemical standards.

Capacity Building
● To establish an expert centre for knowledge exchange in lipidomics and epilipidomics;
● To establish a web-base platforms for data exchange in lipidomics and epilipidomics;
● To promote knowledge transfer between academic and industrial partners in the field of chemical standards, MS method designs, bioinformatics solutions, and diagnostic kits;
● To facilitate expertise exchange between clinicians, laboratory medicine, analytical and medical scientists, promoting the translation of lipidomics to clinical practice;
● To foster the active engagement of researchers from countries with low lipidomics capacities in multi-national collaborations by providing access to infrastructure and computational resources;
● To facilitate the active promotion of Early Career Investigators by involvement in Action decision-making activities.

TECHNICAL ANNEX

1 S&T EXCELLENCE

1.1 SOUNDNESS OF THE CHALLENGE

1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

Over the last two decades, the emergence and advancement of lipidomics, a new omics approach, which is a field of research that investigates pathways and networks of cellular lipids in biological systems have been witnessed. Lipids are characterized by an extremely high structural diversity, reflecting the wide range of physicochemical properties, enabling them to perform various functions, including the organization of cell and organelle membranes, the regulation of membrane fluidity and curvature, the control of energy metabolism of cells and organisms, as well as mediation in several signalling pathways. According to their different functionalities, it is increasingly evident that specific lipids can serve as biomarkers of disease and could be a potential target for pharmaceutical interventions[1,2]. It is therefore not surprising that more human diseases are being associated with significant lipidome alterations and, for many, changes in lipid metabolism have been identified as a major risk factor. Indeed, most metabolic disorders, including obesity, cardiovascular diseases and diabetes, are closely associated with the reconfiguration of lipid metabolism[3]. In addition, a close association between lipidome changes and the onset and course of the disease has been demonstrated in the treatment of cancer and neurodegenerative disorders[4].

Recent studies have shown that lipidomics, as a large-scale study of diverse molecular lipid species, aims to address the identification, cell and tissue distribution of lipids, as well as associated signalling and metabolic pathways, has a very high potential in clinical research[1,5]. The results of lipidomic studies in large clinical cohorts and animal models of human diseases have highlighted the great potential of lipid phenotyping for diagnosis, prognosis and treatment. These studies have had a significant impact on the understanding of disease occurrence and outcomes and can be further translated into biomarker validation, design of new intervention therapies, and diagnostic or prognostic assays[6,7,8]. For example, available data on lipid phenotyping from previously studied cohorts (e.g., the Framingham Heart Study Cohort, PROMISE, FINRISK 2002, LURIC, DIOGENES and Bruneck) allow the selection of panels of lipid species positively associated with development of cardiovascular diseases (CVD), obesity and insulin resistance, and to determine prognostic or predictive factors for personalized medicine and patient stratification. A recent example is the use of a panel of ceramides for the prediction of CVD risk which has been implemented for clinical diagnosis[9,10]. Thus, reliable lipid markers can accelerate clinical developments by (i) enhancing the monitoring of disease progression and changes in clinical status, (ii) measuring the impact of the treatment or therapeutic interventions on the course of the disease, and (iii) providing information on drug-target interactions. In addition, the systematic multidimensional vision of human diseases will guide the development of personalized, predictive, preventive and participatory medicine (P4 Medicine).

Currently, much effort is being made to provide an inventory of natural lipidomes. This may seem surprising, but only a limited number of organisms or tissue-specific lipidomes have been described to date. In fact, for human tissues, blood plasma lipidome is probably the only one that has been thoroughly characterized and verified by different laboratories[11,12]. To provide reliable coverage of different natural lipidomes, researchers need to focus on the development, optimization and standardization of preliminary and analytical workflows, data analysis and reporting solutions for high throughput lipidomics[13]. The combination of modern separation techniques and mass spectrometry instruments

capable of high resolution, mass accuracy, sensitivity, and speed has significantly improved accuracy and dynamic range in lipidomics analysis. This offers the possibility of identifying hundreds of lipid species from natural lipidomes using LC-MS/MS analysis. The reliable identification of lipids forms using LC-MS/MS datasets remains one of the main bottlenecks of high-throughput lipidomics. However, a number of software tools have recently been developed to support MS data processing[14,-19].

The lipidome is also subject to various enzymatic and non-enzymatic modifications. Indeed, chemical modifications of biomolecules (e.g. DNA and proteins) via the introduction of small functional groups are well-known regulators of various biological functions (e.g. epigenetics and protein post-translational modifications). Recently, the concept of epimetabolites, products of enzymatic transformations of primary metabolites leading to new functional activities, has been formulated by Showalter et al.[10]. Similarly, modifications of lipids via enzymatic and non-enzymatic modifications including oxidation, nitration, sulfation and halogenation, constitute a new level of complexity of the lipidomes (epilipidome) necessary for the regulation of complex biological functions[20]. Several excellent examples have illustrated the regulatory role of the epilipidome and lipid modifications in directing cell fate and signalling events. Enzymatically oxidized phospholipids emerge as important regulators of innate immune responses[21]. For example, lipoxygenase (LOX)-mediated oxidation in the platelet lipidome upon thrombin activation results in the formation of over 100 oxidized phosphatidylethanolamine (PE) lipids, including species with pro-coagulant activities[22]. Furthermore, it has been suggested that LOX oxidation of arachidonic and adrenic fatty acyl chains in PE lipids as well as non-enzymatic lipid peroxidation could be associated with the induction of ferroptotic cell death[23]. Other well-known examples of regulatory roles of lipid oxidation include pro- and anti-inflammatory eicosanoid signalling[24] and the regulation of metabolic pathways via the activation of nuclear receptors such as peroxisome proliferator-activated receptors[25]. The particular role of oxidized lipids in the activation of innate immune responses via pattern recognition and scavenger receptors has been shown to contribute to the pathogenesis of many human disorders characterized by chronic inflammation[26]. However, because of the largely unknown structural diversity and low natural abundance of modified lipids, high-throughput epilipidomics analysis of biological samples remains challenging[20,27].

