BOOK OF ABSTRACT

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PLATE-FORME NANO SÉCURITÉ

6th international conference on HEALTH and SAFETY issues related to NANOMATERIALS for a socially responsible approach

5-9 November 2018

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TABLE OF CONTENTS

ORAL PRESENTATIONS

A91267AC

Enhanced protein corona characterisation using novel corona isolation and capillary electrophoresis-mass spectrometry techniques

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Since the nanoparticle corona rose to eminence, it has been investigated by a range of researchers trying to characterise and derive its significance. To date, liquid chromatography-mass spectrometry (LC-MS) is the favoured platform for protein corona characterisation. However, capillary electrophoresis-mass spectrometry (CE-MS) offers an exciting prospect to increase sample throughput and separate and detect highly polar and very large peptides missed by conventional nLC-MS platforms.

Silica NPs were incubated for 1 hr at 37 °C in plasma. On-particle digest particles were washed prior to immediate tryptic digest. The off-particle digest NP-corona complexes were boiled in SDS buffer and run on a SDS-PAGE gel prior to in-gel digestion. A SCIEX CESI 8000 Plus with a 90 cm neutral capillary and 30 kV separation voltage with 2 PSI for separation, detection was with a Thermo QExactive HF mass spectrometer.

Initially an on-particle digest in ammonium bicarbonate buffer was performed and resulted in 1844 peptide and 121 protein identifications. The CE-MS analysis was highly reproducible with 40% of peptide peak areas with <10% RSD. However, the reproducibility for sample preparation was poor, with only 48% of peptides seen in all experimental replicates. To ameliorate this, RapiGest SF and/or urea were investigated to ensure peptides remained solubilized and not re-adsorbed onto the nanoparticle. The addition of RapiGest SF proved optimal compared with urea and pure buffer, enabling the detection of 196 proteins and 2255 peptides. The number of peptides with peak area RSD >50% fell from 32% to <10%. RapiGest SF also resulted in the least number of missed cleavages. The on-particle digest was compared to an in-solution digest and in-gel digest of the protein corona. The on-particle digest resulted in a greater number of peptides and proteins being identified. Interestingly there were proteins groups with significantly improved recoveries for different sample preparation methods. For example immunoglobulins were greatly improved with in-gel digest whereas apolipoproteins recoveries were lower with the RapiGest SF method. Thus highlighting the significance of understanding and valiadating the characterisation method prior to any modelling/QSAR analysis. In addition, this method has a much greater throughput; 12 samples per 8 hr work day compared to 4 samples for LC-MS. This work also represents the first demonstration of CE-MS for the analysis of the protein corona.

Session 1
1. Measurement and characterization of nano objects

A91362AA

CONTRAST ENHANCEMENT FOR LIPID NANOPARTICLES (LNPS) CHARACTERIZATION USING TRANSMISSION ELECTRON MICROSCOPY (TEM)

ARNOULD Amandine[1, 2], CAPUTO Fanny [3], BACIA Maria [4], TEXIER Isabelle [3], BOUTRY Delphine [3], AUGER Aurélien [1], SOULAS Romain [1], DAMLENCOURT Jean-François [2,3]

(1) CEA-LITEN, MINATEC Campus, F-38054 Grenoble, Grenoble, France; (2) Univ. Grenoble Alpes, F-38000 Grenoble, Grenoble, France; (3) CEA-LETI, MINATEC Campus, F-38054 Grenoble, Grenoble, France; (4) IBS, EPN Science Campus, F-38044 Grenoble, Grenoble, France Organic nanoparticles such as Lipid NanoParticles (LNPs) are generally difficult to characterize using Transmission Electron Microscopy (TEM) due to their low contrast [1]. Their characterization is all the more complicated since the suspension media is a liquid and is not compatible with TEM characterization (TEM column being under vacuum). To circumvent these issues, a work needs to be done on sample preparation before observation [2, 3].

This study is based on the characterization by TEM of LNPs, before and after incubation with proteins, to assess their stability. The studied nanoparticles are composed of an oil and wax lipid core stabilized in aqueous medium by surfactants [4]. Particle size distribution (PSD) and shape were characterized by TEM. In order to picture the particle morphology in their close-to-application environment, cryo-TEM and in-situ liquid TEM were performed. PSD collected by TEM methods were compared to the results obtained by batch mode DLS and after fractionation of the sample by FFF, followed by online MALS and DLS analysis.

Particles prepared using negative staining appeared to have different shape according to the oil/wax core ratio but the observation of their core/shell structure was not possible. Preparation using a cryogenic technique to fix the dispersion state of the particle was thus used. Cryo-TEM observation showed particle distortion which may come from the blotting process before freezing because of particle softness [5]. To avoid sample preparation artefacts, LNP were then observed thanks to an in-situ liquid holder but they could not be observed without functionalizing their surface. Particle grafting with metallic nanoparticles was thus performed on LNP surface to enhance TEM contrast. This strategy allowed the core/shell structure to be visualized. Particle interaction with proteins was also performed to mimic blood protein interaction. PSD obtained by AF4-MALS were correlated to TEM results during particle aging, confirming LNP stability. However, PSD obtained for LNP after interaction with proteins showed slight differences.

[1] “Electron Microscopy of Polymers”, ed. H Pasch, (Springer Laboratory, Germany) p. 175-183

[2] Micron 29 (1998), p. 145

[3] Biochimica et Biophysica Acta 34 (1959), p. 103

[4] Journal of Colloid and Interface Science 360 (2011), p. 471

[5] Current Opinion in Colloid an Interface Science 17 (2012), p. 316

Session 1
1. Measurement and characterization of nano objects

A91375TK

Experimental investigation on impact of fine particle less than 10nm on filtering efficiency of particulate respirators

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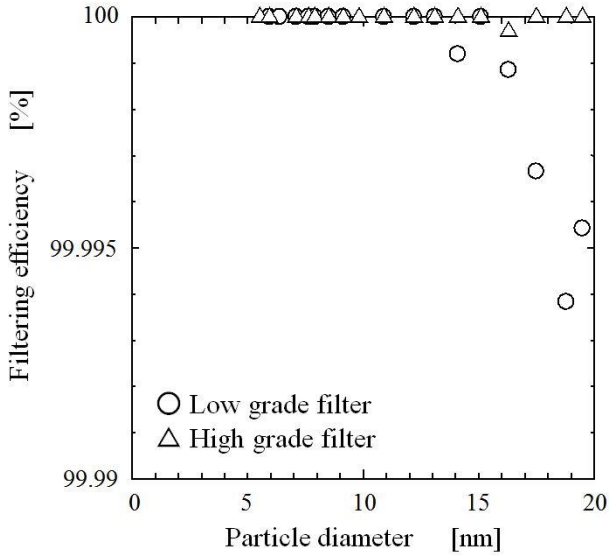
In the field of nanomaterial production, the diameter of nanoparticle such as functional materials tends to become small in order to improve performance of its materials. The risk for the exposure of the nanoparticles having the diameter less than 10nm should be reduced in terms of negative effect on human health. The particulate respirators is the promising way for the prevention from the exposure of the nanoparticles. However, its efficiency for the nanoparticles less than 10nm have not been assessed experimentally.

In this study, the nanoparticle generator based on sublimation of fullerene (C_{60}) was proposed in order to investigate the impact of nanoparticles less than 10nm on the filtering efficiency of the particulate respirators. Its generator consisted of a high temperature furnace for sublimation of fullerene (C_{60}). In order to check the performance of the proposed nanoparticle generator, number concentration with respect to particle diameters was measured with the scanning mobility particle sizer (SMPS). As the result, the nanoparticle generator proposed in this study stably could produce the nanoparticle less than 10nm, and high number concentration of particles more than 10^5 #/cm^3 at 8nm was achieved. It means that it was enough to assess the filtering efficiency of the particulate respirators for the particles less than 10nm by using the nanoparticle generator. Moreover, the filtering efficiencies of the particulate respirators with high and low grade performances were evaluated for the particles less than 10nm by using the proposed nanoparticle generator. As the results, as for the nanoparticle less than 10nm, the particle number concentration in the gas passed through the filter was almost zero regardless of grade of filters. Therefore, it was found experimentally that the particles less than 10nm were collected with the filtering efficiency of almost 100% by using the particulate respirators as shown in Fig.1.



Session 1
1. Measurement and characterization of nano objects

A91549PR

Purchasing Metal Oxide Nanopowders for Research: Buyer Beware!

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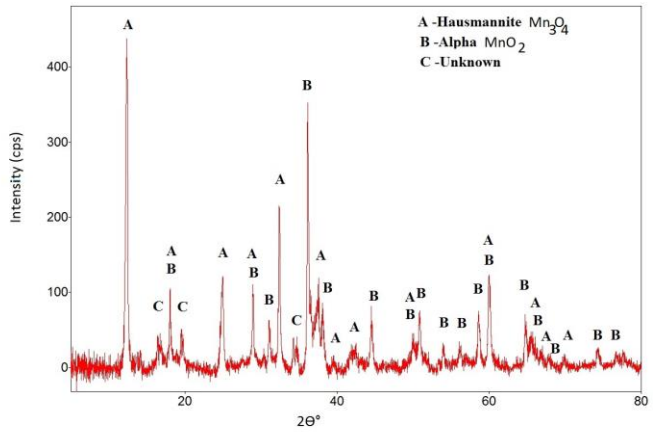
Eight metal oxides were selected for research on the dissolution behaviour of engineered nanomaterials (ENMs) dispersed in water and cell culture media. Suppliers of metal oxide nanopowders were identified by internet search, and products were selected based on particle size (≤50 nm using TEM) and other characterization information available (e.g. specific surface area). The following ENMs were obtained in dry powder form: zinc oxide (ZnO), nickel (II) oxide (NiO), titanium dioxide (TiO_2), cerium oxide (CeO_2), copper (II) oxide (CuO), aluminum oxide (Al_2O_3), manganese oxide (Mn_2O_3) and iron (III) oxide (Fe_2O_3). A Rigaku Ultima IV X-ray diffractometer (XRD Bragg-Brentano geometry) was used to confirm the compounds present in the purchased nanopowders. Additional information about the particle size distribution was obtained using Small Angle X-ray Scattering (SAXS) which works well in the 1 to 65 nm particle size range. Mn_2O_3 was purchased from two suppliers but neither contained Mn_2O_3 according to XRD analysis. One nanopowder sold as Mn_2O_3 (Figure 1) consisted mainly of alpha MnO_2 (avg 21 nm) and hausmannite (Mn_3O_4; avg 46 nm), with a small fraction of an unidentified compound (avg 55 nm). The second nanopowder sold as Mn_2O_3 contained two MnO_2 compounds: akhtenskite (83 wt%; avg 20 nm) and ramsdellite (17 wt%; avg 32 nm). Results for one Fe_2O_3 nanopowder indicated the presence of two different compounds: gamma Fe_2O_3 (88 wt %) and synthetic hematite (12 wt %). As this mixed product was likely to yield inconsistent solubility results, a different supplier was selected whose Fe_2O_3 product was determined to contain >98% synthetic hematite (avg 14 nm). These results underscore the importance of double-checking the physical and chemical characteristics of ENMs obtained for research purposes.



Session 1
1. Measurement and characterization of nano objects

A91606JS

Micro sensor for the capacitive detection of airborne nanoparticles fabricated by combining 3D printing and lithography

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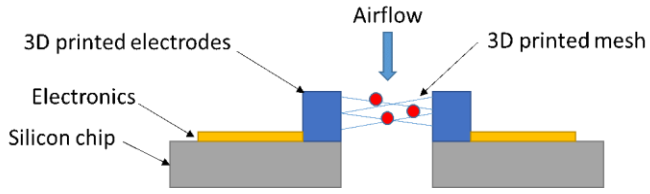
Most of the existing particle sensors are based on optical detection, measuring the light-scattering of the incoming particles. The main disadvantage is the need to integrate optical devices such as laser, photodetector and lenses, making the down-scaling of such sensors challenging. Capacitive methods have been widely used for the detection of gases, based on the change of electrical properties of a dielectric material caused by the physical or chemical interaction with the target gas. The resulting signal is monitored with an electronic circuit integrated on a silicon chip by standard microfabrication processes.

In this study, capacitive sensing is used for the detection of airborne nanoparticles. The sensor is composed of a channel containing two electrodes that measure the change due to interactions between the electric field and the incoming particles. In order to detect nanoparticles, the sensitivity of the capacitive sensor is improved by increasing the electrode area: interdigitated finger-structures as well as 3D electrodes serve that purpose. This study uses 3D printing based on two-photon polymerization in order to add electrodes and functional structures directly onto the silicon chip. The channel between the capacitor plates is also modified by the addition of 3D printed microstructured polymer network able to retain small particles.

With the high precision (100nm resolution) of the 3D printing device, the influence of the structure's geometry (mesh shape and size, number of layers, geometry of the pores) will be investigated as well as the influence of modified photoresists with different additive materials. The selectivity of the sensor towards different types of particles will be evaluated.



Session 1
1. Measurement and characterization of nano objects

A91645OT

Metrology of Nanoparticles with Small Angles X-Ray Scattering (SAXS): from simple cases to nanoparticles in food additives

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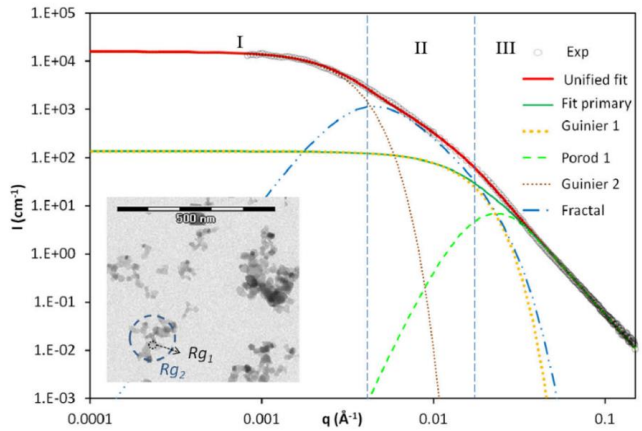
Small-Angles X-Ray Scattering (SAXS) has been established as a metrological method for the determination of nanoparticles size and size distribution. Modern SAXS Laboratory experiments [1], by involving synchrotron-based instrumentation at lower price and very stable X-ray source, are more and more used in nanomaterials metrology.

In the frame of the EURAMET Innanopart project, we have developed a methodology for the size, size distribution and concentration determination of spherical nanoparticles. This protocol involves a precise sample preparation, a rigorous procedure for the data acquisition, and a set of homemade software tools for the data processing - from the acquisition, the absolute scaling, to the analysis.

The SAXS technique is very accurate for the characterization of simple case using nanoparticles: monodisperses, spheric form, unique composition. But it is more complicated in the case of nanoparticles size mixtures and in case of nanoparticles in complex media.

Recent works in the lab shows it is possible to achieve precise measurement on mixture of spheric nanoparticles and nanoparticles in complex media (food additives) using different software or methodology approaches.

[1] Olivier Taché et al., « MOMAC: a SAXS/WAXS laboratory instrument dedicated to nanomaterials », Journal of Applied Crystallography 49, no 5 (1 octobre 2016): 1624?31, https://doi.org/10.1107/S1600576716012127.



Session 1
1. Measurement and characterization of nano objects

A91704MX

Aerosol sampling techniques using TEM grids

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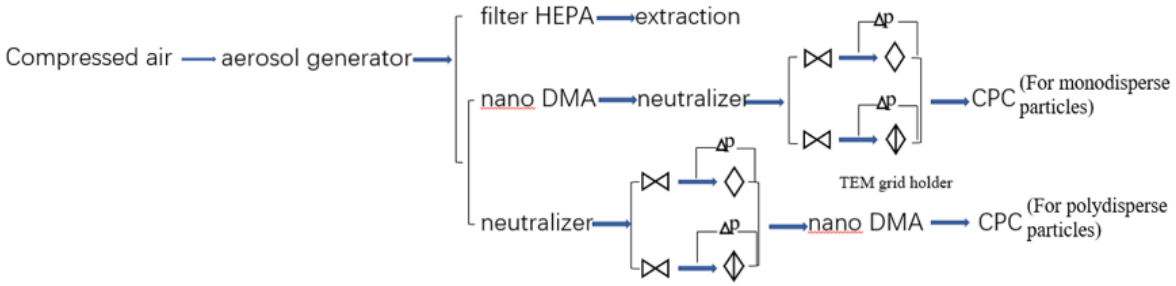
Non-intentional nanoparticle (NP) may occur in aerosol production process. Occupational safety and environment protection associated with the nano-aerosol exposureare serious issues. Nano-aerosol measurement is a key point to characterize NP exposure. Transmission electron microscopy (TEM) is the only technique for gaining sizes distribution and individual particle analysis. However, observation with techniques allowing sampling on TEM grids is crucial to aerosol analysis. There is a need to develop sampling devices that will make possible aerosol speciation and quantification according to class sizes for efficient characterization. Make the measurements quantitative when sample aerosol and analyse particles on TEM grids using MPS developed by INERIS both through experiments and modelling is important. Assess the sampling efficiency and optimize the set up based on TEM analyses technique are the main work.

Aerosol generators, mini particle sampler (MPS) and scanning mobility particle sizer (SMPS) are carried out to evaluate the sampling efficiency. In this way measurement and analysis can be carried out at real time. Three set up method plays an important role. NaClatomizer and WOx nano-aerosol generator are used to generate NP with diameter 10-130nm and 0.8-30nm. For the TEM grid filtration, “Holey” type and “Quantifoil” typecarbon films are fitted with a 400 “mesh” copper grid then installed in the MPS. The overall collection efficiency of each gridand collection efficiency of the holey carbon filmare compared to get the best efficiency. By using MPS and TEM analysis, sampling is made directly and easily. The influence factors are taken into account. According to the experiment and the empirical approach, a theory model is developed to assess the sampling efficiency. Furthermore, the expose risk of the nanoparticles during the processing of the nanoparticles is evaluated using the Short Time Sampling (STS) approach.



Session 1
1. Measurement and characterization of nano objects

A91743MM

CHARACTERIZATION OF NANOMATERIALS IN CONSUMER PRODUCTS AND MEDICINAL SAMPLES. FROM ROUTINE ANALYSIS TO ADVANCED METHODOLOGIES

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Nanomaterials (NMs) are now part of our daily lives by their presence in many consumer products. In spite of the extended use of NPs in diverse consumer products, there is a great concern over the unexpected impact or effects on humans and on the environment. In this context, it has become necessary to assess and control the exposure of the population but also to inform consumers with increased transparency, traceability and regulation of NMs.

