Information to be requested from all CA17104 participants:

Indicate your Working Group(s) in COST Action17104:	**WG4**
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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 nano- sized 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.
Matherials/Methods that could be shared with other members of this COST Action:	Human and animal cell lines of diverse tissue 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, time-resolved 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).