Information to be requested from all CA17104 participants:



Indicate your Working Group(s) in COST Action17104:	WG4
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Link to webpage with biography:	-

Link to webpage		
with group	-	
description:		

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Expertise relevant for this COST Action:	EARLY SAFETY ASSESSMENT OF NEW THERAPEUTIC COMPOUNDS FROM NATURAL AND SYNTHETIC ORIGIN. General toxicity testing of acute, subacute and sub chronic toxicity to evaluate the degree of toxicity in a quantitative and qualitative manner, to provide a reliable set of information on the dose levels, to identify the eventual target organs of toxicity. - In vitro models: cell cultures, isolation of primary cells (hepatocytes, macrophages, lymphocytes), isolation of subcellular fractions, i.e. liver mitochondria, liver microsomes. - In vivo animal models: observations of general condition and behavior by non-invasive methods (general behavior, autonomic and central nervous system (e.g. irritability, somnolence, reduced/enhanced motility, drowsiness, ect.), circulatory system (heart rate, blood pressure), mucous membranes (color, ulcers, moisture), ect. - Clinical pathology assessment by invasive methods: hematology and clinical chemistry analysis, urinalysis. - Post-mortem evaluations (histology preparations for target organ toxicity)

PRE-CLINICAL ASSESSMENT OF HEPATOTOXICITY

In vitro toxicity screening by comparative cell based models:

- *transformed cell lines* (i.e. immortalized human hepatocytes cell i.e HepG2 to predict *in vivo* toxicity through *in vitro* techniques)
- *primary cells* (isolated primary rat hepatocytes the "gold standard" used for predictive toxicology)

Outcomes and detection methods

- Adaptive / pre-lethal mechanistic endpoints: generation of reactive oxygen species (ROS), GSH depletion, lipid peroxidation (MDA assay), mitochondrial homeostasis, inhibition of enzymes (SOD, Catalase)
- Cell death / survival endpoints:
 cytotoxicity evaluation MTT assay,
 Alamar blue, Neutral red assay, etc.,
 loss of membrane integrity, organelle
 swelling (Cytochrome c release), ATP
 and LDH leakage

NANOTOXICOLOGY – IN VITRO AND IN VIVO MODELS FOR NANOTOXICITY EVALUATION.

Biocompatibility assays of the novel nanosized drug delivery systems from organic (biopolymers, i.e. chitosan/ alginate nanoparticles) and inorganic origin (i.e. mesoporous silica nanoparticles, i.e. MCM-41, SBA, HMS).

Available facilities to conduct work, relevant for this COST Action:

Cell Culturing Facilities: Synergy 2 Multi-Mode Reader, laminar flow cabinets, CO2 incubator, inverted microscopes "Optika". Selective automatic biochemical analyzer BS-120; Automatic hematology analyzer BC-2800

	Vet; High-speed centrifuge "Eppendorf", Vacuum centrifuge Beckman, microplate swing- out centrifuge rotor, Universal microscope digital camera. Animal Facilities (certified vivarium) for non- clinical ADME/ Toxicity studies. Human and animal cell lines of diverse tissue
Matherials/Methods that could be shared with other members of this COST Action:	origin – cancerous or normal. Cytotoxicity assays, wound healing migration assay, hemolysis microplate assay, models of oxidative stress-damaged cell culture, in vivo biochemical assays, ADME studies. Measuring fluorescence intensity, fluorescence polarization, timeresolved fluorescence, luminescence and UV-visible absorbance in microplates.

NOTE: By submitting this form to the Grant Manager of CA17104, I agree that this information can be used within the scope of this COST Action (e.g. may be included on the webpage of CA17104).