To date, there is no regulation for the manufacture, handling, and marketing of NMs. However, specific EU regulations for food, cosmetics and biocides aim to ensure that the presence of NMs in the finished product is indicated on the label. Nowadays, no technique can simultaneously determine the main physicochemical properties of NMs. The complete study of consumer products relies on a set of complementary analytical techniques that are often time-consuming and complex to implement. As a result, it is necessary to develop routine analytical approaches in order to respond quickly to the expectations of industrials, control laboratories and consumers. Dynamic Light Scattering (DLS) and Single Particle Inductively Coupled Plasma Mass Spectrometer (SP-ICP-MS) were retained to determine the particle size characteristics (size, size distribution, polydispersity) and/or the chemical composition and the concentration of the metallic nanoparticles. For this purpose efforts were focused on the sample preparation methodology and the optimization of operating conditions. For the validation, results were compared with ones obtained with advanced analytical techniques such as the coupling of Asymetrical Flow Field Flow Fractionation with a particle size detector and an inductively coupled plasma mass spectrometer (A4F-MALLS-ICP- MS) or scanning electron microscopy (SEM).

The second part of this work was focused on the development and validation of analytical methodologies for the characterization of polymer based nanopharmaceuticals according to GMPs (H2020 European Project NanoPilot). Various analytical techniques were employed such as DLS, A4F-UV-MALLS, Size Exclusion Chromatography – UV-MALLS-RI to characterize raw materials and final products. In parallel, the same analytical methodologies were employed for the in-process control to evaluate the production yields and the encapsulation efficiency of formulations.

Session 1
1. Measurement and characterization of nano objects

A91767LG

Optimization of AF4-ICP-MS and Sp-ICP-MS methods for titanium dioxide nanoparticles characterization in food product

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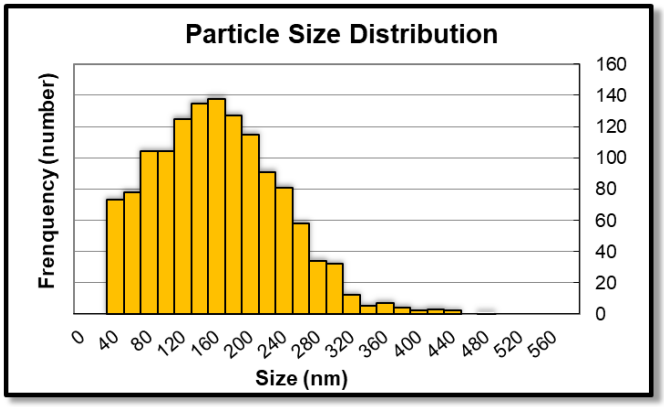
Titanium dioxide (TiO2) is used as food additive (E171) in order to make products whiter and/or shiny. Since 2012, it has been demonstrated that TiO2 in E171 can be partially present under NanoParticle (NPs) form. Despite the regulation imposing the reporting of nanoparticles presence in foodstuff, it remains difficult for food analysis laboratories to accurately quantify the nanoparticle fraction in food products with common analytical approaches.

This study focuses on the development of two complementary liquid methods for TiO2 NPs characterization in food, namely Asymmetric Flow-Field Flow Fractionation coupled with Inductive Coupled Plasma – Mass Spectrometry (AF4-ICP-MS) and Single Particle approach (Sp-ICP-MS).

The AF4-ICP-MS method consists in fractionating particles according to their size along a semi-permeable membrane in a separation channel. Although relatively simple in principle, electrostatic interactions of NPs with the membrane may have a great impact on the separation efficiency and recovery of the particles. In an attempt to evaluate the role of several parameters such as pH, ionic strength and chemical nature of eluent on these interactions and to optimize the analysis, the zeta potential of the particles and of the membrane were measured. From these results, relevant eluents were tested in AF4-ICP-MS analysis of TiO2 and showed that the ionic strength was a crucial parameter for the recovery of particles.

Sp-ICP-MS approach for NPs characterisation is a recent and promising method that allows size measurement of particles without any upstream separation technique. In this study, the impact of spectral interferences on the different Ti isotopes was assessed. Next, the main parameters such as dwell time and chemical nature of the eluent were optimized. The optimised method based on Sp-ICP-MS was applied to the analysis of food products containing the E171 additive.



Session 1
1. Measurement and characterization of nano objects

A91768AS

NANOPARTICLE FORMATION AND EMISSIONS DURING LASER ABLATION OF CERAMIC TILES

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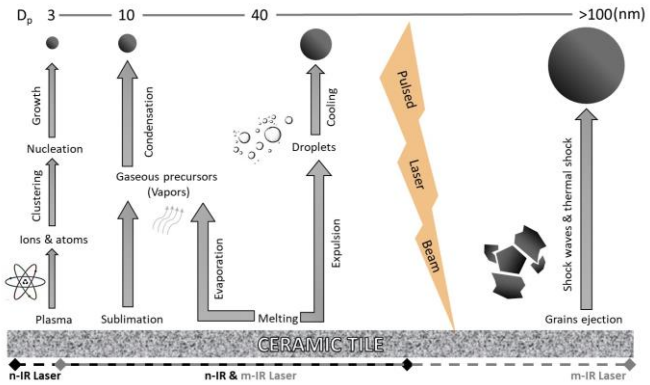
Pulsed laser ablation (PLA) is proposed as an alternative to conventional techniques for surface structuring and tile decoration in the ceramic industry, which is known to generate nanoparticle emissions. This study comprehensively describes the mechanisms controlling NP formation and release during PLA of different types of ceramic tiles (Figure 1), using different laser setups (near-IR and mid-IR).

The measurements took place at laboratory- as well as at pilot-plant-scale, and the process parameters evaluated were laser wavelength, frequency, velocity, and pulse duration. In total, the combination of 4 types of ceramic tiles (conventional and advanced) and 2 lasers was assessed. NP characteristics measured were particle number concentration and size distribution (SMPS, DiSCmini and CPC), particle mass concentration (DustTrak-DRX), and NP morphology and chemical characterization (TEM/EDX).

NP release in high concentrations was evident ($3.5*10^4$/cm^3 - $2.5*10^6$/cm^3) from all of the materials tested and under both laser setups. The formation of NPs <10 nm by nucleation was confirmed. Amorphous SiO_2 NPs (>10 nm) were formed and released during ablation of the porcelain tiles. The release of primary NPs (70-100 nm), linked to melting phenomena (droplets) was confirmed and found to contribute to the emissions in terms of particle number concentration. Different mechanisms were identified as NP sources during ablation of ceramic tiles: nucleation and melting with the near- and mid-IR lasers, and mechanical shockwaves only with the mid-IR laser. Finally, a link was observed between NP number concentration and ceramic tile surface properties. This work presents a synergistic approach bringing together nanoparticle and ceramic tile research to shed light on the mechanisms controlling unintentional NP generation during laser ablation.



Session 1
1. Measurement and characterization of nano objects

A91811ME

OPTIMIZATION OF PHYSICO-CHEMICAL PARAMETERS OF CHITOSAN NANOPARTICLES EXTRACTED FROM EXOSKELETON OF CRAYFISH

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Chitosan nanoparticles are favored due to their small size thus increasing the available surface area to interact with biological support. Consequently, chitosan nanoparticles can be applied in different fields. Various techniques are employed for the preparation of chitosan nanoparticles; however, ionotropic gelation technique is regarded as the best technique, since neither harsh nor inappropriate chemicals are used during the process. Some physico-chemical parameters have been evaluated to the prepared chitosan nanoparticles, such as: particles' size and surface morphology.

The main objective of this study was to allocate the most optimum condition to prepare the chitosan nanoparticles that will, subsequently, give the best physico-chemical characterization regarding: the nanoparticles' size and surface morphology.

Chitosan nanoparticles were prepared by using different concentrations of chitosan and the polyanion sodium tripolyphosphate (TPP). For the determination of the optimum condition for the prepared chitosan nanoparticles, three different ratios of chitosan to the polyanion, TPP were used, 1:1, 3:1 and 1:1.25, respectively.

A novel nanoparticle system composed of low molecular weight chitosan was successfully prepared by ionotropic gelation technique under aqueous-based condition. Results pointed out that using chitosan and TPP in a ratio of 3:1, resulted in the largest particles' size with large range. Whereas, when a ratio of 1:2.5 chitosan to TPP was used, both large size and aggregated particles were spotted. However, the optimum size of chitosan nanoparticles and less aggregation were obtained from the lowest chitosan and TPP concentrations; ratio 1:1, respectively.

Keywords: Chitosan, Chitosan nanoparticles, *Procambarus clarkii*, Ionotropic gelation technique, Physico-chemical characterization.

Session 1
1. Measurement and characterization of nano objects

A91813SJ

Detection of nanoaerosols using ionized air

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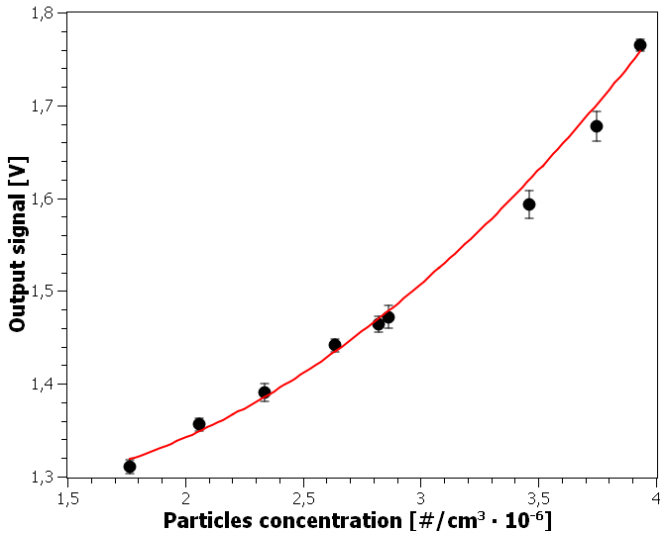
While application of nanoparticles into consumer products grows every year, increasing number of employees manufacturing these products is exposed to their harmful impact. One of the major issues with nanoaerosols is that they can be invisible to human eye, so if emission is caused by a failure (i.e. depressurization of agitator) there is no clear warning about hazard. Therefore there is a need for a simple and low cost device to detect and inform about presence of nanoaerosol, which can be used on industrial plants where nanoparticles are produced, used as ingredients or created as byproducts.

Ionization smoke alarm was modified by exposing three pins connected to ionization chamber voltage, supply voltage and ground. Voltages were measured using microcontroller with analog-digital converter. Output signal was calculated as a difference between supply voltage and ionization chamber voltage. Nanoaerosol was generated using Palas GFG 1000 generator with graphite electrodes. As output signal from ionizing chamber changes with both air flow and particle concentration measurements were performed at constant air flow of 0.012 m/s. Nanoparticles concentration was measured using TSI NanoScan SMPS 3910. Generated nanoaerosol had lognormal size distribution with mean particle diameter of 39.8 nm. Measured sensor output for both still air and in flow with velocity of 0.012 m/s was 1.140 V, although we observed that for higher velocities it drops due to the entrainment of ions from ionization chamber. Device output signal decreases with increasing particles concentration. Relationship is linear for particles concentration range up to 3·10^6 particles/cm^3 (coefficient of determination equal 0.9987). In the whole measured concentration range results can be approximated with quadratic equation (coefficient of determination equal 0.9941). Therefore it was proven that ionization smoke alarm can be used to detect presence of nanoaerosol and determine its total concentration.



Session 1
1. Measurement and characterization of nano objects

A91836MS

CHARACTERIZATION OF DISPERSIBILITY AND STABILITY OF TIO2 NANOPARTICLES IN CELL CULTURE MEDIA WITH STATIC MULTIPLE LIGHT SCATTERING

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Since the last decades, nanoparticles (NPs) have been widely used in a broad range of industries such as cosmetic or food. In this context, concerns had been raised about the toxicity of such nanomaterials on human health. Thus, it is of paramount importance to understand the NPs behavior under conditions like those for in vitro or in vivo nanotoxicity studies.

The preparation protocol of the NPs dispersion greatly impacts their properties and their resulting toxicity [1]. Indeed, it has been proved that NPs agglomerate immediately when added to a cell culture medium and results on false dose estimation and *in fine* false toxicity interpretations [2]. Classically, proteins serums such as bovine serum albumin (BSA) or fetal bovine serum (FBS) are added to the dispersion to coat the NPs and avoid agglomeration. However, the dispersion method (whirling, sonication…), both the BSA and NPs concentrations and the cell culture medium influence the BSA-NP interactions [3]. Then, the characterization of the stability and dispersibility of the NPs over time is very important to obtain a well-controlled dispersion for toxicological studies.

In this study, we propose to use static multiple light scattering (S-MLS) to:

- Evaluate the particle size related to the dispersion state and the stability of a TiO2 NPs stock dispersion in BSA-water solutions.

- Estimate the dispersibility of the NPs stock dispersion diluted in presence or absence of cell culture media (e.g. DMEM) via the mean particle size.

The S-MLS provides a non-intrusive optical characterization of a native sample without dilution. An infrared light source illuminates the sample and the backscattered (BS) and transmitted (T) light intensity signals are collected simultaneously by two sensors over the whole samples height and repeated over time. The resulting spatial and time dependent signals T and BS are directly linked to the fundamental propreties of the dispersion (particles mean size, concentration) as well as physical instabilities (aggregation, sedimentation…).

This all in one technique is promising for controlling the preparation of a well dispersed NPs dispersion for studies on the impact of individual NPs.

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[2] Ji, Z, et al. Environmental science & technology 44.19 (2010): 7309-7314.

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Session 1
1. Measurement and characterization of nano objects

A91837PO

Real-time monitoring, sampling and microscopic analysis of nano-objects suspended in the air at workplaces

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There is currently a rapid growth in production and use of nanomaterials in a form of nano-objects, their aggregates or agglomerates (NOAA), both in research and industry. By reducing the size of particles to a nanoscale we now have a new way of significant change of high-tech materials properties. The largest social group that have a physical contact with NOAA are employees of nanotechnology companies. Exposure can occur during their production, processing, transport, packaging and quality control.

It is very important to study a potential risks of inhalation exposure during the processes of production and handling of nanomaterials. Because nanomaterials are a very diverse group of chemicals, it is difficult to make general statements about their safety. They must be considered on a case-by-case basis, in the same way as any other chemical. Problems with safety of engineered NOAA rise from the lack of knowledge about their properties. Even if we know such properties for microsized counterparts, they can considerably change for the nanoscale equivalents. Risk management, exposure evaluation and prediction of NOAA toxicity requires a real-time monitoring of concentration in the air, sampling and characterization of physico-chemical parameters.

Despite many studies in this field, it is very difficult to compare the results of measurements, build statistical models, and forecast exposure at similar workplaces. In order to harmonize research on emission and exposure to nanoobjects, NECID (Nano Exposure and Contextual Information Database) was created. It is a result of joint project of institutes related to health and safety at work from the European PEROSH group. The NECID database, which is unified way of collecting data, focuses on a detailed description of the activity and material as well as the workplace environment conditions.

One of the tasks of our laboratory group from Central Institute for Labour Protection - National Research Institute (CIOP-PIB) within the framework of database co-creation base is conducting measurements on NOAA exposure at workstations in real-time. Our research is based on WHO recommendations and ISO standards, but we are also conducting experimental work on sampling of nanoparticles suspended in the air and proper methodology for microscopic methods what is a scientific challenge. In this work I would like to present the results of our current studies.

Session 1
1. Measurement and characterization of nano objects

A91891SP

A NOVEL CHEMICAL APPROACH TO REGIO CONTROL SYNTHESIS OF GOLD-BINOL HYBRID NANOSTRUCTURES

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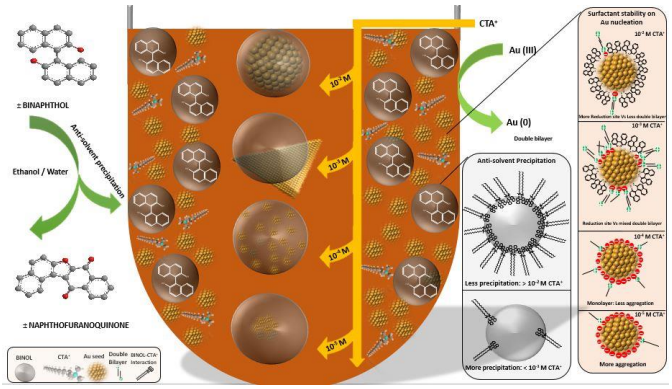
Novel Au-BINOL hybrid nanostructures have been synthesized using a chemical approach via one pot strategical procedure. BINOL [(±)-1, 1´-Bi (2-naphthol)], the organic moiety of the hybrid structure acts as a reducing agent that converts Au (III) to Au (0). One of the key point of this project is the dual behavior of BINOL, where it is oxidized to form Naphthofuranoquinones that leads to the simultaneous reduction of Au (III) to Au (0). In the reaction medium, the BINOL is solubulised between ethanol and water. Therefore, it hereby exhibits solvent-antisolvent precipitation phenomenon, where it precipitates to participate in the formation of the hybrid with Au seed. By tuning the concentration of surfactants (CTA+) in the reaction process, the regio control of Au-BINOL hybrid nanocomposites have been achieved. Moreover, the study on reaction kinetics involved during the early reaction time and the critical micelle concentration of CTA+ ions over the BINOL absorption peaks is determined by Time dependent ICPOES and UV spectroscopy. Both the organic and the inorganic components of the hybrid nanomaterial were characterized by using SEM, TEM, XRD, UV-vis spectroscopy, FTIR, and HR-MS (EI) analysis. Furthermore, the plausible mechanism of the oxidation process of BINOL to Naphthofuranoquinones is reported with water as an oxidizing agent.



Session 1
1. Measurement and characterization of nano objects

A91915CD

AN OPERATIONAL METHODOLOGY TO CHARACTERIZE NANOMATERIAL POWDERS FOR RISK ASSESSMENT

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Nanoparticulate powders are increasingly found in the workplace. Inhalation exposure to airborne nanoparticles (NPs) is possible throughout the life-cycle of the powders. As the lung toxicity of NPs has not been clearly demonstrated to date, it remains challenging to evaluate the risks associated to NPs to propose preventative measures. The first step of a risk assessment strategy consists of the identification of the 'nano' nature of a material and this suffers from a lack of an operational methodology to determine such a nanoparticulate nature. Here, we present a simple and operational strategy relying on the Volume Specific Surface Area (VSSA) determination of powders for nanomaterial identification based on the European Commission definition recommendation. The experimental strategy was tested on a set of 15 representative industrial powders (TiO2, SiO2, CuO, and ZnO) covering a wide range of properties. The VSSA classification was validated comparing it with the particle size distribution (reference criterion) obtained by Electron Microscopy. It was seen that the VSSA parameter is in accordance with particle size for nanomaterial powder classification. Our approach involves relative accessible methods as thermogravimetric analysis, Nitrogen adsorption and Helium pycnometry. Our results suggest with other recent published data, that the VSSA approach allows the nanomaterial powders classification without having to resort to a systematic measurement of the primary particle sizes.

