



4rd CORE GROUP MEETING

COST ACTION CA17112 - PRO-EURO DILI NETWORK

Kaunas, Lithuania 27 March 2020 (cancelled)

Digital CG, MC 14 March 2020 (Actions & Budget approved)

Core Group Digital 26 November 2020

<https://proeurodilinet.eu>

The full Action details available at:

<https://www.cost.eu/actions/CA17112#tabs|Name:overview>



Funded by the Horizon 2020 Framework Programme of the European Union

AGENDA 4rd CORE GROUP MEETING

1. Approval of CG#3 minutes (2019 Palermo, Italy)
2. Submission Progress Report 2y (<https://proeurodilinet.eu/documents>)
3. Discussion about management rules for activities 2020/21
 - a. STSMs ITC Conference Grant (J Cubero)
 - b. Training school (L Nelson, GP Aithal)
 - c. Info Day on DILI (H Glasová)
 - d. Monothematic Conference planning (Thomas Hammond)
 - e. EASL 2021 meeting of the DILI Consortium /EACPT 2021 meeting (H Glasová)
4. Action implementation planning
 - a. Monitoring of the Objective Achievement Indicators for MoU Objectives (all WGs leaders/co-leaders)
 - b. Activity and budget planning (Work and Budget Plan preparation)
 - c. Dissemination strategy/ planning (Publications and outreach activities)
5. Any Other Business
6. Closing

1. Approval of CG#3 minutes (2019 October 11, Palermo, Italy)

2. PROGRESS Report PRO EURO DILI NET 2 years



COST Action
Progress Report at 24 months
(16/10/2018 to 16/10/2020)

CA17112: Prospective European Drug-Induced Liver Injury Network

The Action was approved by the Committee of Senior Officials (CSO) on 13-4-2018 and has the MoU reference COST 023/18.

This report shows the data entered into e-COST to enable the Action Chair to verify the completeness and accuracy of the report with the MC prior to submitting the report via e-COST in fulfilment of the rules for COST Action Management, Monitoring and Final Assessment.

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2nd PROGRESS REPORT CA-17112

COST ITC (network of proposers)

37,50%

NOW → COST Inclusiveness Target Countries 46%

Main Proposer: Spain

Network of Proposers: (15 EU, 13 ITC)

Belgium , **Croatia**, **Czech Republic** , **Estonia**, France , Germany ,
Iceland, Israel, Italy , **Lithuania** , **Portugal** , Spain , Switzerland,
Turkey , United Kingdom

New countries (15): **Bosnia and Herzegovina**, **Romania**,
Serbia, **Greece**, **Norway**, **Slovakia**, **North Macedonia**,
MOLDOVA, **Sweden**, **the Netherlands** , **SLOVENIA**
Ireland, **Denmark**

T 28 countries (15 EU, 13 ITC (46%))

INTERNATIONAL COOPERATION (5)

International Partner Country (IPC): Chile, China, India, United States, Uruguay
Malaysia

INDUSTRIAL DIMENSION

SMEs:

France, CHERRY BIOTECH

Germany, MetaHeps,

Sweden VLVbio, Nacka

United Kingdom, Dr. Olivier Delrieu, C4X Discovery Ltd.,

DestiNA Genomics, Edimburg & Granada, Spain Juan Jose Diaz-Mochon

BIOPREDIC INTERNATIONAL. Dr Christophe Chesne, Rennes, France <https://www.biopredic.com> Liver Systems

Astra-Zeneca, M Merz

Large companies: United States



Liver systems

- Human and animal hepatocytes - Non parenchymal cells - Subcellular fractions - HepaRG - Silensomes

- 1) **to conduct a workshop on HepaRG cell model for prediction of cholestatic DILI risk:** a well differentiated and polarized 2D HepaRG cell culture will be used to assess bile canaliculi alterations in response to cholestatic compounds. These BC alterations induced could be demonstrated by using new fluorescent BC probes and quantified by image analysis.
- 2) **to conduct a workshop on new patented human hepatocyte cell line derived from primary hepatocyte and amplified in vivo.** This cell model could be also used as a good alternative human hepatocyte for in vitro assessment of DILI such as cholestatic prediction

Start of the Action = 1st MC meeting October 16, 2018

Grant Period 1: 16 October 2018 – 30 April 2019 MC Málaga

Grant Period 2: 1 May 2019 – 30 April 2020 MC Lithuania

Grant Period 3: 1 May 2020 – 30 April 2021 MC Nottingham

;; Extended up to 31 October 2021 !!