The goal of (epi)Lipidomics is not only to identify and quantify the thousands of individual lipid species present in cells, tissues and biological fluids but also to decipher the molecular mechanisms of their formation and their action and biological roles, including their interactions with the macromolecular machinery which might regulate major metabolic reactions and functions. The lipidomics community needs reliable tools to establish deep lipidomics profiles, in order to create reference lipidomes and to integrate lipid species data into genome-scale metabolic models describing the whole set of biochemical reactions driven by corresponding enzymes (genes). Such deep lipidomics profiling should be based on the combination of several analytical and computational strategies to ensure high-quality data and, for the moment, cannot be scaled up to high throughput. However, the integration of all lipid species present in tissues (or at least the majority of them) via systems biology and systems medicine tools will enable the design of robust, high throughput analytical solutions adaptable to the clinical translation.

1.1.2 DESCRIPTION OF THE CHALLENGE (MAIN AIM)

Lipidomics is a fast-developing discipline with a constantly growing number of users, applications and methods. At this stage, it is important to provide a platform for open discussion of all aspects of lipid biochemistry, analytical chemistry, systems biology and medicine to ensure community-based standardization, harmonization and integration of available methodological and knowledge base resources. Thus, the overreaching goal of EpiLipidNET is to establish a pan-European expert centre for integrative lipidomics, to facilitate multidisciplinary networking, knowledge building and technology development with a focus on the following areas:

- Community-based survey of lipidomics workflows for the identification and quantification of lipids from a variety of natural lipidomes from various species (human, mammalian, invertebrates, algae, plants and bacteria).
- Establishing a roadmap for clinical translation of MS-based lipidomics through a network-wide and community-wide assessment of strategies for implementing lipid-derived markers in clinical workflows, by taking into account the analytical and clinical performance, cost-effectiveness, and impact.
- Exploring the significance of epilipidomics in the regulation of biological systems in health and diseases by providing a harmonized solution for MS-based analysis of modified lipids, as well as the integration of available information into lipid-centric signalling pathways via the networking of

researchers working on redox and other types of lipid modifications using different model systems and clinical samples (e.g. atherosclerosis, cardiovascular diseases, cancer, aging).
- Integration of the current knowledge on lipid signalling and modes of action with the focus on developing the expertise hub on lipid signalling mechanisms, mainly related to the role of native and modified lipids as well as their protein interactions in a variety of model systems, including cell culture and animal models.

1.2 PROGRESS BEYOND THE STATE-OF-THE-ART

1.2.1 APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE-OF-THE-ART

To set up and operate a pan-European expert centre for integrative lipidomics, EpiLipidNET will provide networking opportunities for existing lipidomics networks including LIPID MAPS, Lipidomics Standards Initiative, Plasma Lipidomics Initiative and the newly created International Lipidomics Society. Importantly, lipid scientists and lipidomics users who were not associated with those activities will have the opportunity to get involved, share and enrich their own expertise. To meet this challenge, EpiLipidNET will provide a platform:

- To establish an active multinational, pan-European, and multidisciplinary network for the exchange and integration of technology and knowledge between universities, hospitals and industrial partners involved in various aspects of lipid biology, chemistry and analysis;
- To provide an open-discussion platform for integration of knowledge and technologies available in previous initiatives and ongoing international activities, as well as for lipid scientists who were not previously involved in the community-wide discussions.
- To facilitate the active involvement of large, medium and small enterprises within EpiLipidNET with the aim of providing a link between end-users and the commercial sector through discussions and collaborations aimed at lipid standardization, optimization of analytical workflows, bioinformatics solutions, and possibilities of clinical translation;
- To initiate community-level discussions and implementation of workflows for standardization and harmonization of pre-analytical, analytical and post-analytical protocols;
- To organize and perform multi-laboratory studies (ring trials) covering various aspects of lipidomics workflows;
- To compile available information on lipidomes of different origins by providing data quality control and integration solutions;
- To provide to all EpiLipidNET members a balanced access to knowledge (via Action website, databases, workshops, meetings), infrastructure and technology (via dedicated training and STSMs), funding and resources (preparation of joint grant proposals within major EC programs dedicated to educational (MSC ITNs), scientific and innovations calls (Interreg, ERC Synergy, H2020 grants);
- To increase the visibility and integration of researchers of all EpiLipidNET members via dedicated training events (training schools, workshops, webinars to initiate knowledge exchange, share know-how expertise, opportunities to get and to provide multidisciplinary teaching and training);
- To disseminate the Action outcomes to the general public via social media, a webpage, and seminars open to the public (e.g. discussion on lipid nutritional values, omega-3 fatty acids, explanation of values behind blood lipogram results, etc) and open science days (demonstration of technology at school days, long night of science, etc).

Using the aforementioned approaches EpiLipidNET will provide and facilitate:

- Development and implementation of lipidomics guidelines based on community-wide discussions and multi-laboratory studies;
- Integration of current knowledge on lipidomes of different origins based on defined and standardized lipidomics guidelines;
- Comparison of intervals of lipid concentrations in human blood plasma using network generated data from a variety of otherwise independent clinical cohorts considering differences in age, gender, ethnicity, diseases and medications;
- For the first time integration, standardization and cross-comparison of the protocols for the analysis of modified lipids;
- Community-wide integration of information and multi-laboratory validation of established lipid biomarkers (including modified lipids, e.g. in oxLDL) with the possibility of further development of clinical diagnostic assays & kits by EpiLipidNET-associated SMEs.
- Systems biology and medicine integration of lipidomics data through network-wide reconstruction and curation of lipid-related networks and signalling pathways.

Considering the current state-of-the-art in the field of lipidomics, it is important to bring together scientists, clinicians and industrial partners from different disciplines for discussion. EpiLipidNET will, therefore, aim to initiate and sustain ongoing interactions between analytical chemists, scientists from molecular medicine, enterprises working on clinical kits and clinicians to define the potential applications of lipids as diagnostic and prognostic markers to be used for clinical diagnostics and requirements for the MS-based diagnostic assays. In addition, close collaborative efforts between chemists, biochemists and molecular biologist and bioinformaticians involved in big data integration (modelling and networks reconstructions) will be supported to ensure the integration of omics data on the (epi)lipidome in systems biology and systems medicine research. Such multidisciplinary and trans-European networking can only be achieved via the COST Action initiative, which will bring together a large number of otherwise independent scientists and industrial partners. None of the other available national and international funding schemes offers the same level of integration of knowledge and technology across Europe.