Session 1
1. Measurement and characterization of nano objects

A90689TH

Development and comparison of different analytical methods to quantify the released graphene from nanocomposites

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Quantification of the released nanoparticles is a necessary step to determine the exposure of them to the environment and human. We developed different analytical methods based on ion selective electrode (ISE), energy-dispersive X-ray-scanning electron microscopy (EDX-SEM), and inductively coupled plasma - optical emission spectrometry (ICP-OES) to measure the released graphene fraction from graphene-epoxy composites. To achieve this goal, we coated the surface of GnPs (graphene nano platelets) with lead and measured the released graphene indirectly via determination of the released Pb^{2+} amount after abrasion of GnP-epoxy composites, following the approach of Schlagenhauf et.al[1]. In the first step, we performed a calibration of the released Pb^{2+} amount from the coated GnP powders. Our results show that it was possible to determine the Pb^{2+} amount released by the coated GnP powders using the Pb^{2+}-ISE method accurately, as proven by ICP-OES measurements. Then we investigated the abraded particles from graphene-epoxy composites. A comparison of different analytical methods to measure the lead amount was carried out, including ISE, ICP-OES and EDX-SEM, which were all able to detect lead on the abraded particles but possessed different characteristics. This study focused on the Pb^{2+}-ISE method, which is less time consuming and less expensive to determine the amount of Pb^{2+} while delivering accurate results. To understand the release process of GnPs, we characterized the GnP-composites concerning the distribution of the GnPs in the epoxy by a suite of methods including terahertz measurements and acoustic microscopy. Furthermore we investigated the particle size distribution of the abraded particles as well as their total amount. Finally we compared our quantification study with previous ones including Schlagenhauf et.al[1] (for CNTs) and Rhiem et al.[2] using a ^{14}C-labeling technique. Our study aims at a better understanding of the release process of graphene particles from composites and an easy-yet-reliable quantification of the amount of the released graphene, and thus delivers data and facilitates future exposure and risk assessment studies.

References:

[1] Schlagenhauf et.al: Environmental Science & Technology (2015) (Carbon Nanotubes Released from an Epoxy-Based Nanocomposite: Quantification and Particle Toxicity)

[2] Rhiem, S., et al., 2016. Release of 14C-labelled carbon nanotubes from polycarbonate composites. Environmental Pollution, 215, pp.356-365.

Session 2
2. Exposure

A91532AV

WORKERS' EXPOSURE TO INCIDENTAL NANOPARTICLES IN DIFFERENT LINES OF WORK

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Nanoparticles originating from anthropogenic sources may be either intentionally produced (i.e. engineered nanoparticles) or side products of some process or work task (i.e. incidental nanoparticles). Workers' exposure to engineered nanoparticles is being studied rather intensively due to the postulated negative health effects of them. Besides this, a number of different work phases and work related processes, such as welding, sanding, asphalt paving and cooking, are known to be an incidental nanoparticle sources meaning that millions of workers' may potentially be exposed to high concentrations.

A comprehensive review on workplace measurements reporting the concentrations of incidental nanoparticles in different work environments was compiled[1]. Peer-reviewed research articles that reported the concentrations of incidental nanoparticles at different work environments were collected and grouped according to the line of work they represented. Also the different measurement techniques used for these studies were analyzed with the information of the measured size range.

Here, the lines of work in which the workers' exposure to incidental nanoparticles is most likely are recognized. Also the challenges related to uniformity of reporting the results of the workplace measurements and available measurement techniques are discussed.

The Finnish Cancer Registry and The Finnish Work Environment Fund (proj. numbers 112132 and 112133) are thanked for funding.

References:

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Session 2
2. Exposure

A91560NS

Powder intrinsic properties as dustiness predictor for an efficient exposure assessment

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Dustiness is not an intrinsic physically defined property of a powder but the tendency of particles to become airborne in response to mechanical and/or aerodynamic stimuli. The present study establishes a set of nine intrinsic physical properties of a powder to which the dustiness can be attributed. By theoretical and experimental investigation of a standardized continuous drop test scenario, we determine the degree of influence of these properties on the aerosolization tendency of powder particles. The inter-particle distance is the most dominant property controlling the particle aerosolization, followed by the ability of powder particles to get electrostatically charged. We observe the kinetics involved during powder aerosolization to be governed by two ratios- drag force/cohesive force and drag force/gravitational force. We propose to use these physical properties as industrial hygiene parameters or dustiness predictors in models used for the assessment of inhalation exposure to airborne particles during powder handling operations.

Session 2
2. Exposure

A91589VS

Process-generated nanoparticles exposure in the ceramic process

SANFÉLIX Vicenta [1], MONFORT Eliseo [1], VIANA Mar [2], SALMANTONIDIS Apostolos [2], GUAITA Luis [3], NÁCHER Francisco [4], BELLÉS M. Carmen [4], RIBERA A. [5]

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Traditional industrial processes, without any relation to nanotechnology and manufacturing or processing of nanomaterials, may generate nanoparticles associated with thermal processes (such as materials heating) and/or high-energy mechanical processes (e.g.: machining of surfaces); these released nano-particles called Process-Generated Nano Particles (PGNPs).

PGNPs can be primary or secondary and in contrast to manufactured nanoparticles, are characterised by their non-specific and highly variable chemical composition and morphology. The potential hazard of the PGNPs depends on factors like particles size, surface, shape and composition.

These findings suggest that the generation and release of PGNPs may take place at any conventional workplace, provided that high-energy processes are involved. Even some processes can be characterized as having a permanent and significant release of PGNPs, hence it is essential to improve knowledge about occupational exposure to them. An exhaustive review of the literature review shows that there is a limited number of industrial studies on workplace exposure to PGPNs.

The present work focuses on the ceramic industry processes, where the presence of different high-energy stages implies a significant potential of PGNPs.

The study was carried out in industrial ceramic plants under real operating conditions. Firstly, a baseline data collection was performed to determine nanoparticle concentrations throughout the manufacturing process. Secondly, the operations that recorded the highest concentrations were selected for a deeper study. The results obtained showed the presence of specific scenarios with significant concentrations of nanoparticles. Finally, in order to reduce the exposure of workers to nanoparticles, some specific corrective measures have been proposed and evaluated for the main sources identified in the ceramic industry. The measures evaluated have permitted efficiencies higher than 50%.

Session 2
2. Exposure

A91627BQ

Metals and metabolites as biomarker of exposure in welder apprentices

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Exposure to welding fumes may result in serious adverse health effects such as respiratory diseases. In fact, IARC has determined that welding fumes were carcinogenic to human with an increase incidence of lung cancer in welders. Evaluation of exposure is generally done by collecting air samples in the breathing zone of a worker. However, it is not always convenient to evaluate exposure from air samples (i.e. if the worker is wearing a respirator). Urinary metals have been uses for exposure to metals compounds, however it proves difficult to measure exposure to welding fumes using urinary metals. In this study, urinary metals and metabolites were quantified in groups of controls and welder apprentices in a longitudinal analysis during their first year of training. Air samples were collected in the breathing zone of the welder the previous day to determine exposure. It was noted when welders wore a respirator.

Fasting urine samples as well as air samples were collected from age- and sex-matched controls (unexposed to welding fumes) and welders on days 0, 1, 7 and 50 of an 8-week welding program. Urine samples were aliquoted and frozen at -80°C prior to analysis. Air samples were digested in an Ultrawave system using a nitric/fluoroboric acid solution. Urine samples were diluted in a nitric acid/ EDTA solution for metal analysis. All analyses were carried out using inductively coupled plasma mass spectrometry in the SWAMP Lab, University of Alberta. Metabolites were determined using 1H-NMR spectrometry at NANUC with peak fitting performed using a Monte Carlo automatic approach.

RM-ANOVA showed differences between controls and welders for metals in urine only for antimony. In addition, Sb was elevated only at day 50, which was the only day it was detected in air samples. RM-ANOVA showed exposure of welders increased as they became skilled since it increased from day 0 to day 50.

Session 2
2. Exposure

A91659AS

EXPOSURE TO PROCESS-GENERATED NANOPARTICLES DURING THERMAL SPRAYING

SALMATONIDIS Apostolos [1], RIBALTA Carla [1], VIANA Mar [1], BEZANTAKOS Spyridon [3], BISKOS George [4], SANFELIX Vicenta [2], MONFORT Eliseo [2]
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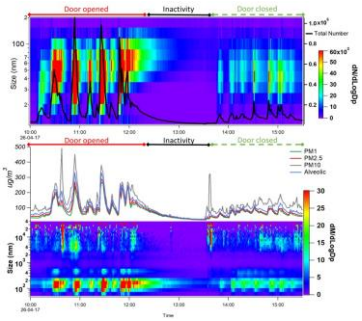
Protective coatings for metal structures used against corrosion and wear are frequently applied by thermal spraying. This study aims to assess exposure to process-generated nanoparticles (PGNP) during thermal spraying at industrial scale under real-world conditions, by means of Atmospheric Plasma Spraying (APS) and High Velocity Oxy-Fuel spraying (HVOF). Particle monitoring performed simultaneously: (a) inside the plasma booth in terms of particle number (N) and mass concentration, mean diameter, TEM sampling for offline analysis; (b) in the worker area outside of the plasma booth, in terms of particle size and mass distribution. In both processes the worker operated inside the plasma booth. The APS was operating with doors closed while the HVOF with open doors. In both exposure scenarios the concentrations in terms of N and mass concentration were high inside the plasma booths and in the same order of magnitude and mean particle diameter (N = 10^6 cm^{-3}; 30-35 nm). HVOF had a major impact on worker area concentrations (Figure 1), as nanoparticles were transported through the open door to the rest of the facility, despite the extraction system (6500 m^3/h). On the contrary, in the case of APS no significant fugitive emissions were observed due to the door sealing and the extraction system.

The main conclusions extracted from this study were:

- High concentrations in terms of N and PM1 were registered inside the plasma booths while the workers were operating.
- In the APS exposure scenario nanoparticle emissions were not released to workplace air due to the closing of doors at all activity times.
- In the HVOF scenario the doors were frequently open, resulting in impacts on nanoparticle exposures in adjacent areas.
- Implementation of mitigation strategies such as optimizing the production routine to keep booth doors closed during the spraying activity could reduce the transport of PGNP outside the plasma booth and therefore impact exposure reduction in adjacent worker areas.



Session 2
2. Exposure

A91751MV

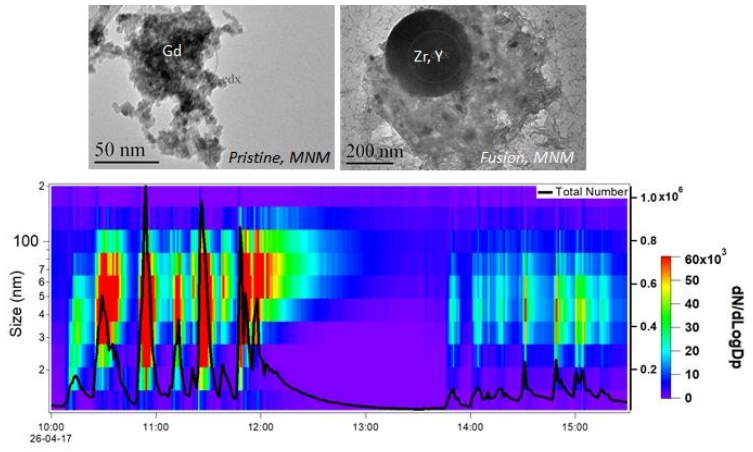
SAFE PRODUCTION AND USE OF NANOMATERIALS IN THE CERAMIC INDUSTRY: OVERVIEW OF RESULTS FROM THE CERASAFE PROJECT

VIANA Mar [1], MONFORT Eliseo [2], SALMATONIDIS Apostolos [1], SANFÉLIX Vicenta [2], CERASAFE CONSORTIUM – [1]. (1) IDAEA-CSIC, Barcelona, Spain; (2) ITC-UJI, Castellón, Spain

The CERASAFE project aimed to understand nanoparticle (NP) release scenarios during industrial processes in the ceramic industry, and to assess exposure by addressing NP characterisation, release mechanisms, toxicity, and mitigation measures. The main results obtained are: - Full physico-chemical characterisation of manufactured nanomaterials Al2O3, SrO, MgO, ZrO2, Y2O3-ZrO2 (YSZ) and CeO2 (Figure 1).

- Assessment of NP release during tile ablation and plasma spraying, evidencing that pristine and process. - Generated NPs may be released. NP emission mechanisms identified were nucleation, droplet ejection and shockwave ejection. Particle concentrations >107/cm3 were recorded. - Exposure assessment during ceramic tile sintering and ablation, plasma spraying, tile packaging and powdered material bagging. Particle concentrations >106/cm3 were recorded (Figure 1). Particle concentrations modelled using one- and two-box models showed ratios modelled/measured ranging 0.89-1.03; this evidences the good performance of risk assessment models. Comparisons with risk assessment models Lycara and NanoSafer are underway. - NP toxicity evaluation via ALI exposure of human epithelial alveolar A549 cells for the MNMs. Two cytotoxicity endpoints were determined: plasma membrane integrity and cell metabolic activity. Process-generated NPs are being tested for cytokine measurements, DNA damage and nanoparticle aerosol uptake analyses. - Particle hypgoscopicity was used as a tool to discriminate between manufactured process-generated and background NPs, using an HTDMA. Particle shape-factors and growth allowed for an effective discrimination between both particle types. - Mitigation strategies were tested, showing that NP reductions of up to 85% may be achieved with proper design, implementation and maintenance. A literature review of mitigation strategies evidenced a knowledge gap regarding process-generated NPs.

Project results will be uploaded to the NECID database.



Session 2
2. Exposure

A91778JL

EXPOSURE TO GRAPHENE IN A PRODUCTION PILOT PLANT

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Workers exposure to graphene was measured in a production pilot plant. Reduced graphene oxide was produced through graphite oxidation and posterior thermal reduction. This work was performed within the Horizon 2020 FAST project which aims to make a new 3D printing technology available for the manufacture of implants customized to the patient at affordable cost (grant agreement Nº685825).

The OECD (2015) harmonized tiered approach was followed to assess potential exposures to graphene nanoparticles. In Tier 1, three main activities were performed: (i) information gathering on graphene hazards (e.j. toxicology data, identification of available exposure limit values), (ii) analysis of the production process to identify potential worker exposure scenarios, and (iii) preliminary Risk Characterisation, using two state-of-the-art control banding tools, Stoffenmanager Nano and CB nanotool. In Tier 2, a basic exposure assessment was performed using handled on-line measurement devices which cover the particle range from 4 nm to 10 µm (TSI- CPC3007 and TSI-OPS3330). Simultaneously, personal and area samples were collected for off line analysis, including gravimetric, elemental carbon analysis and SEM/EDX.

Results obtained in Tier 1 showed that in general expected worker exposures were low since the nanomaterial is mainly handled in water dispersions and adequate engineering controls are kept. Measurements performed in the work place (Tier 2) identified significant releases of particles in two tasks, during the washing of the graphene oxide, and during its milling. However, the analysis of the size distribution and the morphology of the particles observed by SEM suggested that the released particles were not the target nanomaterial but engine generated nanoparticles. The analysis of the collected filters showed that the mass concentration of elemental carbon was below the limit of detection (LOD) and that the graphene concentrations were quite below the selected reference exposure limit (REL) (0.165 mg/m3, BSI 2007).

This work showed that worker exposure to graphene was low in this pilot plant (quite below the selected REL), contributing to guarantee a safe process, previously to its industrialization.

Session 2
2. Exposure

A91828mv

OCCUPATIONAL EXPOSURE TO NANOPARTICLES IN THE CERAMIC INDUSTRY

VIANA Mar [1], SANFÉLIX Vicenta [2], RIBALTA Carla [1], SALMATONIDIS Apostolos [1], GOMES Joao [3,5], ESTEVES Helder [4,5], MIRANDA Rosa [4], MONFORT Eliseo [2]

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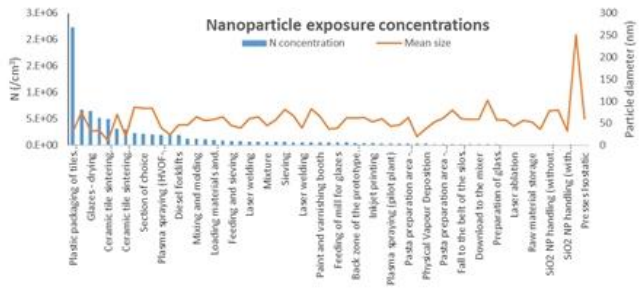
Occupational exposure to nanoparticles is an issue of growing concern in the ceramic industry. While traditionally only micron-scaled materials were used in the production processes, recent advances are favouring the use of nanoparticles (NP) as raw materials for different purposes, e.g., value-added pigmentation or surface properties. In addition, the use of innovative technologies such as laser processing has increased the potential for unexpected NP formation in workplaces. The different emissions generated have the potential to impact worker exposure and health risks. The first step towards risk mitigation is quantification of actual exposures in workplaces.

To this end, SIINN-ERANET project CERASAFE aimed to review a broad range of industrial scenarios with potential for NP release and worker exposure. In total, 59 industrial processes were monitored in Spain, Portugal and France, covering mostly industrial plants. Particle number concentrations and mean size were monitored in the worker area (not in the breathing zone) by means of particle counters (CPC3775, 4-nm-1.5 µm; DiscMini, 10-700 nm) and sizers (NanoScan, 20-420 nm). Mean particle number concentrations monitored in the worker areas, representative of exposure conditions, ranged between 1.5*103 - 666*103/cm3, with only one scenario (thermal packaging of tiles) reaching concentrations up to 2.23*106/cm3. The variability in mean particle diameters was much lower than that of particle number concentrations, ranging between 10-86 nm, with only 2 outliers (102 nm and 250 nm). The two activities with coarser mean NP diameters were related to powder handling, and as a result were more likely to emit NP agglomerates. The industrial processes characterized were correlated with the nature of the processes and the NP emissions generated, and conclusions are extracted regarding potential occupational health risks in the ceramic industry. The database generated will be publicly available through NECID.



Session 2
2. Exposure

A91830CA

Possibilities for workplace exposure assessment by low-cost dust sensors

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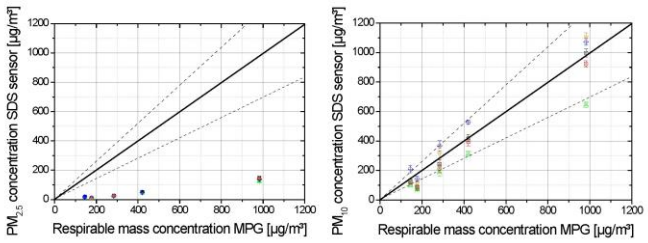
Workplace exposure to airborne dust needs to be assessed in view of worker protection. Conventionally, the exposure is determined in terms of the respirable mass concentration (d_{50} = 4 µm) using filter samplers. Alternatively, the use of optical measurement techniques has raised constantly due to their high sensitivity, high time resolution and simplicity in use. These can be differentiated into particle size-resolving spectrometers and size-integrating photometers. Recently, several low-cost photometers (<20 €) and spectrometers (~400 €) entered the market. Due to their low costs, they may allow e. g. for setting up permanent measurement networks in workplaces to survey the exposure concentrations with high spatio-temporal resolution. Similarly, they can also be used to determine dust concentrations in the atmosphere or in residential buildings.