Grant Period 4: 1 Nov 2021 - 30 April 2022 ¿? MC Prague

Grant Period 5: 1 May 2022 - 15 Oct 2022

Closing Meeting and Final Report Early Sept 2022

End of the Action = 4 years after MC 1st date

Networking Tools	Quantity	Budget
Meetings	2	64 595.65 EUR
Training Schools	1	9 600.00 EUR
Short Term Scientific Missions (STSM) (accepted 4 STSM budget 11.700€)	3	7 500.00 EUR
ITC Conference Grant	2	5 000.00 EUR
COST Action Dissemination	2	2 000.00 EUR
Other Expenses (OERSA)	0	0.00 EUR
Total Science Expenditure		88 695.65 EUR
Financial and Scientific Administration and Coordination (FSAC) - MAX. 15%	15 %	13 304.35 EUR
Total Grant request 3rd GP		102 000.00 EUR

Long Term Scientific planning

3rd Grant Period

- **August 2020** CA-17112 meeting @ The EASL Digital International Liver Congress
- **April 2021**: 3rd WGs meeting, 5th CG & 3rd MC, held by GP Aithal, Nottingham, UK. Training course
- **June 2021**. Digital EASL Conference. Meeting of the COST DILI Consortium. Agenda to be drafted
- **Monothematic Conference on DILI along with the Eurotox Conference. 5th September, Copenhagen, 2020. CANCELLED 26 sept 2021 Sunday**
- **INFO DAY on DILI. Helena Glasova**
- **November 2020 WG 2 & 4 meeting in Montpellier. Prof.D Larrey Will be postponed May 2021 ?**
- **26-27 September 2021 KAUNAS, LITHUANIA**

**4. Discussion about management rules for activities
2019/20**

- a. Short Term Scientific Missions & ITC Grants**
Dr J Cubero

Short-Term Scientific Missions (STSM), COST ACTION 17-112 for the last year:

ECOST-STSM-Request-CA17112-45167

*Title: **Role of Nrf2 in APAP-mediated toxicity**

*Type of Mission: **Basic**

*Applicant: Nuria López-Alcántara

*Location: Institute of Physics of the Czech Academy of Sciences, Prague, Czech Republic

*Responsible: Dr. Oleg Lunov, lunov@fzu.cz

*Dates: 2019-12-02 - 2019-12-22

ECOST-STSM-Request-CA17112-45122

*Title: INTERNAL MEDICINE WARD, OUTPATIENTS HEPATOLOGY CLINIC, LIVER ULTRASOUND AND FIBROSCAN

*Type of Mission: **Clinical**

*Applicant: Enrique del Campo Herrera (UMA, Málaga)

*Location: Internal Medicine & Hepatology, DIBIMIS, University of Palermo

*Responsible: Dr. Anna Licata, anna.licata@unipa.it

*Dates: 2019-10-07 - 2019-10-20

ECOST-STSM-Request-CA17112-45133

*Title: **Viral and autoimmune hepatitis, cirrhosis, acute liver failure, DILI, HILI intrahepatic cholestasis of pregnancy**

*Type of Mission: **Clinical**

* Applicant: Goran Bokan Faculty of medicine, Banja Luka, BA

*Location: Internal Medicine & Hepatology, DIBIMIS, University of Palermo

*Responsible: Dr. Anna Licata, anna.licata@unipa.it

*Dates: 2019-09-30 - 2019-10-31

ECOST-STSM-Request-CA17112-46089

*Title: **Methodology of systematic review of observational studies in DILI**

*Type of Mission: **Clinical**

*Applicant: Cristiana Torres Freixo, Faculdade de Medicina da Universidade do Porto, Porto, PT

*Location: Nottingham Digestive Diseases Centre, Nottingham, UK

*Responsible: Dr. Guruprasad Aithal, guru.aithal@nottingham.ac.uk

*Dates: 2020-01-19 - 2020-02-05

ECOST-STSM-Request-CA17112-46009

*Title: **Training in the use of HepaRGs and monitoring POR expression**

*Type of Mission: **Basic**

*Applicant: Francisco Esteves (Faculdade de Ciências Médicas, UNL, LISBOA, PT)