1.2.2 OBJECTIVES

1.2.2.1 Research Coordination Objectives

- Implementation of the lipidomics guidelines and quality control standards already available for analysis of blood plasma lipidome and other samples (e.g. cells, tissue) in and beyond the EpiLipidNET network;
- Assessment of lipid quantification strategies using different analytical workflows and types of standardization, calibration and data normalization with the aim of providing guidelines for lipid absolute and semi-absolute quantification;
- Establishment of pre-analytical, analytical and post-analytical workflows for the identification and quantification of modified lipids with an emphasis on oxidized phospholipids, cholesterol esters and triglycerides;
- Integration, curation and quality control of structural databases of modified lipids detected experimentally;
- Integration and annotation of available data for lipidomes of different origins (human biofluids, tissues, cell lines, model organisms);
- Optimization of software tools for high throughput identification of native and modified lipids;
- Development and application of new integrated inter-labortory workflows for the detection and identification of lipids and their modified forms - e.g. using relevant clinical samples provided by one member to be used for untargeted LC-MS detection (2nd member) and bioinformatics support for high-throughput identification (3rd member) followed by synthesis of relevant chemical standards (4th member), design of targeted LC-MS methods (5th member) and validation of proposed mechanisms of action using suitable cell culture or animal models (6th member);
- Materials exchange – biological samples, cell culture and animal models materials, chemical standards.

1.2.2.2 Capacity-building Objectives

- Establishment of an expert centre for knowledge exchange in lipidomics and epilipidomics;
- Establishment of web base platforms for data exchange in lipidomics and epilipidomics;
- Knowledge transfer between academic and industrial partners in the field of chemical standards, MS method designs, bioinformatics solutions, and diagnostic kits;
- Expertise exchange between clinicians, laboratory medicine, analytical and medical scientists, promoting the translation of lipidomics to clinical practice;
- Active engagement of researchers from countries with low lipidomics capacities in multi-national collaborations by providing access to infrastructure and computational resources;
- Active promotion of Early Career Investigators by involvement in Action decision-making activities.

2 NETWORKING EXCELLENCE

2.1 ADDED VALUE OF NETWORKING IN S&T EXCELLENCE

2.1.1 ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

EpiLipidNET will provide an open discussion platform for integrating the knowledge and technologies available within former initiatives (FP6 and FP7 funded networks like Lipidomics Net and European Lipidomics Initiative), ongoing international activities and, importantly, lipid scientists, lipidomics and bioinformatics SMEs previously not involved in the community-wide networking. EpiLipidNET will be closely linked and provide networking opportunities between currently existing lipidomics networks including LIPID MAPS (https://www.lipidmaps.org), Lipidomics Standards Initiative (https://lipidomics-standards-initiative.org), Plasma Lipidomics Initiative, newly established International Lipidomics Society (https://lipidomicssociety.org), WikiPathway (https://www.wikipathways.org) and WikiData (www.wikidata.org). Furthermore, lipid scientists and lipidomics users not associated with those activities will have the opportunity to get involved, share and enrich their own expertise.

Moreover, EpiLipidNET will be the first network focusing on epilipidomics layer of the regulation in biological systems by bringing together scientists working in redox biology and biochemistry as well as experts in the analysis of modified lipids. EpiLipidNET will collaborate with the Society for Free Radical Research Europe (https://www.sfrr-europe.org), Society for Redox Biology and Medicine (https://sfrbm.org) and International HNE Club (https://sites.unimi.it/HNECLUB) to facilitate an efficient exchange of the knowledge.

EpiLipidNET will act as an integrative hub to unite different initiatives, individual researches and industrial partners thus supporting, consolidating and increasing research and technology in this field in a truly pan-European way.

Importantly, EpiLipidNET will effectively counterbalance the research and technology opportunities available to developed and less developed countries. EpiLipidNET will bring a significant benefit to all countries involved, and in particular to less research-intensive European countries, by promoting inclusiveness and excellence and providing access to infrastructure and resources.

This COST Action will have a significant added value on the networking in the field of (epi)lipidomics at international level by fostering a collaborative relationship with other international networks in the United States, Singapore, China, and Japan, which are currently among the most advanced countries in this field. EpiLipidNET will encourage the creation of international networks by organizing joint workshops and conferences, inviting international scientists for EpiLipidNET events, thus promoting the international exchange of knowledge and expertise. EpiLipidNET will enable the acquisition of complementary expertise, creating new and reliable networks and building knowledge. Close networking with international experts will promote and increase the visibility of the European researchers and European lipidomics network, thereby promoting future collaborations towards common goals.

2.2 ADDED VALUE OF NETWORKING IN IMPACT

2.2.1 SECURING THE CRITICAL MASS AND EXPERTISE

This Action will involve a wide range of expertise, which will guarantee its successful implementation:

- Organic and synthetic chemistry (synthesis of commercially unavailable and isotopically labelled lipid standards);
- Analytical chemistry (chromatography and mass spectrometry method development and optimization for analysis of lipidomes and epilipidomes);
- Biochemistry (functional assays, targets validation);
- Biophysics (membrane properties, lipid-protein interactions);
- Molecular biology (targets validation, mutagenesis models)
- Cell biology (cell culture models, microscopy);
- Clinicians (laboratory medicine, clinical translation, samples from patients' cohorts, evaluation of clinical parameters, systems medicine);
- Bioinformatics (lipidomics software tools, data integration, metabolic pathways and models, systems biology and medicine);
- Biostatistics (statistical analysis of big datasets, biomarker discovery and validation);
- Pharmacology (target validation, structure-activity relationship);
- MS vendors (optimization of analytical conditions e.g. optimization of in-source fragmentation, a new workflow for targeted, data-dependent and independent acquisitions);
- SMEs with the focus on high throughput lipidomics;
- SMEs with the focus on lipid standards;
- SMEs with the focus on diagnostic kits;

• SMEs with bioinformatics expertise.