To assess the applicability of the sensors for such applications, we challenged both low-cost photometers and spectrometers with various workplace-related aerosols and compared their response with reference techniques. Figure 1 exemplarily shows the $PM_{2.5}$ and PM_{10} concentrations determined with five Nova Fitness SDS011 low-cost photometers vs. the respirable mass concentrations determined gravimetrically. The results show that there is a good linear correlation with the reference, but the sensors need to be calibrated as any other optical measurement technique for the specific aerosol to show the right concentration level. Although their accuracy and comparability will likely not be sufficient for regulatory purposes, the sensors offer new possibilities for permanent monitoring to provide indications of potentially increased exposure concentrations at specific locations and/or times. The presentation will provide an overview of the available sensors. The results of the experimental study will be presented and discussed in view of the sensors' applicability in workplace exposure assessment.



Session 2
2. Exposure

A91839CV

DETECTION OF GRAPHENE IN AIR: A PROPOSAL BASED ON THERMAL PROPERTIES

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Graphene's production and application are growing in accelerated speed. In this scenario, the guarantee of healthy and safety conditions to producers and consumers along the graphene value chain becomes imperative. Due to the unique characteristics of this nanomaterial – major composition of carbon atoms and their interaction with the environment - characterization challenges in these complexes matrices are significant.

This work presents the data of an ongoing methodology development that aims to adapt the current standardized particulate matter sampling methodologies to assess the exposition to nanomaterials released inside and outside of a pilot graphene plant. Thermogravimetric analysis (TGA) is employed to measure the amount of graphene deposited on air sampling filters. A systematic study was performed by preparing different graphene dispersions (0.1; 0.01 and 0.001 ppm), which were deposited on quartz filters via filtration. Filters already exposed, containing dust and ordinary particulate matter were also used as substrate for graphene deposition. TGA was performed in a 40 °C to 1000 °C temperature range, heating rate of 5 °C/min, in high-purity synthetic air atmosphere.

The obtained DTA curves revealed that the thermal decomposition of the deposited graphene (detectable in all samples) occurs around 627 °C. Control filters (with no deposition) remained intact with approximately 2% of weight loss. The thermal decomposition of graphene was also detectable in those filters containing other types of particulate, and occurred in the same temperature range. These results pointed out that thermogravimetric analysis can be used to detect small amounts of graphene suspended in air, and the key factor is the graphene's high thermal stability. The methodology provides a robust way to improve air quality surveillance and exposure evaluation.

Session 2
2. Exposure

A91841cp

Potential workers exposure to ultrafine particles in metal additive manufacturing

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Since 2012, Additive manufacturing (AM) knows an exponential grown in Europe. AM technology defined as the construction layer-by-layer of an object in 3D, is vector of new risks for the worker's health and safety.

In addition of the laser exposure, dust exposure (and its potential inhalation) is one of the main risk to take in consideration in risk analysis. However, in addition of the "classical" dust problematic that is directly link to the nature of the metallic powders used, AM has to deal with potential exposure to particles of much smaller size (to the nanometer). Indeed, this very small fraction is a by-product of the laser beam melting and is met at the end of the process: in suspension in the tool, stacked to the non-used powder, on the parts... In this case, the classical Occupational Exposure Limits (OEL) cannot be used as the only value to check the worker's exposure. Therefore, it is important to complete this regulatory information with additional measurements to take in consideration the all range of particles sizes and the potential worker exposure at the workplace during each step of the process.

Based on this observation, CEA-Nanosafety Platform (PNS) teams decided to work on this thematic by transposing to AM, the worker exposure measurement methodologies1 implemented since 2009 at the workplace when handling nanomaterials. The aim is to have a better understanding of potential emission of ultra-fines particles occurring during the processes and recommended EHS (Environmental Health and Safety) solutions in adequacy to the specific exposure scenarios. In this frame, CEA-PNS teams have performed several measurements campaign in academic and industrial AM lines using metallic powder. All the process steps have been followed (real-time measurements and off-lines characterizations) to have a complete overview of the potential emission form the powder to the final object. These results, combined with CEA good practices and EHS recommendations, allowed adjusting protocols and proposing CPE and PPE (Collective and Personal Protective Equipment) adapted to the emissivity of each working phases.

The ultimate goal of these studies is to offer responsible AM processes by adapting the levels of the protection to the risks incurred; and that with the operators at the center of the concern.

1. OCDE, ENV/JM/MONO (2015) 19, series on the Safety of Manufactured Nanomaterials n°55.

Session 2
2. Exposure

A91858AM

Aging of Wood Stains Containing CeO2 Nanoparticles as UV Filters

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Wood stains need to protect the wood from aging and increase its durability, especially when used as siding. In this context, protection from UV damage is a major issue. CeO2 nanoparticles act as UV filters that do not alter the coloring/staining properties of the product and have an increassed durability compared to organic UV filters. However, exposure to weathering agents (water, UV-Vis illumination, temperature…) can cause the release of the CeO2 nanomaterials, which are known to be of some ecotoxicological concern. Here we examine the released of CeO2 from wood stains under simulated environmental conditions. The aging scenarios (continuous immersion vs periodic spraying, illumination regime…) were found to have a strong influence on the release of Ce from the stain. The mechanisms of release are evolving with time, and are involving transformations of the CeO2 nanomaterial during the course of aging.

Session 2
2. Exposure

A91872SC

STATIONARY INSTRUMENT vs PERSONAL DEVICES TO ASSESS OCCUPATIONAL EXPOSURE TO ENGINEERED NANOMATERIALS IN PILOT PLANTS

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Nanotechnology has rapidly promoted the development of smart and innovative processes and nano-enabled products that have created a tremendous growth potential for a large number of industry sectors. In particular, nanotechnology offers substantial possibilities for improving the competitive position of the EU and for responding to key societal challenges. Ensuring the safe, sustainable and responsible development of pilot lines throughout Europe is a key objective of the Horizon 2020 Work Program.

This work presents the results of experimental campaigns focused on the assessment of occupational exposure during the production of silicon based nanoparticles (plasma processes) and the proposed risk management measures. The methodology used for the exposure evaluation followed the OECD Tiered approach. Thanks to several granulometers, particle counters and personal devices, measurements included particle concentration, size distribution, state of agglomeration / aggregation, specific surface area, morphology and chemical composition.

The authors also investigated the advantages, disadvantages and possible synergies of using personal devices vs stationary instruments to assess release, emission and personal exposure to airborne engineered nanomaterials (ENMs) in the workplace.

The following findings from the undertaken actions will be discussed. Increased understanding of some of the tasks undertaken and the potential for exposure to airborne ENMs. The generated data on release, emission and exposure is used to provide inputs for practical and cost-effective risk management, common safety guidelines, and safer-by-design strategies.

The identification of the remaining experimental challenges to address the speciation of the released particles (i.e. pristine vs aged and transformed) and to discriminate high and fluctuating background in workplaces.

Harmonization of the measurement strategy adapted to pilot plants and small businesses in order to measure potential airborne emissions of ENMs at workplace.

The research leading to these results has received funding from the European Union's H2020 Grant Agreement n.646397 (NanoLeap project).

Session 2
2. Exposure

Personal exposure to ultrafine particles in everyday life - A Pisa study

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Personal exposure to airborne ultrafine particles was measured during a sightseeing tour in Pisa with the help of two personal monitors (PUFP C100 and miniDiSC) with high time resolution.

The PUFP C100 from Enmont, LLC is a condensation particle counter that uses water as working fluid. The miniDiSC is identical with the DiSCmini from Testo and determines, among other metrics, the number concentration of airborne particles on the basis of unipolar diffusion charging. Both instruments can be battery operated for several hours and used to determine personal exposure. The two devices were first compared with different test aerosols in the laboratory. The lab study showed that the devices measure according to their specifications. The PUFP C100, however, is unsuitable for highly hydrophobic particles.

During the measurements in Pisa, the measured concentrations with PUFP C100 (on average 30,340 1/cm³) were about 4 times higher than in the coastal town of Marina di Pisa (7,800 1/cm³). The main sources for the concentrations measured in Pisa (see Figure 1) were road traffic, whereby in some cases concentration peaks of up to >1,000,000 1/cm³ (miniDiSC) were measured, which could be attributed to typical sources such as passing buses or scooters, cigarette smoke or exhaust gases from diesel-powered emergency power generators. The results of the two instruments used were well comparable and correlated. On average, the results differed by a maximum of 20%. The results from the laboratory study and the field measurements will be shown and discussed.

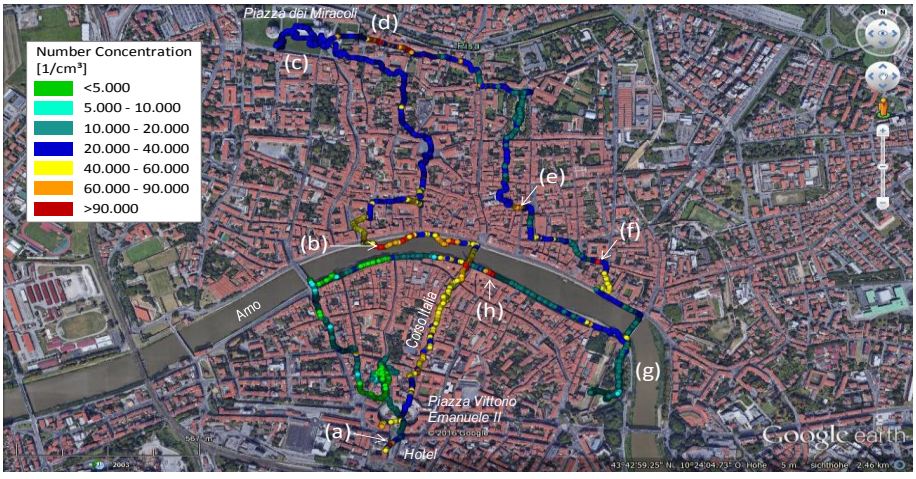

Figure 1: Track and exposure concentrations (color code) during the sightseeing tour in Pisa

Session 2
2. Exposure

A91608OL

Particle emission characterization when incinerating nanowastes using a lab scale tubular furnace operating at 1100°C

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Nanotechnology is said to be the industry of the 21st century. The production of nanoproducts keeps growing at a rapid pace. Consequently, the need to anticipate how to deal with these products at each step of their life cycle is more and more necessary. Nanowaste management including product incineration is to be investigated to assess the impact it could have both on human health and the environment. The growing number of registrations of nanoscale substances (R-Nano in France) clearly demonstrates that the amount of nanowaste to be processed in waste treatment plants will increase in years to come. Though to date French and European regulations relative to nanowaste management do not exist, recommendations may at least be delivered to minimize possible impact on the environment and human health. Data on nanowaste incineration are still scarce. This motivates to better understand the phenomena at stake.

Little is known yet about nanowaste incineration and the ensuing fate of nanoparticles. In addition, literature is scarce. In this context, the Nanowet project supported by the ADEME agency was set up to complement the existing studies. It focuses on the treatment of halogen- and sulfur- containing nanowaste by elevated temperature incineration (1100°C). The objective is threefold, namely to assess the influence of (i) high temperature on the whole process (ii) the effect of the presence of acid gases in the fumes on particle emission and (iii) the effect of the wet scrubber technology installed in the waste treatment plant on nanoparticle capture efficiency. Three polymer wastes were selected and characterized for this project: two of these wastes contained nanofillers (silica and titanium dioxide) in addition with sulfur and chlorine. A lab scale horizontal tubular furnace operating with a temperature of 1100°C was utilized at INERIS nanosafety laboratory for the Nanowet experiments. Criteria relative to combustion requirements when incinerating products were carefully checked. Four series of experiments were carried out. The first three implied the incineration of each waste one after the other. The last series involved the incineration of a mix of the three wastes. It should be noted that at least four incineration experiments were carried out for each series.

Eventually, the obtained results make it possible determining the fate of the nanoparticles and the impact of the mix of the three wastes on nanoparticle release.

Session 3
3.1 Nano-objects release from nano-enabled products

A91618VP

TiO2 NANOPARTICLES RELEASE DURING SIMULATED REAL CONDITIONS FROM A PHOTOCATALYTIC COATING APPLIED ON ROADS

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Long term exposures to nitrogen oxides (NOx), which are highly produced by road transport, are associated with adverse health effects. Nano-enabled coatings were proposed as potential solutions to reduce the generation of NOx during traffic scenarios. The coatings incorporate TiO_2 nanoparticles (NPs) in anatase phase, which can decompose NOx in presence of UV light due to its well-known photocatalytic activity. Although TiO_2 NPs are designed to remain in the coating, external factors as weathering or wheels abrasion can damage it inducing NPs release to the environment.

The present study focuses in monitoring nanoscale materials releases during road transport simulation processes. The simulation processes (weathering and wheel abrasion) were performed in a laboratory controlled environment. The nanoscale-based coating was applied on two different asphalt composites, both highly used in roads, in order to evaluate the matrix effect on the release. The accelerated aging of samples consisted of a combination of two processes: Weathering followed by abrasion of weathered materials (14 and 28 days after being in the weathering chamber) and further weathering of the abraded samples. Weathering of samples was carried out in a climatic chamber for 42 days under accelerated aging conditions (following ISO 4892/06 protocol). The climatic chamber was adapted to collect the water coming from the rain cycles after being in contact with the samples. The collected waters were freeze-dried to isolate the solid residues, which then were characterized to quantify the TiO_2 NPs and their release forms. Preliminary results have shown high NPs release during the first hours, associated to non-attached or weakly attached material. The outcome of these studies is release rates and release forms, which is the main input for nano-specific risk assessment models and tools developed in the framework of the NANOFASE project (a European H2020 funded project).

Session 3
3.1 Nano-objects release from nano-enabled products

A91680CD

POTENCIAL IMPACT OF NANOMATERIALS INCLUDED IN SUNSCREENS: A NANOSAFE CASE STUDY

DELPIVO Camilla [1], ROMER Isabella [1], POMAR-PORTILLO Vicenç [1], VÍLCHEZ-VILLALBA Alejandro [1], VÁZQUEZ-CAMPOS Socorro [1]

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Nanomaterials (NM) are currently present in a large variety of consumer products, including cosmetics. According to the cosmetic regulation (Regulation (EC) No 1223/2009), NM must be labelled in the list of ingredients with the word 'nano' in brackets following the name of the substance. Several studies have been published in literature regarding the physico-chemical characterization of NM used in cosmetics (e.g. TiO2). Some of these studies include evaluations on how this TiO2 NM present in sunscreens are released into lake water or costal seawater directly from beachgoers. Potential risk for the ecosystems were also estimated by analysing accumulation of these released NM in sediments and in the surface microlayer of the water column.

The main aim of this work is to evaluate the potential impact of NM included in sunscreens on aquatic ecosystems. To this purpose, the following studies will be presented: Quantification of NM placed in the Spanish market, physic-chemical characterization of NM from four representative sunscreens and assessment of potential NM releases to the aquatic environment.

A market research work was performed by evaluating the composition of about 300 products (i.e. TiO2, ZnO and SiO2 NM) sold in both pharmacies and big supermarkets, covering the biggest brands dominating the market.

The NM incorporated in four commercial sunscreens were quantified, extracted from the cream matrix and characterized by different analytical techniques. Then, the stability of NM was investigated in fresh and seawater over time to have an insight on their transformation once released into representative aquatic environments. Finally, to simulate the release of sunscreens in water media, it was designed a release experiment aimed to mimic the use phase of these consumer products. Sunscreens were applied on skin and in a synthetic substrate and release experiments were performed in MilliQ water, fresh water and seawater. The release of NM in the different water media was monitored along time and the released NM were fully characterized. The data obtained were used to estimate the amount of NM potentially released in seawater and the results will be compared with real measurement data.

Session 3
3.1 Nano-objects release from nano-enabled products

A92037nb

Impact of product matrix on the exposure, fate and behavior of released nanomaterials

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In recent years, many of the experimental nanotechnologies developed over the last decade have been evaluated by manufacturers, and a few (e.g., nanoscale silver (nanoAg) and carbon nanotubes (CNTs)) are already being incorporated into consumer products. Both toxicity and exposure data specific to realistic releases of nanomaterials are needed to forecast, rank, and manage their potential risks. To usefully forecast risk and possible effects of these nano-enabled materials, it is critical to thoroughly characterize exposure, fate, and behavior of released nanomaterials through the life cycle of nano-enable product. NMs released from product show different speciation: either dissolved, fully or partially embedded in matrix residues, hetero-agglomerated or free. The exposure, fate, behavior, and toxicity of NMs as released from a product are highly influenced by the product matrix. Here we compare the impact of a polymeric matrix on two NMs (MWCNT and nanoAg) showing opposite properties (insoluble/soluble) and shape (tubular/spherical). We simulate the NMs release during mechanical stress and then a release into aquatic media (pure water, wetland water and ocean water). To simulate a mechanical degradation, we design abrading tools. The novelty is the possibility to measure the torque and so on the energy involved in the abrasion process. This allows obtaining for each nano-enable the linear correlation of nano-enabled product abrasion rate versus the energy involve. This data is used to estimate the exposure of nanomaterials during the mechanical stress of real-time event such as car crash, kid chewing. The produced particles were fully characterized (particles size, chemistry) as well as NMs speciation (SEM, TEM, % of NMs is contacted with the surface). In addition, the behavior of the released particle in various aquatic media (milliQ, wetland and ocean water) was determined.

Session 3
3.1 Nano-objects release from nano-enabled products

A91546AS

Practical Implementation of SbD in NanoReg2

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There is not yet a harmonised definition on Safe or Safer by Design (SbD) in the nanotechnology field. Within Nanoreg2 the SbD concept aims at creating safer nanomaterials (NMs), products and industrial/handling processes to reduce the risks to humans and the environment during the product life cycle. Although the concept can be applied at any stage of the value chain, it implies the consideration of safety at the start of the innovation process, not as an additional add-on but as an integral part of the process, together with functionality and cost.

The application of SbD by industry involves an iterative approach where functionality, safety and costs are balanced. The process involves an evaluation of the potential risks arising from the NM, the production process and the product. This step requires collecting hazard and exposure information. Generally, the earlier in the innovation process the greater the uncertainty on the risk and the fewer data will be available. Approaches like grouping and read-across can aid to collect the necessary information for the risk assessment and reduce the reliance upon direct measurements. When a potential risk is identified, the next step is to develop a strategy or to apply safety principles to eliminate or reduce the risk at the design phase, preserving the NM functionality. Once the SbD strategy or principles have been implemented, a new evaluation of the risk is performed to demonstrate the effectiveness of the measure. The process can be repeated at each stage gate of the innovation process as further and more certain information becomes available. The main three stages are NM/process and product design, prototype development, scale-up of production and performance of the nano-enable product.