*Location: Institute of Bioengineering, University of Edinburgh, Scotland, UK

*Responsible: Dr. Leonard J. Nelson, L.Nelson@ed.ac.uk

*Dates: 2020-03-01 - 2020-03-15

STSMs APPROVED 3rd GRANT PERIOD

NAME /SURNAME	Applicant HOME INSTITUTION	COUNTRY	HOST INSTITUTION	COUNTRY	START DATE	END DATE
Lauryna Aukštikalnė	Lithuanian University Health Sciences Inst Physiology Pharmacology	Lithuania	University of Malaga, Spain	Spain	11.01.21	28.02.21
Sonja Trbojevic	Faculty of Medicine, University of Banja Luka	Bosnia and Herzegovina	Faculty of Medicine, University in Novi Sad (Ivan Capó)	Serbia	01.02.21	28.02.21
Daniel Di Zeo	University of Malaga	Spain	University of Lisbon, Joana Miranda	Portugal	01.03.21	30.04.21
Ivan Capó	University of Novi Sad	Serbia	Faculty Natural Sciences & Mathematics, Ss. Cyril & Methodius University, Skopje J Dimitrova-Shumkovska	North Republic of Macedonia	01.02.21	21.02.21

Short-Term Scientific Missions (STSM), COST ACTION 17-112 APPROVED for the next grant period:

ECOST-STSM-Request-CA17112-47460 (Approved)

*Title: *DILI principles in detection, characterization, phenotyping, risk assessment and adjudication. Management of DILI databases. Pathophysiology, therapeutic strategies and new biomarkers in DILI using patient-derived dermal fibroblasts, keratinocytes and hep*

*Applicant: Lauryna Aukštikalnė. Lithuanian University of Health Sciences Institute of Physiology and Pharmacology (Kaunas)

* Location: Universidad de Málaga (UMA), Málaga, Spain

*Responsible: Dr. María Isabel Lucena, lucena@ucm.es

*Dates: 2021-01-11 - 2021-02-28

ECOST-STSM-Request-CA17112-47430 (Approved)

*Title: *COST ACTION 17-112*

*Applicant: Dr Sonja Trbojevic, Faculty of Medicine, University of Banja Luka (Banja Luka, Bosnia and Herzegovina)

* Location: Faculty of Medicine, University in Novi Sad (Serbia)

* Responsible: Prof. Ivan Capo; ivan.capo@mf.uns.ac.rs

*Dates: 2021-02-01-2021-02-28

Short-Term Scientific Missions (STSM), COST ACTION 17-112 for the next grant period:

ECOST-STSM-Request-CA17112-47503 (Approved)

*Title: *Advancing in vitro models of DILI: key techniques for the study of hepatotoxicity in cell cultures*

*Applicant: Daniel Di Zeo, Biomedical Research Institute of Malaga, University of Málaga (Spain) (Málaga)

* Location: University of Lisbon (Portugal)

* Responsible: Prof Joana Miranda, jmiranda@ff.ulisboa.pt

* Dates: 2021-03-01 - 2021-04-30

ECOST-STSM-Request-CA17112-47580 (Approved)

*Title: *Quantification of markers of oxidative damage, lipid peroxidation products, enzymatic and non-enzymatic antioxidant molecules*

*Applicant: Prof Ivan Capo, Faculty of Medicine, University of Novi Sad, Faculty of Medicine (Novi Sad, Serbia)

* Location: Faculty of Natural Sciences & Mathematics, Ss. Cyril and Methodius University in Skopje (North Macedonia)

* Responsible: Prof Jasmina Dimitrova-Shumkovska (jasminad@pmf.ukim.mk)