The close interaction between academic researchers, clinicians and industrial partners will enable effective transfer of knowledge and technology from the initial stages of data acquisition, validation, analysis, method development and optimization

2.2.2 INVOLVEMENT OF STAKEHOLDERS

The relationship between stakeholders and EpiLipidNET Action will be built on the basis of mutual benefit and involve dynamic and active interactions. The Action will promote active involvement and establishment of collaborative initiatives between the network, young scientists, scholars, and stakeholders from the industries (SMEs), biomedical, biotechnological and clinical fields in Europe. EpiLipidNET will address several categories of key stakeholders at different levels:

- Universities will have direct involvement in the Action by participating in all EpiLipidNET activities including scientific, training, teaching, dissemination and explorative actions. Action members with teaching duties will benefit from up-to-date knowledge in lipidomics and (epi)lipidomics. This will allow them to provide a high level of teaching in the area of omics technologies, lipid biochemistry, bioinformatics, and clinical translation via constantly updated courses for bachelor and master students. That will foster the training of highly skilled young scientists targeting research and industrial leadership with complementary and translational competencies in Lipidomics.

- Researchers at Universities and Research Institutes at all levels (Action PIs, advanced and Early Carreer Investigators in their teams all across the Action) will be involved in all scientific activities and dissemination, which will help to promote their future career developments, and translation of the results to industries and clinics.

- Scientific societies, lipid-related databases and web resources (e.g. LIPID MAPS, LSI, LipidBank etc) will be involved in close collaboration with the Action from the start. This will allow worldwide dissemination of the Action results and will help to avoid unnecessary redundancy in research. A representative of all these initiatives will be involved in Action seminars and workshops as well as round table discussions. EpiLipidNET will represent a unique space bringing together European and international organization related to lipid research.

- Industry-level involvement will include scientific instrument manufacturers, software, diagnostic and biotech industries and companies dedicated to analytical/lipidomic services. They will benefit and actively participate in the innovative knowledge and methods development and standardization, databases and bioinformatics tools by the Action that will make the technology amenable to more research groups and may lead to the development of tools suitable for commercialization. Reciprocally they can bring to the Action new challenges within the Action to provide potential solutions. SMEs will be active stakeholders from the start of the Action and will participate in the definition of main scientific challenges, development of the scientific project and its exploitation. Thus, companies will benefit by being more innovative and competitive increasing their economic value and extending the job market in Europe.

- At the clinical level hospitals, clinicians, patients and patients' societies will be considered as main stakeholders of EpiLipidNET. Future members of the Action will provide the support for the translation of (epi) lipidomics to the level of clinical diagnostics by being enrolled in the planning future cohort studies, clinical datasets and patient's cooperation. The dissemination of the Action through diseases related to public societies and social associations will help to bridge EpiLipidNET, patients and clinicians. During the Action duration, more clinicians and patient-related organizations will be actively invited to participate in the mains activities of the Action to reach a critical mass that will trigger fruitful discussions.

- Policymakers will be involved in the dissemination of EpiLipidNET activities by being provided with white papers, reviews, and perspectives defining "hot" areas in (epi)lipidomics research, technological and translational developments. Representatives from health organizations and health and education ministries and from national, international and EU funding agencies will be invited to round table discussions, open days and seminars/workshops organized within the Action.

- General public will be involved in Action activities at dissemination events planned by EpiLipidNET including engagement into social media (Twitter, Facebook, others), open public seminars (e.g. discussing lipid nutrition values, omega-3 fatty acids, explanation of values behind blood lipogram

results, etc) and open science days (demonstration of the technology at school days, long night of science etc).

2.2.3 MUTUAL BENEFITS OF THE INVOLVEMENT OF SECONDARY PROPOSERS FROM NEAR NEIGHBOUR OR INTERNATIONAL PARTNER COUNTRIES OR INTERNATIONAL ORGANISATIONS

International partners from both International Partner Countries (IPC) and Near Neighbour Countries (NCC) will be involved based on a mutually beneficial partnership. All IPC and NNC partners are well-recognized experts in the field of (epi)lipidomics and will strengthen scientific network potential by providing new knowledge and innovation strategies:

- Bayir, Hulyia (Critical Care Medicine Chair, Pediatric Critical Care Research; Environmental and Occupational Health, University of Pittsburgh, USA), expertise in redox/clinical lipidomics, redox biomedicine;
- Kagan, Valerian (Center for Free Radical and Antioxidant Health, University of Pittsburgh, Pittsburgh, USA) - expertise in redox lipidomics; lipid-mediated cell death, apoptosis, ferroptosis;
- Khaitovich, Philipp (Center for Neurobiology and Brain Restoration, Skolkovo Institute of Technology, Moscow, Russia) - expertise in brain lipidomics, evolutionary lipidomics, bioinformatics;
- Shadyro, Oleg (Belarusian State University, Minsk, Belarus) – expertise in radiation chemistry, the chemistry of free radical-mediated reactions in lipid oxidation;
- Uchida, Koji (Laboratory of Food Chemistry, Department of Applied Biological Chemistry, The University of Tokyo, Japan) – expertise in lipid peroxidation products and their protein adducts, pro-inflammatory and autoimmune properties of lipid-protein adducts, antibody development;
- Wenk, Markus (National University of Singapore, Singapore) – expertise in lipidomics, member of Lipid Standard Initiative, leader of Plasma Lipidomics Initiative; clinical translation of lipid-based biomarkers;
- Yin, Huiyong (Laboratory of Fatty Acid Metabolism in Human Nutrition and Related Diseases, Shanghai Institute for Biological Sciences Institute for Nutritional Sciences, Shanghai, China) – expertise in clinical lipidomics and epilipidomics.

Active involvement of international experts will allow not only mutual exchange of the knowledge, clinical translation perspectives and update on state-of-the-art technology in the field but will also provide world-wide dissemination of EpiLipidNET. They will also contribute to the EpiLipidNET training activities (training schools) to foster the training of highly skilled young scientists. From their side, international partners will benefit from having access to the multidisciplinary network, new collaborations at a European level, which will increase their awareness and foster new opportunities for future projects. Participation of international industries, namely scientific instruments manufacturers, chemical synthesis companies, international scientific organizations, scientific societies and public databases can benefit from the awareness of research demands in lipidomics standards and applications, but also provide knowledge and training exchange for EpiLipidNET members through collaborative activities as well as potential jobs placements for early-stage researchers trained by the Action.