As part of the H2020 Nanoreg2 project, we tested this approach in 7 cases studies:

1. Waste reduction in silver-nanofibers production,
2. Improved Biocompatibility and Functionality from QD doped to Dye doped SiO2NPs,
3. SbD considerations for production of pristine graphene
4. SbD scale-up of GA carbon nanofibers (GANF, GAtam)
5. SbD of Si nanoparticles for Li-ion batteries
6. SbD of nanosilver dispersion for coating trolleys
7. SbD professional use of nano- SiO2 reinforced resin

We will present the main outcomes of such implementation. Acknowledgement: NanoReg2 has received funding from the European Union's Horizon 2020 research and innovation programme under grand agreement no. 646221

Session 3
3.2 Safe-by-design nano-enabled products and process

A91561TO

A user guidance on the use of the NanoReg2 database in relation to the safe innovation toolbox: Results from the NanoReg2 project

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A workable Safe Innovation Approach (SIA) requires a toolbox to support the Safe by design and Regulatory preparedness concepts to timely address safety aspects and minimize uncertainty about health risks to workers, consumers and the environment. The SIA Toolbox is a coherent set of tools, guidance and checklists to be used by various actors along the innovation chain and life cycle of nanomaterials and nano-enable products, thereby supporting both the improved dealing with new safety issues of innovative nanomaterials (NMs), nano-enabled products, their production processes and improved regulatory preparedness. Many of these tools, guidance and checklists are self-supporting tools that require specific input data in order to provide users with the relevant output for the purpose of Safe by Design and regulatory preparedness. From various stakeholder investigation in o.a. the H2020 NanoReg2, EC4SafeNano and caLIBRAte projects, it has become clear that users during the innovation process often lack data to provide tools with the proper input. Moreover, users lack the expertise to retrieve these data from various studies. The NanoReg2 database contains information on physico-chemical characteristics and toxicity of a large number of nanomaterials. During the NanoReg2 project this database is being extended to include information on worker exposure and it is envisaged to include information on the functionality of nanomaterials. One task has focused on retrieving the information that a number of tools in the SIA toolbox require to run from the NanoReg2 database and supporting users to find the relevant, physical, chemical, toxicity, exposure and functionality data for their purpose in the database. For this, a user guidance has been developed linking the tools input parameters to the NanoReg2 database and ontology.

The NanoReg2 project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 646221

Session 3
3.2 Safe-by-design nano-enabled products and process

A91566AN

BIMETALLIC GADOLINIUM-CERIUM OXYSULFIDE NANOPARTICLES: TOWARDS A SAFE-BY-DESIGN APPROACH

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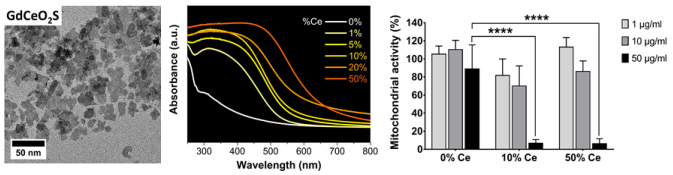
Metal oxysulfides MxOySz nanoparticles have recently emerged as potential contrast agents and photocatalysts among other applications. When developing new nanomaterials, it is crucial to consider their safety. However, studies on toxicity of oxysulfide are scarce. In the present work, we employ Safe-by-design approach for gadolinium-cerium oxysulfide nanoparticles as potential photocatalyst.

We used transmission electron microscopy and X-ray diffraction to evaluate size, shape and crystallinity of the nanoparticles. To assess their photocatalytic properties, UV-visible absorption and radical production were investigated. The Safe-by-design approach aims at reducing potential toxicity of nanomaterials during the design phase. Thus, we studied cytotoxicity of the nanoparticles on murine macrophage cell line RAW 264.7. WST-1 assay was used to evaluate cell viability after exposure to the nanoparticles. Inflammatory response and oxidative stress are being looked at as well. Furthermore, µXRF and µXANES were employed at beamline ID21 at ESRF synchrotron to localize and characterize chemical speciation of the nanoparticles in contact with the cells. In vivo toxicity is also considered to compare with the in vitro model.

We were able to synthesize 20 nm nanoplates (Gd, Ce) 2O2S with cerium content up to 50 % (Figure 1). We found out that cerium shifts absorption of the material towards the visible region which is interesting for photocatalysis. Radical production under visible light is being investigated by EPR. We showed that cerium is likely responsible for the cytotoxicity of the nanoplates. Preliminary results of synchrotron techniques show that oxidation state of cerium in nanoparticles in contact with the cells seems to change.

Altogether, we showed that cerium has an impact on both toxicity and photocatalytic properties of gadolinium-cerium oxysulfide nanoplates. Other key physico-chemical parameters such as surface state is also being considered.



Session 3
3.2 Safe-by-design nano-enabled products and process

A91653MM

Silver nanoparticle assemblies: a promising alternative "less toxic for mammals, active against bacterial strains"

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Silver nanoparticles (AgNPs) are widely used in consumer products for their biocidal activity, which is mainly due to released Ag+ ions [1]. The increasing use of AgNPs in medical devices (as wound dressings, catheters or implants) [2] that can release them directly in the bloodstream, raises several queries concerning the long-term effect of these nanomaterials on the human health and on bacterial resistance development.

In order to design a new biocidal agent with the least possible side effect for human, we have developed silver nanoparticle assemblies in a safer by design approach [3] including: i) nano-object surface modification, ii) decrease of the amount of exposed toxic substance and iii) use of alternative (less toxic) materials to wrap the object of interest, in order to decrease the adverse effects while keeping biocidal properties. Therefore, we made use of a trip odal bio-inspired molecule containing three thiols (L1) [4] that bridge AgNPs together and form stable assemblies with slow and long-lasting Ag+-release properties. We demonstrated that the assembling process is specific to L1, while other thiolate biological and bio-inspired molecules enhance AgNPs dissolution in an uncontrollable way [5].

For the first time, the production of silver nanoparticles assemblies of different sizes (40 to 200 nm), bridged together by thiol-containing bio-inspired molecule is proposed to this end. The extensive physicochemical characterization of this novel nanomaterial revealed that i) the assembly process and the product stability are mainly mediated by thiol binding to NP surface Ag, ii) the organic coating provides a full coverage of the AgNP surface. In addition, and as opposed to AgNP aggregates, these assemblies can be produced with controlled sizes and have well defined optical properties. More importantly, our results showed that these assemblies have a preserved bactericidal activity but a very low toxicity on hepatic cell-line compared to AgNPs.Therefore, we achieved a proof of concept for the production of size controlled AgNP assemblies where AgNP are entrapped into the bio-inspired organic coating and we demonstrated their potential as safer biocide.

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Session 3
3.2 Safe-by-design nano-enabled products and process

A91665RH

TRANSFORMATIONS AND ENVIRONMENTAL IMPACT OF NEXT-GENERATION ENERGY STORAGE MATERIALS

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The Center for Sustainable Nanotechnology is a multi-institutional, multidisciplinary research effort aimed at understanding the fundamental chemical and physical transformations of nanomaterials in the environment, with a focus on nanomaterials of potential environmental importance. The rapid increases in use of lithium-ion batteries for mobile electronics bring with it a concurrent increase in the synthesis and utilization of a range of new materials, many in nanostructured form. Metal oxides such as $LiCoO_2$ and the broader class of complex transition metal oxides such as $LiNi_xMn_yCo_{1-x-y}O_2$ ("NMC") and $LiNi_xCo_yAl_{1-x-y}O_2$ ("NCA") have the potential for adverse environmental impact through the release of transition metals into the environment, and are being synthesized and used in quantities exceeding 100,000 tons/year. These materials are chemically reactive and undergo a number of chemical transformations in aqueous media. One transformation of NMC and NCA materials is incongruent dissolution, wih preferential release of Ni>Co>Mn; this transformation leaves behind a chemically transformed, Mn-enriched nanoparticle with significantly greater stability against further reaction. Toxicity studies using bacterial species such as Shewanella oneidensis show toxicity that is largely attributed to interaction with the released ions. However, more detailed studies of gene expression using higher-level organisms such as Daphnia magna show ingestion and nanoparticle-specific effects on growth, reproduction, and gene expression even at low concentrations. One approach to mitigating potentail environmental impact is to alter the composition and/or morphology of the nanomaterials to control the rate at which metals are release. Ultimately, our goal is to develop a molecular-level understanding of the chemical and physical transformations of these materials in the environment. In this talk I will summarize our current knowledge of the chemistry and potential environmental impact of complex oxides used in the energy storage field, and the potential for mitigating adverse impact through physical and chemical alteration of the materials.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91674EH

Machine learning and QSAR Meta-analysis of nanobiomaterials used as nanocarriers within a Safe by Design (SbD) context

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Nanomedicine research has gained more importance in the past years due to the revealed potential of nanomaterials for wearable devices, vaccine development, imaging tools, therapy or drug delivery to name a few. The latter being the area of research for this present study, and more specifically, the use of nanobiomaterials as mobile nanocarriers. Human toxicity and its relationship to intrinsic/extrinsic nanobiomaterial properties play an important role when designing and developing new drug delivery systems. Moreover, having toxicity screening techniques before in vivo/in vitro testing can also help developing the most suitable nanocarrier design and at the same time decrease unnecessary animal testing. In this project we propose to combine the QSAR (Quantitative Structure-Analysis Relationship) approach with machine learning techniques to develop a prediction tool, which is trained by using a large set of extracted data from available peer-reviewed papers of polymeric nanocarriers (i.e., PLA, PHA, chitosan). We aim to relate nanobiomaterial properties with in-vitro data on human toxicity (cell viability). The gained knowledge provided by the QSAR meta-analysis is intended to contribute to the safe design of developing new nanobiomaterials used in drug delivery systems.

A91677MU

Real-Time Deep In Vivo Imaging of Biliary Excretions of NIR-II Fluorescent Polymer Nanoparticles

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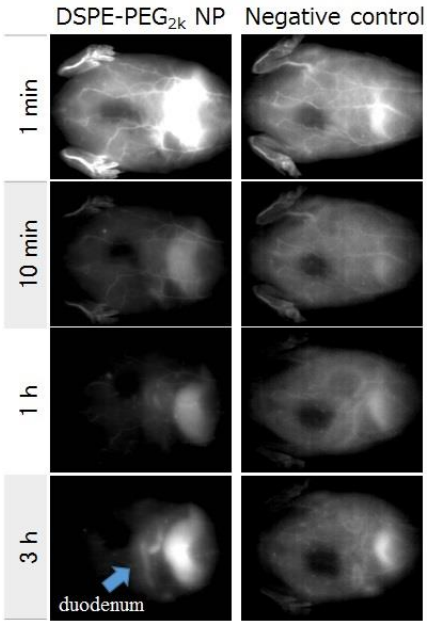
Understanding the mechanism of nanoparticle (NP) clearance from the body is important for safer biomedical use of nanomaterials in various fields. However, the main route, renal clearance via glomerular filtration, is restricted according to NP size (<6 nm in diameter) and water solubility not to aggregate in the blood. Here we show that hepatobiliary excretion, another potential clearance route, can be monitored by a real-time *in vivo* deep imaging system using near-infrared (NIR) fluorescence. We prepared 9-nm-diameter micelle NPs composed of a biocompatible and amphiphilic polymer, DSPE-PEG_{2k}, labeled with IR-1061 NIR fluorescent dye. IR-1061 emits fluorescence peaked at 1110 nm, which is in the over-thousand-nanometer (OTN-) NIR wavelength region, also called NIR-II, available for *in vivo* deep fluorescent imaging under 980-nm excitation. Therefore, labeling NPs with IR-1061 allows us to trace their distribution and clearance non-invasively. The NPs were administered intravenously to six-week-old ICR mice. Whole-body blood vessels were visualized by the IR-1061-loaded NPs using a portable *in vivo* NIR fluorescent imaging system SAI-1000 (Shimadzu. Co., Japan). The NPs were then trapped by the reticuloendothelial system and mostly distributed to the liver within 60 min post-injection. After 90−180 min post-injection, fluorophores were excreted from the liver with bile to the duodenum while the mice were fed a high-fat diet to enhance bile secretion. We found some other NPs were excreted with bile after intravenous injection but others were not. The hepatobiliary excretion route may allow efficient clearance and may be the major clearance route for NPs with >6 nm in diameter. Furthermore, the OTN-NIR fluorescent imaging technique is useful for screening hepatobiliary excretion of administered substances.



Session 3
3.2 Safe-by-design nano-enabled products and process

A91717HW

INVENTORY OF SERVICES FOR NANOSAFETY ASSESSMENT AND MANAGEMENT BASED ON COMPETENCES, EQUIPMENT AND INFRASTRUCTURE

WITTERS Hilda [1], VERCAUTEREN Sven [1], DUUREN-STUURMAN Birgit [2], MARCOULAKI Effie [3], RISSLER Jenny [4], FREJAFON Emeric [5], CAILLARD Bastien [6], VIITANEN Anna-Kaisa [7]

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EC4SafeNano is a 2016-2019 Coordination and Support Action, funded by the European Commission (Grant Agreement No 723623), coordinated by INERIS, and operated together by major European human health and environmental risk institutes with the support of associated partners, gathering stakeholders in the field of Nanotechnologies (regulators, industry, civil society, NGOs, service providers etc.). EC4SafeNano aims to bridge the gap between scientific knowledge on hazard and risk, and 'fit-for-purpose' risk management tools and strategies. The main objective of EC4SafeNano will be to develop and promote a harmonized vision of expertise and services in risk assessment and management, to enable the safe development and commercialization of nanotechnology and develop a sustainable structure to deliver these services. In this respect, two work packages were dedicated to gathering information on stakeholder needs and available services, by means of an online survey.

Information was collected on the ability to provide technical services for testing and measuring, and/or to perform consultancy and desk top studies. For these services, detailed information on available technical equipment, software tools, methods used and application fields was requested. Alongside specific technical details, the service providers were asked to give a general overview of their current and future offers for nanosafety services by scoring a matrix table.

The online survey resulted into 82 responses from 22 countries, including 2 non-European countries. An overview of current types of services demonstrated that testing and measuring and consultancy studies represented the majority of the offered services (each >20% of total), followed by training (12%). Across all the types of services, physicochemical characterization (12.5%), emission studies (6.8%), fate (5.1%), human health hazard studies (5.7%), occupational exposure assessment (8.8%), occupational risk assessment (5.2%), occupational risk management (5.5 %) and risk prevention (5.7%) were the main application fields for nanosafety.

The information from service providers will be compared to the inventory of stakeholder needs, as part of a fit and gap analysis in another work package, and provide the basis for a catalogue of services to be offered by the EC4Safenano Centre.

We will present the set-up of the survey to create an inventory of the competences and infrastructure of service suppliers, as well as the obtained results.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91725IT

SAFE BY DESIGN FOR INNOVATIVE NANOMATERIALS

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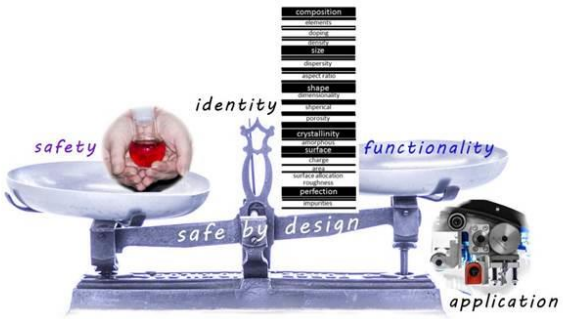
The implementation of Safe by Design (SbD) for manufactured nanomaterials (NM) is still in its infancy. The SbD concept developed in frame of the NanoReg2 project aims at reducing risks and uncertainties of NMs related to human health and environmental safety starting at an early phase of the innovation process. The aim is to eliminate or minimize potential adverse effects during the whole NM's life-cycle by modifying the material or process rather than using protective measures. SbD will not only result in balancing safety and functionality, it is also expected to positively impact cost/benefit.

The application of SbD requires comprehensive knowledge of the relationship between safety and functionality of NMs. This knowledge can also be used to apply SbD measures aiming at reducing either the hazard potential of NMs or release and exposure levels. The functionality defines the relationship between the properties and the application of NMs. A concept was developed that enables correlating use-oriented and safety-related properties of NMs through their identity. Future implementation of such a concept can be used to support SbD measures in a predictive way, a long term goal in the field of NMs research.



Session 3
3.2 Safe-by-design nano-enabled products and process

A91758JR

The SERENADE project: toward safer and eco-designed innovative nanomaterials

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Nanotechnology appears as one of the most promising fields of science and technology that will bring beneficial effects in our lives (medecine, environment, electronics…). Nanotechnology therefore appears as strategic and a key of success in the globalized economy. However the fast development of nanomaterials and the estimated production for next years has triggered many debates concerning their safe development and use.

To reach the forecasted level of economical development, the public acceptance of nanotechnology is essential not only in terms of human health safety but also concerning the environmental impact. Nanotechnology faces a big challenge that requires to develop a new paradigm in the concepts of design and production of nanomaterials.

The SERENADE project (French Government, the Investments for the Future programs, LABEX call)) proposes an integrated scientific and educational approach to develop new concepts and tools for the Safer and Ecological Design in Nanomanufacturing Processes and Products. The concepts developed in SERENADE will give new momentum to the sustainable and responsible development and the competitiveness of companies in the nanotechnologies sector.

SERENADE is not only focusing on the design phase, but addresses nanosafety during the entire life cycle of nanoproducts, from the earliest production stages (pristine nanoparticles) to the end-of-life (recycling, disposal).

SERENADE initiated 7 integrated Case studies aiming at testing the SERENADE 'Safer by design' methodology on various product types: photocatalytic paints, sunscreen, Nano and food packaging, Nano-wire, End-of-life and nano-wastes. The talk will present the several design strategies to both reduce hazard and exposure within the dedicated case studies.

Acknowledgment:

The project leading to this presentation has received funding from Excellence Initiative of Aix-Marseille University - A*MIDEX, a French "Investissements d'Avenir" program, through its associated Labex SERENADE project. This work is also a contribution to the OSU-Institut Pythéas. Finally, the authors acknowledge the CNRS funding for the GDRi iCEINT.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91847JL

SAFE DESIGN AND RE-DESIGN OF PILOT PRODUCTION LINES FOR THE MANUFACTURE OF CARBON NANOTUBE-BASED NANO-ENABLED PRODUCTS

LOPEZ DE IPIÑA Jesus M. [1], **VAVOULIOTIS Antonios [2], LATKO Paulina [3], DURA?EK Pawel [3], GAZTELUMENDI Idoia [4], SEDDON Richard [4], FLOREZ Sonia [4], GUTIERREZ-CAÑAS Cristina [5]**

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The PLATFORM ecosystem for the pilot production of pre-commercial CNT-based nano-enabled products consists of three pilot lines (PPLs) to manufacture buckypapers, CNT-doped prepregs and CNT-doped veils. Buckypapers are continuous self-supporting thin sheets consisting of 100 % of entangled CNTs; CNT-doped prepregs are the result of the combination between commercial prepregs and a tailored CNT-thermoplastic powder formulation and, finally, CNT doped veils are an ultralight polymer non-woven fabric, consisting of thin fibers bonded together thermally.

This paper shows the safe-by-design strategy followed for the prevention and control of aerosol emissions containing CNTs in the three PPLs, as well as the verification and optimization of their designs, based on the results of a measurement campaign of emissions and exposures to CNTs performed in the PPLs.