* Dates: 2021-02-01 - 2021-02-21

List of topics for STSM proposed	List of centers willing to HOST STSM candidates	Expected duration	
DILI Principles in detection, characterization, phenotyping, risk assessment and adjudication. Management of DILI databases	Spain University of Malaga (RAUL J. ANDRDE/ MARIBEL LUCENA)	From 1 to 3 months from January to March	Clinical proposal
3. Internal medicine ward, out- patients hepatology clinic, Liver ultrasound and fibroscan (Italy)	3. Italy. Internal Medicine & Hepatology, DIBIMIS, University of Palermo (ANNA LICATA)	One month 15 September to 30 October 2019	Clinical proposal
1. Advanced physical methods in hepatotoxicity studies (Czech Republic)	1. Czech Republic. Institute of Physics (OLEG LUNOV)		Basic proposal
4. Production of hepatocytes from human pluripotent stem cells (Norway)	4. Norway. UiO (GARETH SULLIVAN)		Basic proposal
5. 3D culture facilities, expertise in stem cell differentiation into hepatic cells, hepatotoxicity studies, metabolism studies, etc... (Portugal)	5. Portugal. Faculty of Pharmacy of the University of Lisbon (JOANA MIRANDA)		Basic proposal
6. In vitro and in vivo models. Basic - models of advanced chronic liver disease (Spain)	6. Spain. UCM (JAVIER CUBERO)	One week	Basic proposal
7. Preclinical models of toxicity in hepatic surgery and liver transplantation (Spain)	7. Spain. IDIBAPS (CARMEN PERALTA)	1 Week in 2020. 3 students	Basic proposal
8. In vitro models (Spain)	8. Spain. UCM (YULIA A. NEVZOROVA)		Basic proposal

List of topics for STSM proposed	List of centers willing to HOST STSM candidates	Expected duration	
9. Exosomes (Spain)	9. Spain. CIC bioGUNE (JUAN M. FALCON-PEREZ)	3 months (October-December)	Basic proposal
10. Emerging technologies in DILI ; New in vitro models of DILI (Spain)	10. Spain. IDIBAPS (PAU SANCHO-BRU)	3 months (October-december)	Basic proposal
11. Bioengineering and Bioprinting of Hepatic Tissues: Novel Tools for DILI Research and Drug Discovery (Spain)	11. Spain. IIS Aragon (PEDRO M. BAPTISTA)		Basic proposal
12. Zebrafish as a model for DILI; bioinformatics(Turkey)	12. Turkey. Bilkent Univ (OZLEN KONU)	3-4 weeks in Fall 2019	Basic proposal
15. Able to perform epigenetic studies (Turkey)	15. Turkey. KU (MUJDAT ZEYBEL)		Basic proposal
16. Human liver modelling, DILI/ Liver disease preclinical models and non-invasive screening technologies (United Kingdom)	16. United Kingdom. Institute for Bioengineering, Edinburg University (LEONARD J NELSON)		Basic proposal
17. Lab equipped for preclinical in vitro and in vivo experiments (DNA analysis, mass spectrometry, cell cultures). vivarium with small rodents	17. Serbia. Faculty of Medicine Novi Sad. (NEBOSJA STILINOVIC)		Basic proposal
18. Optimization of preclinical testing of hepatotoxic drugs	18.Serbia. FMUNS (IVAN CAPO)	up to 2 months (end of 2019 or beginning of 2020)	Basic proposal

List of topics for STSM proposed	List of centers willing to HOST STSM candidates	Expected duration	
19. Quantification of markers of oxidative damage, lipid peroxidation products, enzymatic and non-enzymatic antioxidant molecules and their alterations on drug induced animal	19. Republic of North Macedonia (JASMINA DIMITROVA-SHUMKOVSKA)	1-2 candidates during the third grant period	Basic proposal
21. Liver cell population isolation and culture models for DILI	21. United Kingdom. Nottingham University (ANDREW BENNETT)		Basic proposal
22. Development of 3-D culture for modelling DILI	22. United Kingdom. Nottingham University (NICK HANNAN)		Basic proposal
23. <i>In vivo</i> evaluation of mitochondrial function using Liver Magnetic Resonance Spectroscopy techniques	23. United Kingdom. Nottingham University (Guru GURUPRASAD AITHAL)		Clinical proposal

Application extended UNTIL 31st of December 2020!!!

**4. Discussion about management rules for activities
2020/21**

b. Training schools

4. Discussion about management rules for activities 2019/20
b. Training schools

TRAINING COURSES DONE

Assessment of Drug-Induced Liver Injury: Key Rules And Common Pitfalls.