3 IMPACT

3.1 IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAK-THROUGHS

3.1.1 SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

Combination of EpiLipidNET networking activities will ultimately lead to the establishment of a pan-European scientific and technology cluster, focused on integrative (epi)lipidomics, providing scientists with high-level scientific information to understand the role of lipids and their modifications in human health and diseases with potential clinical translation.

The immediate scientific impact of the Action will include:

- Harmonization of (epi)lipidomics research through the development and implementation of standardization guidelines for pre-analytical, analytical, post-analytical and reporting workflows based on evidence-based community-wide validation and agreements;
- Development and implementation of Lipidomics Bioinformatics hub for the processing and integration of big (epi)lipidomics datasets using Action validating and quality-control software tools for lipid identification, quantification, functional annotation, and pathways integration;
- Roadmap to clinical translation of (epi)lipidomics including evidence-based guidelines for human blood plasma lipidomics in large population and clinical cohort studies, including the introduction of reference materials and analytical workflows aiming to define consensus and possibly reference ranges for selected lipid markers in heterogeneous human populations;
- Establishment of (epi)Lipidomics Educational and Training Hub of freely accessible to the community.

All of these will allow definition of the Roadmap for the creation of a European Lipidomics Research Infrastructure and Clinical Translation hub based on state-of-the-art technologies integrated by the Action with the aim of providing coordinated and harmonized access to the facilities, services and educational resources.

The long-term technological impact of EpiLipidNET will be mainly related to academia and clinics but also to a large number of industrial applications including analytical instrumentation manufactures, bioinformatics enterprises, pharmacological, diagnostics, biotechnology, food, and cosmetics companies. Through networking between industries and academia, EpiLipidNET will provide access to the newest developments in analytical and technology platforms. Furthermore, the results gathered by the Action will provide new insights, allowing to propose innovative strategies to better understand the chronic and non-communicable disease as well as new opportunities for supporting innovation in diagnostics solutions and pharmacological interventions. New bioinformatics tools designed and fine-tuned via multidisciplinary collaborative efforts will be commercialized by software companies. These innovations will provide opportunities for patent applications. Collaboration with European companies, including SMEs involved in EpiLipidNET, as well as other stakeholders will strengthen the translation of the results into the market.

As a short-term socio-economic impact, EpiLipidNET will provide highly qualified training to a new generation of scientists in the broad range of analytical, technological, clinical and industrial applications. Furthermore, the close involvement of industries, the access to new innovative platforms and their exploitation will generate new jobs, thus increasing the European labour market. The ultimate, long-term socio-economic impact of EpiLipidNET will focus on the contribution of knowledge and human actions to reduce disease, morbidity and mortality, mainly associated with chronic, non-communicable diseases (NCDs) and ageing by improving prognostic, diagnostic and therapeutic measures against disease and thus promote health of European citizens and the whole world. NCDs, including cardiovascular diseases, cancers, chronic respiratory diseases and diabetes, pose a major threat to human health and development. According to the WHO, NCDs are responsible for about 41 million deaths each year, corresponding to 71 % of all deaths worldwide, 80% of which are in low- and middle-income countries. Better management of NCDs is essential, and significant efforts are needed to improve detection, screening and treatment of these diseases to improve world health. This has been recognized as a major challenge for sustainable development according to 2030 Agenda for Sustainable Development (Goal 3,4 - to reduce by one-third premature mortality from NCDs through prevention and treatment). Improved well-being and disease prediction will reduce the cost of treatment in hospitals and have a positive impact on the health economy in all countries and citizens.

The scientific, technological and socioeconomic impacts of EpiLipidNET are in line with the societal challenges addressed in the UN-defined Sustainable Development Goals blueprint under Goal 3 (Good Health and Well-Being), Goal 4 (Quality Education) and Goal 7 (Industry, Innovation and Infrastructure).

3.2 MEASURES TO MAXIMISE IMPACT

3.2.1 KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

The creation of knowledge is a fundamental pillar of research and innovation, and both drive the sustainable development of science, business and economy around the world. EpiLipidNET unites highly skilled researchers with complementary scientific expertise ranging from analytical chemistry and biochemistry to the biomedical sector. Close networking will foster the development of bottom-up

research-orientated to new findings, methods and protocols, diagnostic tools in the field of (epi)lipidomics. The multidisciplinary collaborations will boost knowledge creation in an active and interactive process with the development of new ideas and concepts, completely achieved through dynamic interactions among individuals, research institutions, and industrial partners. Networking between researchers, health centres, bioinformatic companies SMEs and industries from different sectors, including lipid supplies, biotech companies and instrument manufacturers, will actively contribute to the shared knowledge, helping to define strategy and working processes, new technologies, products and services. The transfer of knowledge between academia and the industrial sector will be actively promoted by collaborative research programs, meetings, industrial days, round tables and workshops organized during the Action.

Knowledge exchange between researchers using cellular and animal disease models, and clinicians involved in lipidomics analysis of human clinical samples will provide the link necessary to promote clinical translation of (epi)lipidomics via integration of clinical research, laboratory medicine, and SME involved in the lipidomics services and development of diagnostic assays. This will foster the development of new commercialized products and protocols for sample collection and preservation, lipid analysis in clinics and biological medicine. This could contribute for the future development of diagnostic tools and kits for disease diagnostic and monitoring. It will also offer new tools to support the transfer of knowledge to clinical practice, which will be developed in close collaboration with regulatory entities, fulfilling bioethics requirements. These actions will foster knowledge creation and transfer by producing new results and products with clinical and biotechnological applications, to be exploited by the industrial partners, favouring new business strategy and competitiveness, maximising the impact of the knowledge creation and the innovation in Europe.

One important part of the Action will be the Short Term Scientific Missions (STSMs), which will greatly contribute to knowledge creation and transfers. Thus, a significant part of the budget will be allocated to STSMs. Young and Early Carer Investigators in particular from ITC will be encouraged to apply to STSM to visit other excellent research centres to broaden their expertise and to gain experience in new technology and instrumental facilities.