The potential hot spots were firstly identified in the three PPLs through risk assessment methodology (EN ISO 12000). Then aerosol field measurements were performed in PPLs, combining the use of portable direct reading instrumentation (CPC, OPS) with filter-based sampling at source, area and worker breathing zone. Samples collected were later analyzed by thermal-optical analysis and electron microscopy (SEM/TEM), to quantify the concentration of elemental carbon (NIOSH 5040) and the number of CNTs structures (ISO 14966 and NIOSH 7402 modified). Measurement strategy was based on standards EN 689 and EN 17058.

Results of the measurement campaign were used to provide recommendations to improve the designs of PPLs and the associated workplaces, through the implementation of the corresponding measures for risk prevention and control (EN 14123-1). This work has been supported by projects PLATFORM and I.NANO. These projects have received funding from the European Union's Horizon 2020 and the Basque Country´s Hazitek 2017 research and innovation programmes, under grant agreements Nº 646307 and ZE-2017-00025.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91857AM

Spectroscopic monitoring of the aging of sunscreens with TiO2 UV filters

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There is an increasing variety of nano-enabled consumer products on the market. Besides food, personal care products are a particularly sensitive category since they come in direct contact with the skin and mucosas, and might even be (accidentally) ingested (e.g. toothpaste). In an effort to make these products benign for both humans and the environment, the strategy aims to address safety issues from the very beginning following the "safe(r) by design" approach. Here we show the implementation of this approach applied to the design of sunscreens. These products contain nano-sized TiO2 as mineral UV filters. Since, besides being an efficient UV filter, TiO2 is also a photocatalyst, it is necessary to protect the skin against these harmful effects. This is achieved by applying one or multiple shells around the TiO2 core with the purpose of blocking photocatalysis and facilitating dispersion of the nanocomposite in the lotion. These nanomaterials need to be safe for human use and benign when released into the environment. Several formulations of the TiO2 based sunscreens were artificially aged so as to determine and quantifiy the alteration. To counteract photocatalytic effects, SiO2 and AlOOH shells were selected to coat the TiO2 core. These shells behaved very differently: whereas dissolution/degradation of the Al based shell was slow and limited, the SiO2 shell was far more sensitive to aging and most of the coating was eliminated from the nanocomposite. Spectroscopic data suggest dissolution as the main mechanism.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91860VB

AGEING AND NANORELEASE OF PHOTOCATALYTIC PAINT PRODUCTS: TOWARDS A SAFER BY DESIGN APPROACH

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The main objective of the project SafeTiPaint (part of the LabEx Serenade) is to formulate a new photocatalytic paint containing Nanoparticles (NPs) of Titanium Dioxide (TiO_2) with an effective air pollutant removal and with respect of the collateral parts. This is why a Safer by Design approach was considered for the all life cycle of the product, meaning from the formulation, application, using conditions and finally the end of life. This presentation shows results of the paints degradations by physical and mechanical ageing processes once applied.

A first study performed upstream revealed an accelerated degradation of an initial photocatalytic paint during the ageing process leading to high number of particles released during the abrasion. In fact, the physical ageing of the paint was carried out under UV light, and so high amount of hydroxyl radicals were generated by the NPs of TiO_2 in order to oxidize air pollutants in CO_2, however the side effect observed was the degradation of the organic matrix in the paint, leading to isolated and free particles and NPs at the surface, easily aerosolized with a mechanical stress.

To improve the initial formulation and avoid the matrix degradation, two new approaches were considered: The first consisted to improve the TiO_2 NPs with a coating addition to avoid the matrix degradation. The second entailed to coat NPs of TiO_2 on Cellulose Nano Cristals to limit the quantity of TiO_2 and obtain a better dispersion of NPs for an enhanced photocatalytic yield. At the end, seven new paints were formulated and applied for the experiments.

An accelerated physical ageing of the paints was performed in Q UV chamber (Q-lab), with cycles of light and water spray over a period of 0, 500, and 1000 hours. Then, samples were fixed on a rotative Taber, to generated mechanical soft abrasion. The system was in a glove box with the inlet air controlled to obtain a particle background less than 10 particle per cm^3. Particles emitted during the abrasion were analyzed on line with CPC and FMPS instruments and collected on PolyCarbonate filters for further analysis like SEM EDS to obtain particles chemical composition and the geometric size of the particles emitted during all the abrasion process.

Finally, results obtained will be presented and this work will allow the selection of the best candidates for the formulation of new photocatalytic paints with a reduce matrix degradation to limit the people exposure during abrasion processes.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91867SO

Safe-by-design approach applied to the production of antibacterial textiles

ORTELLI Simona [1], PARIDE Mantecca [2], BELOSI Franco [3], RAVEGNANI Fabrizio [3], BALDISSERRI Carlo [1], SIMEONE Felice Carlo [1], BLOSI Magda [1], COSTA Anna Luisa [1]

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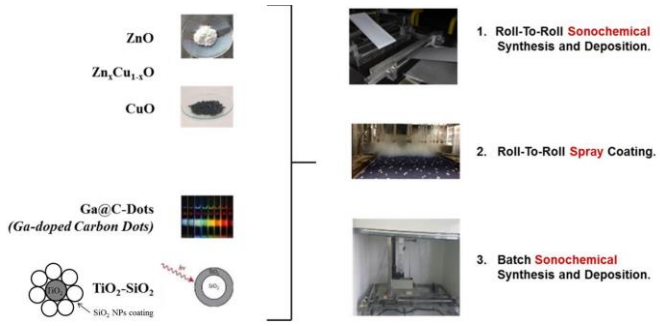
Safe-by-design applied to nano-manufacturing processes faces a multitude of challenges, and its practical implementation aims to reduce, from the early stage of product development, material intrinsic hazard and likelihood of exposure, thus improving the safety profile of nanomaterial (NM). Within European project PROTECT (PILOTS-02-2016), we are tackling some of these challenge right at the first two stages of a nano-enabled product development: 1) selection of material, and 2) deposition of a nanostructured coating. The target materials are bactericidal nanoparticles (NPs) manufactured in three pilot plants (Figure), in which we analyze the exposure scenarios for monitoring the potential release of NM; intrinsic properties of the nanomaterials and evaluation of exposure in the three plant provide the background information to predict risks and elaborate measure to minimize it. We combined results from in-vitro test with evaluation of exposure in a control banding approach that allowed to identify safer alternatives in terms of material and processes, making sure that they fulfill regulatory requirements. To this end, we proposed a material design alternative and we encapsulated photoactive TiO2 NPs with SiO2, an already investigated strategy to mitigate human and environmental toxicity. The final goal was to demonstrate that the silica coating preserves the TiO2's photocatalytic antibacterial performance while decreasing its hazard potential. Looking to the process we initially performed a risk control banding assessment of the pilot lines, performing a preliminary nano-monitoring campaign that was expected to improve risk prediction. We present the results of two different activities: 1) sampling of solutions and suspensions directly from the tank and analysis of particles present in the environment collected on filters; 2) control of the air quality by measuring the concentration of particles to estimate the workers' exposure through inhalation.



Session 3
3.2 Safe-by-design nano-enabled products and process

A91903DT

SAFER BY DESIGN: A RESPONSIBLE WAY TO INTEGRATE SILVER NANOWIRES ON COMMON APPLICATIONS

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Transparent conductive films are widely used in common optoelectronics devices like organics photovoltaics, displays and transparent heaters. The fabrication of transparent conductive films is currently realized with thin films of transparent conductive oxides, and in particular indium tin oxide (ITO). The as-made ITO transparent conductors lead the market with outstanding optoelectronics performances (R? >50 ohm/sq. and T >90%) but suffer from limitations like costly fabrication process and brittleness under mechanical stresses.

The existing market is evolving towards new types of devices, low cost, high-performance and flexible. Candidate replacement materials for ITO include carbon nanotube networks (CNT), graphene thin films, conductive polymers, metallic grids and metal nanowire networks. Metal nanowires appear the most promising alternative. In particular, silver nanowire networks offer flexible transparent electrodes with similar performances to ITO and less fabrication cost, above all a simple and controlled way of synthesis. We have developed a solution synthesis method, based on polyol process that can produce nanowires with diameter and length modulated separately able to cover a large panel of applications. This laboratory synthesis method is close to becoming an industrial process.

At the dawn of massive use, the interactions between silver nanowires and the human body are not well known. Knowledge of the chemistry and toxicity of silver nanoparticles and of the potential health impacts of one-dimensional particles justifies concern about nanowires. However, there are currently no clear conclusions about the links between nanowire properties and biological interactions.

We will describe our “safer by design” strategy to synthesize high-performance and non-toxic silver nanowires. Until now, investigations are mainly focused on length effects on toxicity, but diameter could also influence cellular uptake and clearance. We will show successful synthesis of nanowires with modulated length and diameter, quantify their performance for transparent conductive film production, and discuss the toxicity carried out on skin cells and immune cells identified as the main exposure routes (manufacturing, usage). This study set the guidance to determine the best compromise between performances and toxicity.

Session 3
3.2 Safe-by-design nano-enabled products and process

A91954IM

Safer-by-design conception of TiO2 nanoparticles coated with bio-inspired ligands for applications in paints

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Due to their unique intrinsic properties nanomaterials (NMs) have a significant technological impact [1]. As an example, NMs such as Ag or TiO2 nanoparticles are already used in paints for their antimicrobial and self-cleaning properties, respectively. Nowadays, more than 1 800 nano-products are on the market [2] and the production of NMs is predicted to increase exponentially to reach several millions of tons in 2024 for TiO2 [3]. Consequently, the question of their release in the environment by weathering or mechanical stress and the growing risk of human exposure have become a major concern. A safer-by-design approach e.g. a responsible development of NMs through all the life cycle (manufacture, use and end of life) must be taken into account. The objective of the SafeTiPaint project was to develop a novel TiO2 nanoparticles-based paint via a “Safer-By-Design” approach in order to reduce drastically the release in the environment and the risk of human exposure. Preliminary studies by B. Fiorentino et al.[4] have shown a rapid and intense degradation of the paint due to very small uncoated nanoparticles of TiO2 presenting very efficient photo-catalytic properties compared to micrometric TiO2 traditionally used as pigment. The aim of our work was to modify the surface of the TiO2 nanoparticles used by a paint manufacturer with a bio-inspired approach in order to reduce the degradation of the organic part of the paint while maintaining an appropriate photo-catalytic effect. We will present our strategy to disperse and stabilize the particles in aqueous media with the use of bio-inspired ligands (amino-acids, iron chelators, biodegradable polymers) as electrostatic and steric stabilizers. The photocatalytic activity of the new composites materials was investigated by measuring the degradation of methylene blue in solution under UV irradiation. Finally, the best candidates have been dispersed in paints in order to evaluate their release during ageing.

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Session 3
3.2 Safe-by-design nano-enabled products and process

A91358GV

Tuball ™ Single wall Carbon Nanotubes: Health, Safety & Environmental status

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The company OCSiAl is been founded in 2009 and is also the first SWCNT manufacturer who has completed his EU-REACH registration for a tonnage band of up to 10T/a. Later on this year we will be placed on the US-TSCA inventory, our PMN file will be dropped meaning we will have a signed consent order with the EPA.

Because Tuball™ is used and also tested in various applications on an ongoing basis, also receiving a lot of interests worldwide. That is why it is obvious that the company OCSiAl is establishing the necessary regulatory and quality standards worldwide.

The first part of this presentation will aim at providing a short introduction of our Tuball™ substance and his product line, a second part of the presentation will be an overview of the status and plans of the ongoing registrations an compliance. The third and last part of the presentation will focus on the health, safety and environmental aspects of our Tuball™ substance and the different applications.

As SWCNT manufacturer, OCSiAl is doing continues investments in improving our understanding of our different (new) Tuball products themselves and potential hazards through their (entire) life cycle. We are involved in generating additional test data and collaborating with industry associations and networks.

This presentation will describe the steps being taken by the company H&S Lead manager, Van Kerckhove Gunther to successfully introduce our carbon nanotubes (SWCNT's) regulatory status and outline our (future) plans for numerous of studies and qualifying our Tuball™ substance including the different kind of compositions.

References

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Session 3
3.3 Pilot plant production / Industrial issues

A91435AV

UTILIZING SAFE-BY-DESIGN PRINCIPLES IN NANO-ENABLED MATERIAL DEVELOPMENT FOR PRINTABLE ELECTRONIC

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Nanotechnology is applied in many fields of industry such as electronics, healthcare and energy production. In industrial applications and consumer products utilization of nanomaterials may provide many advantages including improved durability, and functionality compared to traditional products. However, the use of nanomaterials has raised some concerns related to occupational and environmental safety. Therefore, the risks needs to be assessed throughout the innovation process of nano-enabled materials.

In the EU H2020 funded project NECOMADA (www.necomada.eu), new materials and methods for printable electronics are being developed. The ambition of the project is two-fold, firstly the intention is to develop these new materials and methods that are beyond state of the art which will enable the increase in the effectiveness, productivity and speed involved in the automated processes opening up the market and possibilities for the Internet of Things (IoT). The second ambition is to deliver an open access pilot line facility that will be able to develop, evaluate and produce nanoparticles, inks and adhesive materials and devices beyond the life of the project.

In the development process, nanomaterials have an important role as a raw material of inks and adhesives. As part of the life-cycle analysis (LCA) occupational safety is assessed throughout the process. Safe-by-Design (SbD) approach is utilized in order to ensure the safety in every step of the production.

Nanosafety is assessed throughout the production chain utilising among other things questionnaires, discussions, literature reviews on toxicological effects of nanomaterials and workplace measurements of workers' exposure to engineered nanoparticles. The potential hazards of the materials used as well as the hot spots of possible occupational exposure to nanoparticles will be reviewed. The advantages and challenges of using SbD in industrial innovation processes will be discussed.

Acknowledgement:

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 720897.

Session 3
3.3 Pilot plant production / Industrial issues

A91832TA

Continuous synthesis of colloidal fluorescent quantum dots

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In the past decades, many types of nanomaterials have taken a leap from the development phase to commercial use. Depending on the desired size and type of material, either bottom-up or top-down approaches may be favorable for their production. For the case of quantum dots (QDs), i.e. semiconductor nanocrystals with sizes well below 10 nm, bottom-up chemical wet-synthesis can yield a high quality product featuring a narrow size distribution and low number of crystal defects.

In order to fulfill safety requirements and EU regulations (such as RoHS[1]) for the final product, the QDs should consist of a non-toxic material (e.g. InP, $CuInS_2$). But despite the QD material itself, also the precursors needed for the synthesis and the production process should be critically reviewed and optimized regarding safety, toxicity, material consumption and product yield.

When aiming for industrial production of QDs, a continuous synthesis process offers several advantages compared to the pure scale-up of a batch reaction. Often mentioned are inherent advantages of using flow reactors, such as a high reproducibility due to exact control of process conditions. As shown in a recent work[2], the use of flow reactors for the synthesis of $CuInS_2$ QDs enables better control of product properties (e.g. size-distribution narrowed by 30%) due to process intensification. Furthermore, flow reactors are known to enable a safer operation, especially in case of toxic intermediates or exothermic reactions.

Here, we will present the setup of a continuous production process for InP QDs, a material that is currently used in commercial display applications (e.g. TVs). By developing a new synthesis routine, we were able to avoid expensive and highly toxic and pyrophoric silylphosphine as phosphorous precursor. In our contribution, we will discuss safety and operational issues faced when transferring the batch synthesis of InP QDs to flow reactors, such as reactor clogging upon using commercial aminophosphines as phosphorous precursors. Alternative precursors will be presented, together with new solvent concepts necessary for a continuous production of QDs in flow reactors. All approaches will be discussed within the context of mechanistic considerations.

References

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Session 3
3.3 Pilot plant production / Industrial issues

A91862CS

Industrial drivers for nanomaterials pilot plant scale up.

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For any technology to achieve commercial success, there needs to be a transition from producing the materials at the bench scale to producing them at the pilot scale and beyond to industrial production levels. Whilst it is true that some processes are not scalable for one reason and another, there are many reasons why a company will look at scaling up their production.

There are many reasons how these scale-up processes can be achieved, but each material, application and company has different needs. So, it is more beneficial to look at why a company should consider scaling up their production.

There is an industry-wide issue across the whole nanotechnology sector (and not just in functional inks) in trying to produce nanomaterials that are of low cost without compromising their performance or how they affect the environment. Cost often causes both a positive and negative thought process to those looking to scale up, in that there are more costs involved with taking a material to a higher production level, but also, many companies undertake it to try and bring the cost of their materials down.

There are high upfront costs, but the introduction of optimized bulk production methods enables the company to produce much higher volumes at a lower cost than if they were to produce the same amount of material using multiple smaller volume methods.

Another main reason why companies look to scale up their production is because of demand, and this can be a result of lower costs (as mentioned above) or can be an independent factor due to general market demand. If the demand for the product is already there, then companies should look at scaling up their production to meet this demand and to avoid being forced out of the market by competitors with greater volume capacity.

Better collaborations between supply chain partners is needed in the nanotechnology sector, and higher production volumes and tailored materials provides the opportunity for companies to explore more options within the supply chain. Additionally, many companies outsource aspects of the scale-up process to universities and research centres. This approach enables companies to build long-term relationships with these establishments and enables the company to acquire the use of specialists through these relationships; which often provides a win-win scenario for all parties involved and a greater number of advancements for the industrial partner.

A91894MM

Safety by design in nanomaterials production

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The use of nanotechnology in different facets of industry has gathered momentum in recent years. Nanotechnology has been considered; owing to its well published benefits that manifest due to its small, unique sizes, which in turn bring enhanced properties than conventional products. However, the issue of nanotechnology safety, health and environmental implications is a key factor that tends to limit the commercialization of nanomaterials. This report seeks to promote a systematic approach to nanomaterials development that begins with predefined objectives and emphasizes product and process understanding and control, based on sound science and safety risk assessments. This entails designing out potential hazards in nano production including the design of nanomaterials, and measures to minimize exposures and eliminate risks that may be related to the manufacturing processes and equipment throughout the entire nanomaterials development lifecycle.

Session 3
3.3 Pilot plant production / Industrial issues

Current to the near-future in risk assessment and management methods for manufactured nanomaterials

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Coordinator of the EU H2020 Project caLIBRAte: www.nanocalibrate.eu. National Research Centre of the Working Environment, Copenhagen, Denmark, www.nrcwe.dk

While several different methods, tools and strategies have been developed and used over the past two decades for nanospecific risk assessment. So far most of these methods have been established and applied in research and specialist consultancy companies. While measurement methods are generally accepted by regulatory authorities, nanospecific risk assessment models and tools are not due to lack of documentation. However, such methods can still be used at daily nano-risk management level, covering both nano-risk innovation and established industrial production and downstream use. Unfortunately, there appears to a critical capacity barrier to use and implement state-of-art knowledge and methods at company levels in general. This presentation aims to provide an overview of the state-of-art and prospective methods in nano-risk assessment and management and some lessons learned regarding stakeholder knowledge and needs for nano-risk assessment and overall governance.