How To Make a Clinical Narrative (Spain) March 2019

Pending ERT Recognition by EUROTOX as an educational course

COST-DILI supported fellowship Oct 2019. Lisbon Conference Eurotox **Stem cells technology** (a side meeting on stem cells in DILI) October 2019

Suggest topics that you wish to be covered in the new Training Courses
/School organized by the Cost Action

EASL School of Hepatology Thematic Workshop. WG3 propose to apply to EASL in 2021-2022 to establish a high-profile hybrid (taught/ practical) workshop on DILI focusing on basic liver cell science.
Major sponsors will be sought such as Gilead and Biopredic International to provide financial/ in-kind support.

To Make Training courses on line?

4. Discussion about management rules for activities 2020/21

- a) STSMs ITC Conference Grant (J Cubero)
- b) Training school (L Nelson, GP Aithal)
- c) Info Day on DILI (H Glasová)
- d) EASL 2021 meeting of the DILI Consortium (Agenda)
/EACPT 2021 meeting (H Glasová)
- e) Monothematic Conference planning (Thomas Hammond)
- f) Dissemination

EASL CONFERENCE 2021 JUNE

Make a Info DAY in DILI with ELPA ?

EACPT CONFERENCE 2021 GREECE

DILI SESSION-WORKSHOP-ROUNDTABLE

Topic – preliminary title: DRUG-INDUCED LIVER INJURY: INNOVATIVE APPROACHES IN DIAGNOSIS AND MANAGEMENT

Chairpersons/Moderators: *Prof Lucena / prof Andrade (Spain) + Helena Glasová / Co-chair (tbi)*

Topics to be possibly covered:

1. New biomarkers in DILI. From drug development to post-marketing
2. Management of DILI related to immune check points inhibitors
3. Clinical trials in DILI. Where do we stand?
4. RECAM: revised causality assessment method in DILI: a collaborative initiative
4. Hypersensitivity syndrome and DILI. What do they have in common?
5. Chronic DILI: Risk factors and diagnosis
6. DILI in patients with pre-existing liver disease
7. Acetaminophen overdose: biomarkers for early DILI recognition and translation into clinical practice

**4. Discussion about management rules for activities
2020/21**

d. Monothematic conference. Thomas Hammond

DISSEMINATION ACTIVITIES 2020

ProEuro DILI network we have received a request to provide a speaker for the

23rd International Symposium on Microsomes and Drug Oxidations conference, to be held **30th August – 3rd September 2020** in Prague, Czech Republic.

Title: “Pharmacogenomics in Mechanisms of Idiosyncratic DILI in Man” in the session **_Metabolizing enzymes in drug-induced toxicity _**

Speaker: **Prof Ann Daly, Newcastle, UK Confirmed European DILI Consortium and Newcastle University**

POSTPONED SUMMER 2021

DISSEMINATION ACTIVITIES 2020

NEW SCENARIOS OF COLLABORATIONS HAVE BEEN OPENED

- **Upcoming collaboration between The International Autoimmune Hepatitis Group (IAIHG) Led by Diego Vergani and the Pro-Euro DILI Network CA-17112.** Prof Vergani couple have listed a huge number of connections such as the IAIHG Registries or the Swiss Autoimmune Liver Disease Register. A priori a **Consensus Conference** proposed by Prof Andrade between IAIHG experts and the CA members to agree upon definition and diagnostic criteria in DILI-AIH was very well welcomed.
- **Setting-up of a working group on pediatrics by Prof. Cigdem Arikan, Turkey.** To harmonize definitions, causes needed to be excluded on DILI in children taking advantage of what we have learnt from adults.
- **Collaboration with the European Liver Patient Association (ELPA): the relevance of a patient perspective in DILI .**

Publications funded by COST shall be a direct result of work performed by Action Participants and shall be co-authored by Action Participants **representing at least 3 different Participating COST Full Members / COST Cooperating Members.**

Whenever possible, publications should be made available under Open Access licences.