EpiLipidNET will provide an active and continuous process of training and improving skills, to support career development and to provide better job opportunities. An important part of this Action is the training of new professionals highly specialized in technology and research in the different fields of lipidomics, and redox lipidomics. EpiLipiNET intends to train specialized professionals in this emerging area with high demand but that lack employees. The COST Action will enhance career skills for future professionals and leaders with the ability to work in industrial, commercial, research and clinical contexts. At the academic level several specific and local courses will be provided. Hands-on courses & training school will be organized at the institutions with top technology available with the involvement of industrial partners. Theoretical workshops and seminars will be organized in ITC & NNC. Visits and technical sessions to the industry sites will be organized, such as industrial days, promoted by the companies involved in the network and/or other companies that are interested in training and collaborating with the network. These will support new jobs opportunities for young people, adding value to their experience, promoting career development independently of age, gender and nationality.

3.2.2 PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

Dissemination and exploitation of EpiLipidNET results will be one of the most important Action outcomes. Due to its importance, one Working Group (WG5) will be entirely dedicated to these activities, focusing on implementation, monitoring and updating of the proposed dissemination and exploitation plan. WG5 will actively interact with the other WGs1-4 from the start of the Action at different levels.

The first actions will be the generation of a EpiLipidNet website and the Social network accounts for the Facebook, Twitter and Linkedin. These will be setup in the first month of the Action and will be used as main dissemination routes to all participants, stakeholders and to attract future participants and users. EpiLipidNet website Social network accounts will be regularly updated with major findings and news from all participants and will have private specific sections for participants and public open pages to stakeholders and for general public. Young researchers will be particularly motivated to actively update Facebook and Twitter by providing posts and likes.

Other specific dissemination actions will be:

Dissemination and dialogue with researchers, clinicians and industry:
- Publication of research articles, reviews and white papers in international journals according to EC recommendation on Open Science work program;
- Publication of protocols for sample preparation and analysis and practical clinical guidelines;
- Open access sharing of protocols, reports and data;
- Active participation of Action members at the relevant international conferences, meetings, workshops and training events;
- Events organized by the Action at national, European and international levels including training schools, workshops and satellite symposia at major scientific and public events;
- Community sharing of teaching and educational resources (e.g. recordings of the webinars, teaching lectures);
- Interaction with other European and International networks and scientific societies, COST Actions and international projects.

Dissemination and dialogue to the general public and policymakers:
Outreach activities directed to the general public will be developed to inform local communities and organizations, including patients' organizations, about the potential of advanced lipidomics analytical technologies in the framework of personalized and P4 medicine. Overall, those strategies will include:
- Dissemination via media press releases (newspapers, radio and TV programmes);
- Outreach activities to the public and schools via open public seminars (e.g. discussing lipid nutrition values, omega-3 fatty acids, explanation of values behind blood lipogram results, etc) and open science days (demonstration of the technology at school days, long night of science etc);
- Organization of "orientation days" for students;
- Presentation of the project to general public including students of secondary and higher education via for instance "Open Campus" and "Open Week of Science and Technology" events; round tables debates on science and innovation with wider audience including researchers, stakeholders & general public.
- At the last year of the Action, the main outcomes of EpiLipidNET will be presented at a closing meeting to which stakeholders, end-users, and policymakers will be invited.

4 IMPLEMENTATION

4.1 COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

4.1.1 DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

This COST Action will include five closely interacting Working Groups (WG) uniting leading European researchers and prominent International collaborators. EpiLipidNET Working Groups will cover WG1: Harmonization of lipidomics workflows to increase natural lipidomes coverage, WG2:Epilipidomics analysis and data integration strategies, WG3:Clinical significance and applications of (epi)lipidomics, WG4:Lipid signalling and mechanisms of action, and WG5:Dissemination and outreach.

WG1: Harmonization of lipidomics workflows to increase natural lipidomes coverage. Lipids are recognized as an important structural, regulatory and signalling molecules with numerous functional roles in biological systems and metabolic pathologies. Such functional diversity and a high degree of specialization are possible due to the variety of chemical structures and large number of individual lipid molecular species. Available data demonstrate an extreme complexity of natural lipidomes which further underline the analytical challenges in lipidomics profiling for each biological matrix. Indeed, despite active research all over the globeworlwide, the only lipidome more or less fully characterized and, importantly, confirmed by several laboratories is the human plasma lipidome. The use of different analytical strategies including methods used for lipid extraction, separation, analysis, and identification can lead to dissimilar results impairing robust comparison of data between studies or labs. Thus harmonization and standardization of protocols are urgently needed, and are the only way for a unique identification of the lipidome of specific biological samples and conditions. Clearly, to foster the development of lipidomics and increase the coverage and reliability of reported lipidomes, joint networking efforts are required.

WG1 objectives – To promote a community based survey of lipidomics workflows for identification and quantification of lipids from a variety of natural lipidomes. This includes lipidomes from various species (human, mammalian, invertebrates, algae, plants and bacteria). For animal lipidomes, body fluids (e.g.

blood plasma, CSF, saliva), different tissues (e.g. cardiac tissue, liver, adipose tissue), cell types, and exosomes, can be studied. EpiLipidNET will perform a community-wide survey to collect feedback and discussion aiding Lipidomics Standards Initiative (LSI), which is a working group belonging to International Lipidomics Society (ILS), to establish the initial guidelines in lipidomics. The obtained material will be transferred to ILS, who will perform the evaluation, reformatting and adaptation according to the necessary standards. For that WG1 will focus on the following tasks:

T1.1 Establishment of guidelines for sample preparation strategies for different biological matrices
T1.2 Establishment of guidelines for workflows for MS based lipidomics
T1.3 Establishment of guidelines for quantitative lipidomics
T1.4 Multi-center evaluation of pre-standard protocols
T1.5 Benchmarking and inter-laboratory evaluation of existing software tools for lipid identification
T1.6 Definition and implementation of reporting standards
T1.7 Facilitate development, enrichment and curation of lipid databases, ontology, functional annotation for reconstruction of lipid signalling pathways (WG4) in collaboration with LSI and LIPID MAPS consortium. Guidelines will be used in WG2 and WG3.