Session 4
Plenary Talk

A91460EB

Risk assessment during explosion severity tests of carbon black and MWCNT in a laboratory

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Risk assessment has been conducted by quantitative and qualitative methods during explosion severity tests for two nanomaterials (NMs) in a laboratory.

First a quantitative assessment was performed in order to assess the exposure of the operator during explosiveness testing in the 20 L sphere for carbon black (N990) and MWCNT (NC7000TM).

The methodology was based on general recommendations for exposure measurement assessment (e.g. [1]), and an easy-to-use operational sampling approach [2]. Exposure was measured with a Condensation Particle Counter (CPC) in background field as well as in the immediate vicinity of the operator. The operator was also equipped with a portative particle counter DiscMini. Samples for Transmission Electron Microscopy (TEM) analysis were collected with a Mini Particle Sampler (MPS) system. The testing procedure was clearly split into different steps to allow identifying the emitting activities. Background concentrations were monitored using a scanning mobility nanoparticle sizer (SMPS).

The measurements campaign enabled to assess the air flow in the laboratory, the performance of the local exhaust ventilation and to monitor the particle number concentration, nature and morphology both in the immediate vicinity of the operator and in the background.

The measurements allowed to identify a few sources of NMs emission during the tests and to come up with recommendations to reduce the operator exposure. It led also to the finding that the dynamic barrier provided by the local exhaust ventilation system can be temporarily weakened during overpressure events.

Second, a qualitative assessment was performed using two control banding tools, i.e. CB Nanotool 2.0 and the StoffenManager Nano 1.0. The risk levels assessed by the control banding tools are not in full agreement. The subjectivity associated with some input parameters for the risk assessment and the lack of information in the safety data sheets (SDS) and literature are discussed for several parameters.

Third, the results from measured versus estimated exposure to NMs were compared. The results from comparing airborne nanoparticles concentrations are in line with estimated exposure. However risk assessment with control banding tools remains questionable in some cases. Causes and consequences are investigated.

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Session 4
4.1 Occupational risk assessment

A91564FK

ADDITIVE METAL MANUFACTURING EMISSION CHARACTERIZATIONS USING A MULTI-METRIC METHODOLOGY

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The main objective of this study is to characterize the emissions of airborne particles generated from a metal additive manufacturing machine. A complete measurement methodology involving direct-reading instruments associated with conventional aerosol sampling was deployed around a Direct Metal Deposition (DMD) machine. The number and mass concentrations as well as the number size distribution profiles of airborne particles emitted during repeated manufacturing cycles were simultaneously measured at the source and in the near field (1.2 m away from the door). Different instruments were used to characterize the machine emission: 2 Nanoscan (TSI, 3910), 2 OPS (TSI, 3330), 3 Discmini (Testo). Therefore, a wide size range from 10 nm up to 10 µm is covered, and the number concentration of airborne particles can be measured up to 106 #/cm3. The same piece was produced by means of 3 different nozzles with varying deposition rates to provide new elements on the impact of the metal deposition rate on the emission generated from the process.

The measurements were performed during both the manufacturing process and transient operating phases such as machine door opening and part removal by the operator. The extraction ventilation operating on the machine was recorded and analyzed. Number of particles and size distribution profiles obtained for the different machining phases show low exposure to airborne particles under normal conditions along with a higher rate of particle emission during transient phases. In addition, the results relative to the different deposition rate nozzles will be discussed.

Session 4
4.1 Occupational risk assessment

A91601LD

3D MODEL AND SUBCHRONIC REPEATED EXPOSURE TO AEROSOLIZED GRAPHENE OXIDE: PRELIMINARY CONSIDERATIONS IN PRECAUTIONARY CONTEXTS

DI CRISTO Luisana [1], SABELLA Stefania [1]

(1) Instituto Italiano di Tecnologia, Genova, Italy

Graphene family materials (GFMs) are receiving increased attention due to their application in many industrial fields, and therefore, the unintentional exposition of humans may pose risks in both occupational and environmental settings. However, little knowledge is currently available on exposition limit value for humans. Also methods simulating realistic conditions for most of the exposure routes (e.g. lung, gut, liver, sewage, etc.) and the employment of realistic doses (long terms, sub-chronic) are currently missing. Regarding toxicity, at present, available results appear contradictory. Mimicking the cellular functionalities and in vivo tissue microenvironment, organoids or 3D tissues would be greatly beneficial in this context, in a first instance, to provide more realistic responses to chronic exposure to nanomaterials (NM).

In the current study, within an Italian National Project focusing on Occupational Exposure of NM (NanoKEY), we show an advanced in vitro tool that combines a 3D human bronchial tissue which is chronically exposed to aerosolized graphene oxide (GO) through the coupling of a nebulizer system (Vitrocell®Cloud) that enables dose deposition monitoring. To allow for a sub-chronic repeated exposure of GO, low doses were selected based on exposure limit values for nanocarbon based materials currently available for humans. Different biological endpoints (cytotoxicity, barrier integrity, uptake, inflammation, oxidative stress) were assessed in relation to GO biotransformation, which, in turn, has been studied by TEM and SEM. Results showed that none of the investigated parameters was altered at cumulative doses of 10µg/cm2. Although no clear toxic effects were detected, chronic GO exposure elicited a significant autophagosomes accumulation (since ca. 2 weeks since the first exposure), a process resulting from blockade of autophagy flux, rather than induction of autophagy. This study highlights the potential toxic mechanism of sub-chronic doses of inhaled GO, indicating the importance of advanced exposure/toxicity testing methods for risk screening of NM. Importantly, the doses tested and their correlation to limit exposure values in occupational settings is expected to advance the functionality of the in vitro tool in precautionary context, providing information on “no adverse effect dose” and risk classification for humans.

Session 4
4.1 Occupational risk assessment

A91604RF

OCCUPATIONAL EXPOSURE TO LTA NANOZEOLITES: STRATEGIES OF EXPOSURE MONITORING AND TOXICITY EVALUATION

FERRANTE Riccardo [1], URSINI Cinzia Lucia [1], BOCCUNI Fabio [1], FRESEGNA Anna Maria [1], CIERVO Aureliano [1], MAIELLO Raffaele [1], IAVICOLI Sergio [1], CAVALLO Delia [1]

(1) Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, INAIL-Italian Worker's Compensation Authority, Monteporzio Catone, Italy

Nanozeolites (NZs) are increasingly used in several sectors. The few available studies demonstrated that the cubic LTA NZs display clear toxicity compared to those with spherical or quasi-cubic morphology. We aimed to apply a standardized strategy to assess the occupational exposure and an in vitro model useful to evaluate toxic effects in the case study of LTA NZs produced in an industrial workplace. A harmonized methodology based on the OECD standard were applied. The multi-metric approach included real time measurements of particle number concentration, surface area, size distribution, environmental pollutants and indoor climatic parameters for the distinction of NZs from background airborne particulate matter. Personal and workplace sampling were performed using inertial cascade impactors for the following chemical and morphological off line analysis. Since lung represents the main target organ for workers exposed to nanomaterials, cyto-genotoxic effects on alveolar cells (A549) induced by exposure to NZs produced in the factory were investigated. CPC measurements highlighted values greater than background significant level of about 6000 #/cm3, when workers performed the cleaning of workstations and devices; FMPS size distribution compared to background values showed an increase in the typical size range of produced NZs, ranging from 56 to 100nm. ICP-MS and SEM-EDX analysis on sampled filters confirmed the chemical composition and the morphology of airborne NZs and their aggregates in the workplace. SEM and DLS were used to characterize the NZs. After 24h exposure to different concentrations (10-100µg/mL), we evaluated cell viability, apoptosis and mortality by cytofluorimetric viaCount and membrane damage detecting LDH release. Genotoxicity was evaluated by fpg-comet assay to evaluate simultaneously direct/oxidative DNA damage. Primary cubic particle analyzed by SEM ranged from 32-295nm. DLS analysis of NZs dispersed in RPMI medium (with 10% FBS) at the used concentrations, showed dose-dependent increase of Zav Diameter ranging from 100 to 299nm. We found a slight increase of % apoptotic cells at 50 and 100µg/mL and LDH release at 100µg/mL. A slight direct DNA damage from 25µg/mL and slight oxidative DNA damage were found. In conclusion, these findings represent the first data integrating the exposure characterization and the genotoxic effects of NZs and highlight the need to perform further studies to quantify NZs used in industrial applications.

Session 4
4.1 Occupational risk assessment

A91612VM

Pulmonary and remodeling effects of repeated exposure to low doses of silica dioxide micro- and nanoparticles in mice

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Rationale

Silica dioxide (SiO_2) micro- and nanoparticles (NP) are non-intentionally produced from building materials, such as drilling or sandblasting, or intentionally incorporated in building materials. However, concerns are emerging about their potential health effects. Previous studies in animal exposed to crystalline silica (quartz) by respiratory administration at very high doses have shown pulmonary inflammation and remodelling. Our hypothesis is that building materials dusts containing micro- and NP of silica could be also implicated in pulmonary inflammation and/or remodelling. The aim of this preliminary study was to analyse pulmonary inflammation and/or remodelling in mice exposed to repeated and realistic doses of building material dust containing silica.

Methods : C57/Bl6 mice were weekly exposed by pharyngeal aspiration during 1 or 3 months to SRM 679 (brick clay) or SRM 1887b (cement) dust at 5 or 50µg doses, representing 10% and 100% of the non-specific Threshold Limit Values (TLV) for occupational exposures to respirable particles, respectively. Bronchoalveolar lavages (BAL) were performed at time of sacrifice. Lungs samples were included in paraffin or stored at -80°C. Pulmonary remodelling was evaluated by optical microscopy after HES staining. Presence of NP in SRM 679 and 1887b samples was analysed by TEM-EDX analysis. Pulmonary inflammation in BAL was studied by total cellularity evaluation, as well as quantification of total protein and cytokines levels by ELISA.

Results: Presence of SiO_2 micro- and NP in SRM 679 and 1887b samples was confirmed by TEM-EDX. Massic fraction of silica was about 50% with 0.1% of quartz in SRM 679 and about 20% with 0.3% of quartz. Lung inflammation was observed only in mice exposed to 50µg of SRM679 (100% of TLV) at 3 months with a significant increase of neutrophils in BAL and macrophages in BAL and pulmonary tissues associated with significative secretions in BAL of KC and MCP-1 proteins, respectively. Bronchus-associated lymphoid tissues have been also identified after exposure to 50µg of SRM679 at 3 months.

Conclusions: Repeated instillations of mice to NP at doses representative of those present in occupational aerosols at TVL lead to lung alteration. Those results confirm the necessity to reconsider the limit value for occupational exposure to non-specific dust and study the effects of crystalline and amorphous silica micro- and NP.

Session 4
4.1 Occupational risk assessment

A91808CR

MODELLING NANOPARTICLE EMISSIONS IN INDUSTRIAL SETTINGS: TESTING BOX MODELS PERFORMANCE UNDER HIGH AND LOW CONCENTRATION SCENARIOS

RIBALTA Carla [1], KOIVISTO Antti Joonas [2], SALMATONIDIS Apostolos [1], LÓPEZ-LILAO Ana [3], ESTUPIÑÁ Sara [3], MINGUILLÓN María Cruz [1], MONFORT Eliseo [3], VIANA Mar [1]

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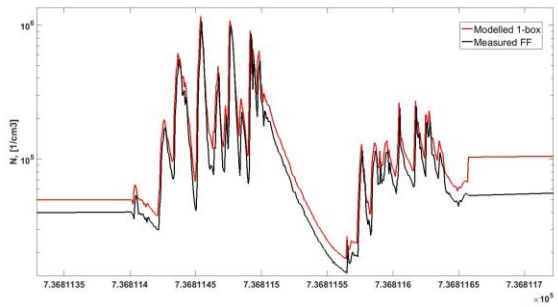
In order to implement prediction models as trustable tools for worker risk assessment, real-world cases need to be evaluated to validate model performance under different type of nanoparticle (NP) emission scenarios (e.g. engineered or process generated particles) and concentrations (high and low). To this end, NP concentrations were modelled during two emission scenarios: high NP concentrations (>106 cm-3; 30-40 nm) generated during thermal spraying of ceramic coatings (a widely-used technique in diverse industrial sectors; Viana et al., 2017), and low concentrations (279 to 668 µg m-3) monitored during packing of a fertilizer (Ribalta et al., 2018).

Worker exposure during both industrial processes was assessed. Aerosol measurements were carried out in near- and far-field locations by using online devices to obtain particle number and mass concentrations and particle size distribution for particles between 10 nm to 35 µm. Additionally TEM samples were collected. Exposure modelling was performed with one-box (Hewett and Ganser, 2017) and two-box (Ganser and Hewett, 2017) models. Modelling results were compared with actual worker exposure in order to validate model performance and to provide additional experience on real applications of the prediction models.

Results showed that one and two box models were able to predict low exposure concentrations with a relatively high accuracy during packing of a granulated inorganic fertilizer. The emission source was characterized by using the dustiness index. Ratio modelled/measured NP concentrations ranged between 1.05 (±0.08) and 1.22 (±0.07).

For the high concentration scenario, the emission rates were calculated by convolution using far field particle size distribution and near field total particle number. Preliminary results show that the one box model using estimated emission rates is able to satisfactorily predict actual far field concentrations.



Session 4
4.1 Occupational risk assessment

A91815TO

NANOSTREEM TO ASSESS EXPOSURE AND RISKS OF NANOMATERIALS IN NANO-ELECTRONICS MANUFACTURING WITH GENERIG NANO RISK ASSESSMENT TOOLS

LE FEBER Maaike [1], **OOSTERWIJK Thies [1]**, L'ALLAIN AND ROQUET Catherine and Pascal [2], BELDE Peter [3], GEERTS Lieve [4], MOCLAIR Fiona [5], MORELLI Attilio [6], PRODANOV Dimiter [7]

(1) TNO, Zeist, Netherlands; (2) CEA and ST, Grenoble, France; (4) VITO, Mol, Belgium; (5) Intell, Leixlip, Ireland; (6) LFoundry, Chiet, Italy; (7) IMEC, Leuven, Belgium; (3) NXP, Nijmegen, Netherlands

In order to maximize the benefits of nanotechnology and avoid unwanted consequences, additional data are needed to better understand potential health risks and necessary control measures across the life cycle stages of novel nanoscale or nano functionalized materials. In the meanwhile, we must rely on generic nano risk assessment tools.

By comparing and testing various risk assessment approaches and sharing good practices, the European NanoStreeM project will contribute to the improvement of the awareness and safety of workers in the semiconductor industry. The goal of this project is to gain insight in the potential pathways of exposure to and release of nanomaterials, to compile risk management practices enabling better risk governance in the European semiconductor industry, and to serve as benchmark for other industries.

From the available generic tools for nano risk assessment, the state-of-the-art tools have been selected to assess scenarios in four different source domains: manufacturing processes, exposure to nanopowders, to liquid nanodispersions and to nanodebris coming from abrasive activities. This tiered approach has published as a guidance document.

The proposed generic models were evaluated for their applicability in the semi-conductor industry, by testing them in real-life exposure scenarios. To fill gaps in the exposure assessment, recommendations were made for use of exposure monitoring complementary to risk and control banding in the semiconductor industry. The findings will be presented and lead to conclusions on how to improve the applicability of generic tools for specific sectors.

The NanoStreeM project (Nanomaterials: strategies for safety assessments in advanced integrated circuits manufacturing) receives funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement n° 688194.

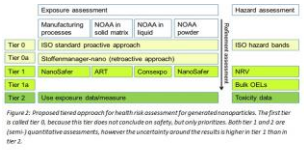


Figure 2: Proposed tiered approach for health risk assessment for generated nanoparticles. The first tier is called tier 0, because this tier does not conclude on safety, but only prioritizes. Both tier 1 and 2 are (semi-) quantitative assessments, however the uncertainty around the results is higher in tier 1 than in tier 2.

Session 4
4.1 Occupational risk assessment

A91816DP

Three-Tiered risk assessment for engineered nanomaterials. A use case for the semiconductor industry

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Nanomaterials offer a wide range of possibilities for new applications in major economic sectors, for example automotive, cosmetics, consumer electronics. At the same time, the industrial use of novel manufactured nanomaterials raises questions about potential unintended risks for the workers, consumers or the environment. Among the challenges the field of nanosafety is facing are the insufficient amount and quality of nanotoxicological data and the ambiguity in the metrics describing the exposure. This results in substantial difficulties in the actual quantification of risk in terms of dose-response relationships and exposure limits, which is a cornerstone of chemical risk assessment.

Challenges in the traditional chemical risk assessment approach can be traced to the assumption that the hazard and the risk can be quantified absolutely. Since hazard profile data for novel materials are inherently uncertain, the risk can be estimated only in a relative way. A way to do that is by grouping of materials based on certain similarity metrics. Such an approach favors categorical or qualitative risk assessment tools, which results in a classification into hazard and control bands for the process under investigation. The risk assessment approach developed in NanoStreeM focuses on the specific conditions present in the semiconductor industry – notably almost particle free working environment.

This presentation will outline the 3 tier risk assessment approach developed within the H2020 project NanoStreeM. The method can be summarized as follows: Tier 0 consists of hazard and risk categorization. Tier 1 consists of risk modeling, however, without performing emission measurement. Finally Tier 2 consists of designating of specific monitoring and control strategies for the exposure or emission of nanomaterials, which confirms the identified control strategies.

The presentation will focus on the application of the Tier 0 method -- ISO Technical Standard ISO/TS 12901-2:2014 to the process of Chemical Mechanical Planarization and its comparison with several other tools. The data have been collected during a structured survey conducted among the industrial project partners for several typical semiconductor facilities across Europe. Use cases will be presented along with identification of the hotspots of risk.

The work is supported by the NanoStreeM project, funded under H2020 grant agreement 688194 of the European Commission.

Session 4
4.1 Occupational risk assessment

A91831mv

CHEMICAL CHARACTERIZATION OF AIRBORNE NANOPARTICLES IN AN INDUSTRIAL SCENARIO

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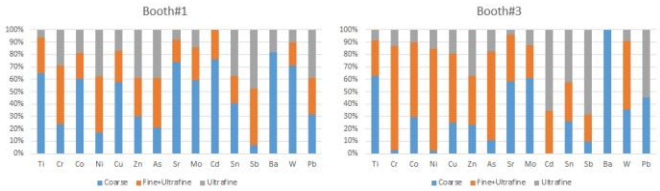
Atmospheric plasma spraying is applied at industrial scale to produce high-resistance coatings of metallic surfaces. Due to the high energies applied, it is a known source of nanoparticles (NP) which are released to workplace air and impact worker exposure in industrial facilities. NP emissions in this kind of scenario are characterized in terms of particle number concentrations, mean diameter and size distribution (Viana et al., 2017; Salmatonidis et al., under review), but data are lacking regarding the chemical properties and toxicity of these particles.