1.State in the acknowledgement : "**This article/publication is based upon work from COST Action "CA17112 - Prospective European Drug-Induced Liver Injury Network" supported by COST (European Cooperation in Science and Technology).** www.cost.eu"

2.QUALITY & IMPACT criteria:

- the article processing fees (APF) charged to COST may not exceed the APF published on the journal's Web site.*

- Peer-review process:** *All of a journal's content, apart from any editorial material that is clearly marked as such, shall be subjected to peer review. Peer review is defined as obtaining advice on individual manuscripts from reviewers, expert in the field who are not part of the journal's editorial staff. This process, as well as any policies related to the journal's peer review procedures, shall be clearly described on the journal's Web site.*

- Impact of the publication to be assessed along the SCImago Journal**

Rank (SJR)³: *Any journal that is situated in the first three quartiles⁴ Q1-Q3 is considered of sufficient impact, while journals in the last quartile Q4 or journals not contained in the SCOPUS database need an assessment by the responsible SO; the SJR and quartile (Q1, Q2, Q3 or Q4) for each journal contained in SCOPUS can be obtained from the SCImago web page (accessible at <http://www.scimagojr.com/journalrank.php>)*

Montpellier meeting Dominique Larrey, Sept 2021

to organize a meeting in April or May 2021 .

The estimate is presented in the joined piece.

The simulation has been done for a meeting on 12 and 13 April according to the availability and COVID.

The meeting room for 196 persons and space for reception for 2 days 2200 EUR instead of 4400 EUR (as I am a member of the university we would have a 50% discount).

The social program might include :

- Visit of the old university of Medicine in the center of the City founded in 1221
- Visit of the Museum of Anatomy and the botanic garden for medicinal plantes.
- Conference in english about the history of the school of medicine which is in its 800th birthday in the old school in the historical Theatrum Anatomicum.

There is no fee for the social counterpart which is managed by the Association of History of Medicine. But a donation would be wellcome.

WGs KAUNAS Meeting , Simona, last quarter of the year, f2f




4. Action implementation planning

- a. Monitoring of the Objective Achievement Indicators for MoU Objectives**
- b. Activity and budget planning (Work and Budget Plan preparation)**
- c. Dissemination strategy/ planning (Publications and outreach activities)**

a. Monitoring of the Objective Achievement Indicators for MoU Objectives

Input from all WGs Leaders, co-leaders

Create a collaborative group of members in this COST action and reach out other potential cost initiatives to advance knowledge on the diagnosis and management of DILI in patients with COVID 19 with and without preexisting liver conditions

	TASKS	DELIVERABLES
WG 1. IN DETH PHENOTYPING DILI	Standardize forms for prospective data collection, improved CAM 	<ul style="list-style-type: none"> ✓ Review: DILI diagnosis and management ✓ Conduct a system  review of published data on DILI diagnosis and (management WG4) ✓ A monothematic conference on DILI jointly with European Professional Societies
WG 2. DILI RISK STRATIFICATION	Systematically review techniques to evaluate DILI risk, and model clinical outcomes	<ul style="list-style-type: none"> ✓ Scientific publication on the current knowledge DILI risk modifiers ✓ Set up STSMs for ECIs to learn about systems biology networks and pharmacometrics
WG 3. PRECLINICAL EVALUATION OF DILI	Review in vitro and in silico models of hepatotoxicity: strengths, limitations, applications in pre-clinical evaluation	<ul style="list-style-type: none"> ✓ A review of current and potential <i>in vitro</i> and <i>in silico</i> models of hepatotoxicity 

	TASKS	DELIVERABLES
WG 4. CLINICAL TRIALS	<p>Define design and outcomes measures to optimally plan future clinical trials</p> <p>Review and evaluate therapeutic options for patients with DILI</p>	<ul style="list-style-type: none"> ✓ Set up STSMs and exchange programs for ECIs with the Regulatory Agencies ✓ To standardize procedures and remove bottlenecks at each participating center that would facilitate the future conduct of a multicenter clinical trial in DILI (mapping network of centers for conducting clinical trials in DILI)
WG 5 KNOWLEDGE DISSEMINATION	<p>Coordinate the set-up and maintenance of the Website and social networks promotion of the Action and maintain updated information on recent activities and downloadable resources</p>	<ul style="list-style-type: none"> ✓ Mid-term review of the COST Action proposal with the Management Committee (MC) to implement corrective measures if deemed necessary

Quality plan and good practice policies

Web

<https://proeurodilinet.eu/>

SOCIAL MEDIA PLATFORMS

Twitter: under "@EuropeanDILInet"

Linkedin:

<https://www.linkedin.com/company/12989961>

COST ACTION' PLANS Progress Report 2019

1. To **grow EIC/ITC leadership**. next two meetings held in ITC AND organized by ECIs. **Setting up an ECI forum** for further developing leadership skills.
2. **Provide mentorship to ECIs particularly from ITCs.**
3. **To assist in the development of ECIs through education and capacity building:** We will encourage ECI oral presentations and look to incorporate poster sessions into our future CA17112 meetings.
4. **Establish links with Regulatory agencies** to initiate training programs.
5. **Update website (<https://proeurodilinet.eu/>) to advertise funding opportunities and open a public page** run by ECIs
6. Organizing a one-day **Drug-induced liver injury Monothematic Conference, and an INFO DAY**, primarily organized by ECI participants within the action.
7. **Reach out** to other groups, societies
8. **Ensuring strong representation of ECIs and gender balance on all Committees/WGs.**
9. The setting of principles **to ensure family-friendly practices**

Action budget status

❖ Grant Holder

Biomedical Research Institute of Malaga (IBIMA)- FIMABIS Foundation

Grant Holder Manager: Marina Lozano (marina.lozano@fimabis.org)

1st GP REPORT (01/11/2018 - 30/04/2019)

Total Networking expenditure	43.896,59 €
15% of Eligible Networking expenditure	6. 584,49 €
TOTAL ELIGIBLE COSTS until 30/04/2019	50. 481,08 €

Cash Balance = 68.735,50 € - 50.481,08 € = 18.254,42 € (*Budget not executed*)

Action budget status

❖ Grant Holder

Biomedical Research Institute of Malaga (IBIMA)- FIMABIS Foundation

Grant Holder Manager: Marina Lozano (marina.lozano@fimabis.org)

2nd GP

Total Eligible Networking expenditure	95.652,16 €
15% of Eligible Networking expenditure	14.347,82 €
TOTAL ELIGIBLE COSTS	109.999,98 €

Estimated Expenditures 2nd GP

3 th Core Group & 2 nd Working Group (Palermo)	15.563,44 €
2 nd Training School (Lisbon)	12.789,95 €
3 th MC & 4 th CG (Lithuania)	€
Dissemination	3.084 €
ITC Conference Grant (Helsinki)	1.140 €
STSM	20.835 €
Total	45.102,39€

Action budget status

❖ Grant Holder

Biomedical Research Institute of Malaga (IBIMA)- FIMABIS Foundation

Grant Holder Manager: Marina Lozano (marina.lozano@fimabis.org)

2nd GP Report (01/05/2019-30/04/2020)

Total Networking expenditure	45,102,39 €
15% of Eligible Networking expenditure	6. 765,36 €
TOTAL ELIGIBLE COSTS until 30/04/2020	51,867,75€

Cash Balance = 109.999,98 € - 51.867,758 € = 58.132,23 €

(Budget not executed. This amount includes the budget not executed in the 1st GP)

Action budget status

❖ Grant Holder

Biomedical Research Institute of Malaga (IBIMA)- FIMABIS Foundation

Grant Holder Manager: Rosa Gómez (rosa.gomez@ibima.eu)

3rd Grant Period (01/05/2020-30/04/2021)

Total Eligible Networking expenditure	88.695,55 €
15% of Eligible Networking expenditure	13.304,35 €
TOTAL ELIGIBLE COSTS	102.000,00 €

Estimated Expenditures 3rd GP

4 STSM	11.700,00 €
Other Expenses related to Scientific Activities (Zoom Networking tool)	265,78 €
TOTAL	11.965,78 €

MoU Objectives

Objective 1

To develop a shared understanding of the key issues related to signals of hepatotoxicity in preclinical models/ experiments, clinical trials, and large electronic medical records, methods of detecting these in experimental models and clinical practice in addition to monitoring this for regulatory as well as pharmacovigilance purposes.

Objective 2

To systematically review potential risk factors associated with hepatotoxicity and biomarkers indicating DILI throughout the life course of a drug including pre-clinical development, in vitro investigations, clinical trials and post-marketing phase.

Objective 3

To establish standardized prospective data collection procedures and to develop an infrastructure for heterogeneous data and sample sharing.

Objective 4

To develop a functional strategy that is adaptable Europe-wide and beyond for an early identification of DILI, evaluate the performance of established and novel near patient DILI diagnostic tools, harmonize the criteria used for DILI diagnosis and its in-depth Phenotyping.