WG2: Epilipidomics analysis and data integration strategies. Nowadays it has become evident that, similar to the other level of biological organisation (genome, transcriptome and proteome), the lipidome is also subjected to different enzymatic and non-enzymatic modifications. Modified lipid species (epilipids) can be formed by derived from enzymatic and non-enzymatic reactions and can have multiple biological functions dissimilar from their native forms. They are a subset of natural lipidomes (epilipidome). Oxidized lipids represent the fraction of epilipidome that has attracted high scientific attention and are involved in the onset and development of numerous human disorders. Development of high-throughput analytical methods such as LC coupled on-line to MS provides the possibility to address epilipidome diversity in complex biological samples. Furthermore, the lack of optimal computational tools for robust, accurate and specific identification of already discovered and yet unknown modified lipids still needs to be addresses through community-based networking.

WG2 objectives – To explore the significance of epilipidomics in regulation of biological systems in health and diseases by providing integrative solution for MS-based analysis of modified lipids. To integrate the available information in lipid-centric signalling pathways via networking of researchers working on redox and other types of lipid modifications using different model systems (e.g. cellular models of ferroptosis and apoptosis) (from WG4) and clinical samples (e.g. atherosclerosis, cardiovascular diseases, cancer, aging) (from WG3). This area will be developed in coordination with Society of Free Radical Reseach and International HNE club. For that WG2 will focus on the following tasks:

T2.1 Establishment of pre- and analytical workflows for MS-based detection and identification of modified lipids
T2.2 Exchange of the protocols and definition of SOPs for qualitative and quantitative analysis of different modified lipids, such as including oxylipins, oxysterols, reactive aldehydes, oxidized PLs, TGs, and CEs.
T2.3 Benchmarking, further development and optimization of bioinformatics tools for high-throughput identification of modified lipids
T2.4 Collaboration with companies producing lipid standards to initiate commercialization of standard chemically defined modified lipids (including isotopically labelled standards for quantitative epilipidomics)
T2.5 Exploring potential of oxidized lipids as markers for clinical diagnostics (e.g. in oxLDL) and their future translation into design of diagnostics methods/kits together with SMEs involved in the Action
T2.6 Integration of the data on involvement of modified lipids in physiology and pathophysiology by combining results from different models and clinical samples (together with WG4)

WG3: Clinical significance and applications of (epi)lipidomics. Lipids and their modified forms have a large translational potential for clinical implementations, especially for inflammatory diseases and other disorders characterized by dysregulation of the metabolism such as cardio-vascular diseases (CVD), obesity, diabetes (DM), neurodegeneration and cancer. All are major causes of morbidity and mortality worldwide and with high health costs. Decoding lipid deregulation in each disease will have a significant impact on understanding disease pathophysiology and will aid, in the future, to propose new markers for high diagnostic, prognostic, and therapeutic values. Moreover, clinical translation of reliable and validated lipid markers will guide the development of personalized, predictive, preventive, and participatory medicine (P4 Medicine). Indeed, several clinical diagnostics parameters of lipid metabolism

including plasma cholesterol levels (LDL-C, HDL-C) and triglycerides are commonly used in laboratory diagnostics all over the globe. Further development of the (epi)lipidomics technology at clinical level will allow to gather new inputs, and design new assays based for the detection, identification, and quantification of specific lipid species involved in the pathogenesis of diseases.

WG3 objectives – To establish a roadmap for clinical translation of MS-based lipidomics by bringing together participants working in clinical diagnostic and laboratory medicine, clinicians, researchers involved in method development and validation, biostatisticians and commercial enterprises developing lipid standards and diagnostic kits. The main focus of WG3 is a network- and community-wide assessment of the putative implementation strategies of lipid derived markers in clinical workflows considering analytical and clinical performance, clinical and cost effectiveness, and impact. EpiLipidNET will aid the Clinical Lipidomics working group of ILS by performing a community wide assessment for establishing a roadmap for clinical lipidomics. The work will be done in coordination with ILS and Plasma Lipidomics Initiative. The obtained material will be transferred to ILS, who will perform the evaluation, reformatting and adaptation according to the necessary standards. For that, WG4 will focus on the following tasks:

T3.1 Standardization of preanalytical workflows for sample collection, biobanking, storage and management in clinical environment for biofluids and tissue samples
T3.2 Assessment of the inter-individual variability factors in clinical lipidomics including age, gender, ethnicity, diet and lifestyle, medication history and disease conditions
T3.3 Development of a workflow for the establishment of reference values for selected lipids
T3.4 Definition, assessment and promotion of reference materials to increase comparability of large scale lipidomic studies
T3.5 Development, optimization, implementation and exchange of biostatistics tools and machine learning algorithm for lipid biomarker discovery and validation in large clinical cohorts.

WG4: Integration of (epi)lipidomics with lipid signalling and mechanisms of action. The lipidome is a very dynamic structure participating in the regulation of numerous biological functions and is tightly maintained by complex metabolic networks. It dysregulation often results in the development of pathologies. Synthesis, regulation, and modes of action for native lipids and their modified forms (e.g. oxidized lipids) are closely interconnected with other levels of biological systems such as regulation of gene transcription, enzymes and lipid-protein or lipid receptor interactions(y covalent or non covalent). Understanding of the signalling and metabolic pathways related with alteration of lipidome and epilipidome is urgently needed to understand the development of several diseases and requires joint multi-disciplinary efforts of analytical scientists, biochemists, biophysicists, molecular and cellular biologists, as well as bioinformaticians. Acquisition of big lipidomics datasets provides opportunities for systems-wide data integration. However, comprehensive solutions such as functional enrichment, pathway mapping and integration into genome-scale metabolic networks, are almost not available in (epi)-lipidomics. Combined community efforts under the EpiLipidNET umbrella are absolutely necessary at this stage to provide a collaborative networking platform to define the strategies for data integration in system biology level, normalization, reporting, and functional annotation.

WG4 objectives - Integration of the current knowledge on lipid signalling and modes of action with the focus on developing the expertise hub on lipid signalling mechanisms, mainly related to the role of native and modified lipids as well as their protein interactions in a variety of model systems, including cell culture and animal models. It will be based on analytical, molecular, cellular and biophysical approaches to tackle the mechanisms of action of lipid species. For that, WG4 will focus on the following tasks:

T4.1 Collection and exchange of the model systems (cell lines, animal models; material and knowledge exchange) used by the network as a joint resource available to the EpiLipidNET participants(that can be used in WG1 and WG2);
T4.2 Collection and exchange of the SOPs and expertise of analytical, biochemical and biophysical methods for the detection and functional assessment of lipid-protein interactions, covalent and non-covalent;
T4.3 Development of a database on protein-lipid interactions and associated functional effects;
T4.4 Integration of available data on lipid signalling and metabolic pathways;
T4.5 Integration and curation of pathways summarizing lipid related signalling

WP5: Dissemination and outreach. Dissemination is a key aim and outcome of the COST Action as it is required in order to achieve Impact. This will be delivered via a variety of mechanisms, including scientific publications in biological and analytical journals together with Special Issues, conference

organization, public engagement and outreach events, and well as the use of social media. These different types of dissemination are chosen to address the specific objectives below.

WP5 objectives - The goals of WG 5 are to reach 4 key target beneficiary groups: (1) the academic community in a wide range of subject areas where lipidomics is relevant and useful; (2) clinicians and medics working on diseases involving dysregulation of the lipidome; (3) the industrial sector where lipidomic information underpins products or product design; (4) the public, in order to educate about how lipidomic research can help understand aspects of health, ageing and disease. For that, WG4 will focus on the following tasks:

T5.1 Set up a website with pages suitable for specialist and non-specialist readers giving information about (redox)-lipidomics role in health and disease, and analytics, advertise events and training, and include links to published articles as these become available.
T5.2 Set up EpiLipidNET accounts on Facebook, Twitter and LinkedIn, and identify people responsible in each country to support a multilingual approach. This will facilitate communication both with scientists and the public.
T5.3 Communication to the scientific community via journals. Joint primary articles resulting from STSMs carried out by Early Career Investigators, to be published in Quartile 1 and 2 journals. Joint review articles involving 2 or more teams to overview emerging concepts in (epi)lipidomics and summarize recent findings in the field, bringing together complementary specialities. Some articles will be published individually, while others will be combined into one or more Special Issues.
T5.4 Presentations at scientific meetings. EpiLipidNet will organize open meetings and training schools. The training schools will disseminate theoretical knowledge, practical skills and good practice to Early Career Investigators. The meetings will discuss current and emerging concepts, and present findings from EpiLipidNet research.
T5.5 Dissemination to non-academic beneficiaries. Industrial and clinical contacts will be invited to attend the open conferences. Information sheets summarizing relevant findings and protocols will be prepared and distributed.
T5.6 Information leaflets on the importance of lipids in health and disease will be prepared and disseminated. Generic material will be prepared in English and translated for local use. Teams will organize trips to schools and public speaking engagements appropriate to their local community as well as patients organizations.

4.1.2 DESCRIPTION OF DELIVERABLES AND TIMEFRAME

D#	Description	WG	Month
1	Website and Social Media of EpiLipidNETaccounts set up and available	WG5	3
2	Web-based resource for collection of analytical protocols for shotgun and LC-MS based lipidomics established	WG1	12
3	Web-based resource on available model systems and clinical studies in (epi)lipidomics established	WG4	12
4	Shared resources on lipidomics open-source software tools established and available via Action Website	WG1§2	14
5	Web-based database of the data integration strategies in (epi)lipidomics methods established and made available to the EpiLipidNET community	WG4	16
6	Open access guidelines for quantitative lipidomics analysis established and made available to the EpiLipidNET community	WG1	18
7	Publication of ring trial study the coverage of selected lipidomes	WG1	22
8	Publication on inter-laboratory benchmarking of software tools for lipid identification	WG1§2	26
9	Open access guidelines for quantitative epilipidomics analysis are published on Action website	WG2	30
10	Position paper on pre-analytical workflow for clinical lipidomics published open access	WG3	31
11	Publication of ring trial study the quantification of selected lipidomes	WG1	32
12	White paper on standardization acquisition and processing of (epi)lipidomics datasets	WG1§2	34

13	Publication of a ring trial study on the identification and quantification of selected modified lipids	WG2	38
14	White paper on standardization of lipid annotation tools published	WG1§2	40
15	Position paper on the interindividual variations in clinical lipidomics published	WG3	44
16	Roadmap to the establishment of European Lipidomics Research Infrastructure and Clinical Translation hub prepared	all	48
17	Position paper on human plasma lipidome in heterogeneous population cohorts	WG3	48
18	Special Issue on Action results organized and in press	WG5	48

4.1.3 RISK ANALYSIS AND CONTINGENCY PLANS

The Action will have a coherent interaction of participants. The Management Committee (MC) and the WG Leaders will be responsible for evaluating every 6 months the outcomes and deliverables of the Action. If necessary, relevant recommendations and incentive actions will be planned and delivered. Although most participants have experience in collaborative work and in project networking, some problems could arrive at several levels:

- Poor involvement of participants and poor interdisciplinary cross activities - It is expected that new collaborative interactions will arise from the network, but this process may occur slowly. This will be actively monitored by the MC and Core Group (CG) and will be discussed in the WG meetings and in the annual meetings. If events do not occur as expected, new workshops and round tables will be planned and new collaborative projects and STSMs will be discussed and proposed.
- Low involvement of young researchers - Actively involve young researchers in developing the tasks and organizing meetings, workshops, training schools and in dissemination activities.
- Poor outcomes - MC and the WG Leaders will foster preparation of joint publications, by suggesting a relevant topic and proposing inter-laboratory studies.
- Conflicting parties - The success of the Action requires mutual trust and confidence. Best results are expected from the open and dynamic discussion and sharing of knowledge and ideas. If some conflicts exist, this will be discussed at the WG level, and the MC Chair will propose specific measures, such as confidentiality, and if necessary, non-disclosure agreements.

4.1.4 GANTT DIAGRAM

Activity	Year 1				Year 2				Year 3				Year 4			
	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Kick-off meeting																
MC meetings																
Website launched																
LipidNET annual meetings																
STSM calls																
Workshops, seminars and webinar																
WG meetings																
Training schools																
Dissemination to general public																
Final Action meeting																

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