Objective 5

To harmonize nationally and internationally funded research activities towards a common goal and providing bench, bedside and population perspectives. Mutual understanding between academia, clinicians, pharmaceutical and regulatory agencies will establish a strong scientific base for European regulatory decision-making processes, public awareness and education.

Objective 6

Create a mutual strategy to optimize the training capacities related to DILI currently available at different cross-border stakeholders via exchange programmes.

Objective 7

Improve institutional capacities of participating centres by providing support to reach a minimum set of standards that would ensure high-quality research activities through STSMs.

Objective 8

Establish effective channels of communication between preclinical researchers, clinicians, scientists in different disciplines, SMEs, industry representatives and regulatory bodies through annual DILI conferences and joint meetings with regulatory Authorities.

Objective 9

Facilitate exchange of professional expertise, research material/ data between experienced researchers and ECIs through workshops and training summer schools.

Objective 10

Provide mentorship to ECIs with the adequate induction into DILI and preparing them to be actively involved in future cross-border multi-centre, multi-disciplinary studies.

Objective 11

Develop strategies to involve patients who have suffered DILI and to provide public education for the purpose of prioritising research questions in DILI field, identifying gaps in clinical service relevant to DILI subjects and improving public awareness.

Deliverables

Deliverable 1

Capitalizing on already existing databases in DILI to develop a standardized approach to diagnosis and to prepare standard operating procedures (SOPs) for the most appropriate collection and storage of all biological samples (liver biopsy, serum, plasma, DNA, urine and stool) related to DILI.

Deliverable 2

WG1-Coordination of the development of pre-funded database of DILI patients providing a framework for the access to patient cohorts from different EU countries.

Deliverable 3

WG1-Conduct a systematic review of published data on DILI diagnosis and management.

Deliverable 4

WG1- Development of a classification system for HDS which may increase HDS induced-liver injury recognition, improve causality assessment and foster research in this area.

Deliverable 5

WG1- Development of a consensus document on the diagnosis, classification, assessment and treatment of DILI in addition to standardization of nomenclature and causality assessment to harmonize the criteria used for DILI diagnosis in clinical practise across Europe.

Deliverable 6

WG2-Focus on the array of existing research techniques and expertise among the Action members in order to come up with an EU Framework translational research plan for biomarker development - as well as cutting edge research techniques tailored to this need.

Deliverable 7

WG2-Scientific publication to summarize the current knowledge on 1) Drug properties associated with hepatotoxicity; 2) Host factors considered to modify an individuals' risk of DILI and clinical phenotypes; and 3) Drug-host interactions to improve risk stratification in patient care.

Deliverable 8

WG2-Written input to one or more commercial enterprises necessary for Future Market Exploitation of biomarkers.

Deliverable 9

WG2- Scientific publication to summarize the current knowledge on Drug properties associated with hepatotoxicity.

Deliverable 10

WG3- A review of current and potential in vitro and in silico models of hepatotoxicity.

Deliverable 11

WG3- Identify and list the most appropriate control compounds for testing new in vitro models.

Deliverable 12

WG3- Define a roadmap for the development of in silico, in vitro and experimental models incorporating host determinants of DILI.

Deliverable 13

WG4- To standardize procedures and remove bottlenecks at each participating centre that would facilitate the future conduct of a multicentre clinical trial in DILI.

Deliverable 14

WG4- A proposal for study design for risk or biomarker evaluation, pathway for evaluating of diagnostics and appropriate statistical methods.

Deliverable 15

WG4- Design of clinical trials in DILI to assess the effect of an intervention on disease course or clinical outcomes.

Deliverable 16

WG5-Set up a Website and social networks to translate scientific efforts into public dissemination and regulatory bodies.

Deliverable 17

WG5- Write a Quality Plan and Good Practice Policies that apply to all COST partners.

Deliverable 18

WG5- Mid-term review of the COST Action proposal with the Management Committee (MC) to implement corrective measures.

Deliverable 19

WG5- Preparation of large-scale European projects, searching topics of interest at H2020, 9 EU Framework Programme and other funding programmes.

Deliverable 20

WG5- Organise the Closing meeting and Final Report in which a roadmap to DILI research in Europe will be presented.