In this framework, this work aimed to characterize the chemical composition of course, fine and ultrafine aerosols emitted during plasma spraying in a real-world setting, with the ultimate goal to support ongoing toxicity assessments of the same aerosols. Two different scenarios (Booths #1 and #3) were assessed. Particles were sampled onto Teflon filters and in suspension using an aerosol concentration enrichment system (VACES; Kim et al., 2001), and analyzed by means of ICP-MS, ICP-OES and XRF. An inter-comparison between analytical methods was used for quality assurance. Results evidenced a major enrichment in potentially health hazardous metals (Cr, Ni, W) sourcing directly from the feedstock in both scenarios, as well as in major elements (Al, Ca, Fe) with different possible source origins (including outdoor infiltration). The elements with the highest enrichments in the ultrafine fraction were Zn, As, Sb and Ni in Booth#1, and Cd, Sb and Pb in Booth #3, highlighting the potential health risks linked to exposure to this kind of aerosols. Aerosol chemical properties were correlated with bulk material composition, to understand the relationship between bulk composition and NP emissions in the three size fractions analysed. Toxicity assessments will provide further quantitative insights into the health hazards of this kind of exposure.



Session 4
4.1 Occupational risk assessment

A91835AF

Value-chain case-studies with high quality conceptual information for model testing in caLIBRAte project

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In the EU H2020-funded project caLIBRAte (http://www.nanocalibrate.eu/home), different models and tools were selected in order to support a risk governance framework for the assessment and management of human and environmental risks of manufactured nanomaterials (MN) and MN-enabled products. Before becoming part of the framework, the performance of the tools and models need to be thoroughly analyzed and tested against data from comprehensive value-chain case-studies with high quality conceptual information about MN release and exposure.

This study highlights the specific methodology followed in caLIBRAte to create an inventory of case studies with high quality data potentially available for further use for model performance testing:

Compilation of compulsory parameters requested by the selected models, related to human exposure and environmental release and fate;

Identification of data sources (databases, data generated in EU Projects or literature); Evaluation of data availability to cover requirements by the different models; Evaluation of data quality.

Suitability of risk assessment with different exposure assessment models ranging from simple ones applied in control banding tools (e.g. Stoffenmanager Nano v. 1.0 (Duuren-Stuurman et al. 2012) and NanoSafer v 1.1 (www.nanosafer.org) to advanced and full quantitative aerosol dynamic models (Jensen et al. 2018) will be discussed by comparing with the gathered exposure measurement data.

ACKNOWLEDGMENTS

This work is part of the caLIBRAte project funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No 686239.

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Session 4
4.1 Occupational risk assessment

A91854PK

Safety Observer app for use in measuring safe working conditions and behaviour with nanomaterials

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Introduction: Occupational safety and health are often measure reactively with lagging indications such as accidents, injuries and illness. The objective of this presentation is to present preliminary results in developing a tool for use in safety rounds in workplaces and laboratories that work with or are exposed to chemicals and manufactured nanomaterials (MN). The tool is to be intuitive and easily useable by students, workers, faculty, lab directors and OSH professionals in assessing safety and health risks.

Methods: Safety observation templates are being developed for the free app 'Safety Observer'. Safe and unsafe work conditions and behaviour regarding MN in a workplace are counted, e.g. use of personal protective equipment (e.g. protective clothing, one observation per person) and technical assistive devices (e.g. fume exhaust hoods, one observation per hood). Comments, smileys and photos can be added, and a final report containing leading safety indicators is generated and made available in the app and sent to one's email for immediate use in reinforcing and improving OSH initiatives.

Results: The 'Safety Observer' app allows each user to either use the templates, or adapt them to the local context, language and culture. The templates for a MN lab could include topics such as: 1) Signage, marking and labelling (one of more observation for each room, storage area, piece of equipment or tool, etc.); 2) MN handling, storage, transport (one observation for each process in a given area); 3) Ventilation and filters (e.g. one observation for each HEPA-filer as to whether it is properly maintained and cleaned); 4) Personal protective equipment (e.g. gloves, lab coats, long pants, safety glasses, ear plugs, face shields, closed-toed shoes, respiratory masks); 5) Technical aids (e.g. fume exhaust hoods, glove boxes); 6) Order and tidiness (work and transport areas); First aid equipment; 7) Hygiene (e.g. no food or drinks in the lab); 8) Waste storage, recycling and disposal (e.g. labelling); 9) SOPs and risk assessments (e.g. chemical and MN specificity, use of hierarchy of controls).

Conclusion: The templates are an important contribution to providing positive, proactive and leading safety indicators in the daily promoting of healthy and safe work with MN.

Acknowledgement: The research leading to these results has received funding from the European Union's Horizon 2020 research and innovation program under Grant Agreement No.686239 'caLIBRAte'.

Session 4
4.1 Occupational risk assessment

A91481NM

Trends on environmental transformations and effects of nanomaterials mixtures in aquatic systems: an overview

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In the environment, organisms are potentially exposed to numerous engineered nanomaterials (ENMs) as complex mixtures whether as ENM-ENMs, or ENMs and other environmental pollutants. Similar to the approaches aimed to assess the risk of individual environmental chemicals, to date, a large body of scientific articles (> 10 000) have been generated on the fate and effects of individual ENMs in the environmental systems. This raises the question as to whether individual ENMs data on fate and effects is adequate to account for their potential risks in the environmental as mixtures. Forty studies were retrieved from scientific literature databases (e.g. google scholar, international council on nanotechnology) that have reported the fate and effects of ENMs mixtures (ENMs-ENMs) in the environmental systems. Results of data analysis revealed: (i) in a mixture where one or more of the ENMs is stable and has low solubility/dissolution (e.g. nAl_2O_3, nTiO_2), and under visible light antagonistic effects were observed due to their ability to adsorb particulates and ionic species of highly toxic ENMs (e.g. nAg, nZnO), (ii) synergistic or additive effects mostly occurred under ultra violet light conditions due to photoactivity of one or more ENMs in the mixture, and (iii) forty three percent of the studies were done in actual environmental matrices (freshwater and wastewater); thus offering insights on likely implications of ENMs mixtures in actual ecological systems where organisms under certain conditions showed tolerance to ENMs. However, current data has several gaps that require attention. First, only limited ENMs mixture studies reported the interplay of ENMs characteristics and exposure media water chemistry to the observed effects, or absence thereof. Secondly, limited “Trojan horse” effects were investigated although is known to increase uptake and bioaccumulation as well as potential transfer of ENMs mixtures from lower to higher trophic levels through the food chain. Given the knowledge gaps on factors that influence the environmental fate and effects of ENMs mixtures, there is a need to develop tools that can address current challenges such as standardization of methodologies suitable to determine the potential risks of ENMs mixtures. Such proactive approaches may aid to protect the ecological systems from adverse implications of ENMs mixtures.

Session 4
4.2 Environmental risk assessment

A91484NY

Assessment of metal oxide-based nanoparticles stability in the aquatic systems using fuzzy logic

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Increasing use of engineered nanoparticles (ENPs) in consumer products and industrial applications have raised concerns as their emissions to the environment continue to increase, though their implications remain partly addressed. To date, large data has been generated on ENPs hazard and exposure in an effort to address their potential risks in the environment. However, the data is fragmented and complex, therefore making it difficult for use by policy- and decision-makers to determine the potential risks of ENPs in the environment. Here, we report the application of fuzzy logic to assess the exposure of ENPs for environmental processes like dispersion in the aquatic systems. Fuzzy logic is suited to handle data characterized by ambiguity, uncertainty, and incompleteness. The developed fuzzy logic model comprised of nine deterministic inputs in three broad categories: inherent physicochemical properties (e.g. particle size), water chemistry (e.g. natural organic matter), and product-specific characteristics (e.g. frequency of product used by consumers) as antecedent variables; whereas two outputs variables (the consequents) as the deposition and dispersion. Aggregation/agglomeration, dissolution, and adsorption processes were identified as intermediate inputs-outputs in this model. A total of 86 IF and THEN inference rules were developed linking the antecedents to consequents; and used to derive the model results. Two cases (for nZnO and $nTiO_2$) based on data collected from the literature are presented to illustrate the functionality of the proposed approach. Results suggest that the proposed tool can support policy- and decision-makers to conduct initial screening of ENPs likely degree of exposure using the available data without the need for additional costly laboratory experiments. The modular approach adopted to develop the fuzzy logic-based decision support systems (DSS) render it easy to update as new data become available without the need to re-configure the entire model.

Session 4
4.2 Environmental risk assessment

A91654HW

NEXT STEPS IN ENVIRONMENTAL RISK ASSESSMENT OF ENGINEERED NANOMATERIALS CONSIDERING MATERIAL-SPECIFIC PROPERTIES

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Engineered nanomaterials (ENM) are advocated due to their unique material properties and their options for modification leading to various products and applied ENMs, e.g. with respect to mineral phase or coating. ENMs are specifically designed for a certain purpose in order to meet the required properties in applications. So far, different environmental exposure assessment models and hazard testing strategies have been developed to identify potential environmental risks. Generally, environmental exposure models have considered a “generic ENM” (i.e. material class) while experimental studies on adverse effects refer to specific ENMs in a certain configuration, e.g. crystal form. This aggravates the risk characterization step that compares both results of potential exposures and hazards in the risk assessment.

This work analyzed all major ENMs that have been investigated in material flow models and determined if a differentiation is possible for both exposure and hazard assessment. We can only perform a form-specific risk assessment if both form-specific exposure and hazard data are available. Subsequently, we have selected nano-TiO_2, CNTs, nano-Al_2O_3 and nano-ZnO due to the expected production volume as well as the possibility to create ENM subclasses. For these ENMs we estimated the predicted environmental concentration (PEC) and/or in the hazard assessment we derived an ENM subclass-specific predicted no-effect concentration (PNEC) by means of the probabilistic material flow analysis and probabilistic species sensitivity distribution, respectively.

We were able to show that a differentiated assessment leads to varying estimated PECs for nano-TiO_2 (crystal form: anatase vs. rutile), CNTs (SWNT vs. MWNT) and nano-Al_2O_3 (crystal form: alpha vs. gamma) as well as subclass-specific estimated PNECs for nano-TiO_2, nano-Al_2O_3, nano-ZnO. By doing so, we are able to obtain risk characterizations for specific forms of one ENM class that should be considered in future risk assessments.

Session 4
4.2 Environmental risk assessment

A91656HW

REDEFINING ENVIRONMENTAL NANOMATERIAL FLOWS: CONSEQUENCES OF THE REGULATORY DEFINITION ON THE RESULTS OF EXPOSURE MODELS

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All nanomaterial exposure estimates require fundamental knowledge about the production volumes of the nanomaterials. Published values of production volume can vary by orders of magnitude, mainly caused by ambiguities in the definition of what a nanomaterial actually is. The recommendation for a definition of “nanomaterials” by the European Commission has to some extent clarified this issue. In the meantime, first data are available for registered production volumes of nanomaterials in France based on a mandatory registration scheme. We have compared the tonnages of registered production and import of substances in nanoform in France with the estimated total market volumes of these substances, which include both non-nanoforms (bulk) and nanoforms. These substances comprised $CaCO_3$, carbon black, TiO_2, SiO_2, ZnO, AZO-based and diketo-pyrrolo-pyrrole-based (DPP) pigments as well as carbon nanotubes. The results show that some materials such as SiO_2 and DPP have a good match between reported nanoform and total production volumes, whereas for other materials such as TiO_2 and ZnO the reported nanoform production volumes are only a fraction of the total production volumes. This means that for SiO_2 and DPP the “conventional form” and the nanoform are identical, while TiO_2 and ZnO have been used as bulk materials in several applications. With this knowledge that for SiO_2 the global production of “conventional” silica is in fact all nano-silica, we can apply the information on the uses of conventional silica to refine the material flow model for nano-silica. The results of this updated modeling show an input mass flow of (nano) silica to environmental compartments that is four to five times larger than previously modelled. The flows to natural and urban soils even increased by a factor of 13, because not only the production but also single specific applications (such as the use in tires) may have a considerable impact on the environmental exposure. Future environmental risk assessments ought to prioritize both by production volume and/or by the probability of direct environmental releases, considering that data on conventional substances may often represent forms of the substances that are nanomaterials in terms of the definition that is recommended by the European Commission.

Session 4
4.2 Environmental risk assessment

A91793CA

NON-CANCER AND CANCER RISK OF COMMUNITIES SURROUNDING GOLD MINE DUMPS IN SOUTH AFRICA DUE TO NANO-SIZED SILICA DUST INHALATION

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Despite the known association between occupational exposure to crystalline silica and adverse health effects (e.g. silicosis and cancer), the risk associated from exposure to crystalline silica from environmental sources has not yet been fully studied. Gold mine dumps, also known as tailings storage facilities (TSFs), are known to be such a dust-generating source in South Africa, particularly in Gauteng and the North-West Province. The objective of this study was therefore to assess the potential of exposure to nano-sized tailings dust by surrounding communities as well as the presence of crystalline silica in tailings dust samples and the determination of risk associated in developing respiratory diseases. Environmental PM10 filters and personal PM4 filters were collected in communities surrounding the TSFs and the crystalline silica polymorph (quartz, tridymite and cristobalite) content on the filters were determined using direct-on-filter X-ray diffraction (XRD) methodology. Their size distribution analysis was also conducted using a scanning mobility particle sizer and aerodynamic particle sizer. The risks for both cancer-related and non-cancer-related endpoints were calculated based on the crystalline silica levels measured on the personal PM4 filters. Environmental PM10 and personal PM4 sampling showed that surrounding areas experienced silica levels as high as 90 µg/m³ and 51 µg/m³, respectively. All samples consisted mostly of quartz (73 - 87%) with only trace amounts of tridymite and cristobalite. A large percentage of incidental nanoparticles were identified (67 - 71%) indicating the potential of the dust to lodge deep within the lungs. These results, as well as the frequency of exposure to dust obtained from meteorological data were used to calculate risk of disease, with hazard quotients between 5.5 and 16.2 for potential non-cancer risks and 3 to 9 individuals out of 10 000 potentially developing cancer over a 70 year life-time period. These results have therefore clearly indicated unacceptable risk to surrounding communities from exposure to crystalline silica emanating from these TSFs.

Session 4
4.2 Environmental risk assessment

A91855DK

RISK ASSESSMENT OF SYNTHESIZED ZERO VALENT IRON NANOPARTICLES (NZVI) ON ENVIRONMENTAL BACTERIAL ISOLATES AND ITS CONSORTIUM

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Nanoparticles are used in different consumer products and industrial applications such as cosmetics and food preservatives etc. Presently, nanoparticles and its application has become an important aspects in day to day life. The present study deals with the chemically synthesis of nZVI (CS–nZVI) and its characterization using different advance technologies. Polyvinylpyrrolidone (PVP) was used as stabilizing agent. The characterization of nanoparticles was confirmed by XRD. The obtained XRD spectra were corresponding with the database of JCPDS card file no. 00–006–0696. The advanced characterization techniques were used to undrestand the surface morphology of nanoparticles i.e SEM-EDAX and FT−IR. Elemental analysis was done using EDAX analysis and confirmed the presence of iron. FT−IR analysis showed the presence of functionel groups. The surface area was analyzed using BET analysis. The antibacterial effects was studied using five different bacteria and its consortium which was isolated from the contaminated sites. The toxicity assessment data showed an important and vital effects of nZVI and it was found that the nanopartixles were least toxic towards the consortium (mixed cultures). Therefore, NPs may not have the specific toxic response towards the consortium compared to individual isolates.

Keywords: BET; consortium; SEM-EDAX; Risk assessment, Zero Valent Iron (nZVI)

Session 4
4.2 Environmental risk assessment

A91809AN

THIRD GENERATION RAPID HIGH THROUGHPUT SCREENING PLATFORM FOR NANOMATERIALS (NM)

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OBJECTIVES: Developing high throughput NM screening system. Validating this system on standard toxicants. Relating the concentration, size, shape, coating and polydispersity of NM to their bioactivity. Streamlining and automating the modular flow system

METHODOLOGY: The screening device is composed of a flow cell with individual biomembrane-like sensor element on fabricated electrode1, 2 interfaced to miniature resevoirs by microfluidic flow networks. The endpoint is registered as damage to the continually replaceable lipid sensor element and recorded electronically3-5. The HISENTS vision of individual modules within parallel flow systems is being extended to biologically more complex sensor elements and the functional operation of the platform is being underwritten by a physiologically based pharmokinetic (PBPK) model.

RESULTS: The structure, workings and performance of the platform has been recorded against standard intercalibrant water soluble toxicants, where limits of detection (LoD) and response “fingerprints” are shown for each toxicant. The application of the screening platform to Au and Ag NM is reported. In particular the relation between the extent of the electronic response and the concentration, size, shape, coating and polydispersity of the NM particles will be shown and related to the mechanism of interaction of the particle with the biomembrane-like sensor element. The screening platform has been streamlined and automated. The importance of rapid screening at point of synthesis is established through the subtle changes in NM conformation within short time scales.

CONCLUSIONS: Screening system measures biomembrane damage. The platform can “fingerprint” molecular and nano interaction mechanism with biomembranes. Particle interaction with sensor element is directly related to particle type, particle aspect ratio, coating, concentration and polydispersity.The HISENTS modular vision has now been successfully streamlined and automated.

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Session 4
4.3 Tools and commercial equipment

A91900RD

Measuring chemically-specified size distributions and agglomerate density with PARTICLEVER

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As every expert in nanoparticles measurement knows, elemental mass concentration is not the sole metric to be considered when measuring exposure. It should be combined with other relevant metrics. When considering dose-relevant metrics, specific surface was suggested as best correlated (Öberdoster et al, 1994; Tran et al, 2000).

More recent publication contradicted this hypothesis (Elder et al, 2005; Pauluhn, 2014) as lower toxicity has been obtained with high surface-area carbon compared to low surface-area carbon (surface area dose adjusted accordingly).

Therefore, BAUA recommended to modulate the mass concentration by the agglomerate density (Assessment criterion (reference value) for nanoscaled GBP, BAUA, 2015), considering that the lowest the agglomerate density, the more hazardous the substance is.

But the agglomerate density is still a challenge to be measured by commercial equipment on site and PARTICLEVER (formerly NANOBADGE) has developed a protocol to measure it. PARTICLEVER has begun to use this metric for several exposure measurements to nanomaterials under powder form and found its use very promising.

Session 4
4.3 Tools and commercial equipment

A91988PB

Industrial and Laboratory Engineering for Nanoparticles Related Projects

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Infrastructure projects in the field of nanoparticle design and handling require a set of skills related to nanosafety (staff and environmental protection) which are specific. On the other hand, standardization is not possible given the great variability of products and applications.

In order to meet the expectations of customers in this area, FAURE QEI asked CEA/PNS to join a traditional engineering team in order to provide the specific skills needed by such projects.

A 10 years collaboration history through projects in the field of industrial environment measurements and R&D projects concerning nanoparticles containment, makes a solid background and a strong bond between the two organizations. This project team also relies on hardware resources and calculation tools that, pooled together, make it possible to characterize and size an installation with accuracy.

We propose to present the operating principles of this skills combination and to explain:

- The nature of the knowledge we pool
- The role of each structure at different stages of a project

We will illustrate with an example, how a support mission makes it possible to guarantee the success and to adapt to each customer specificities.

Our presentation will be complemented by an example of an energy study that will provide an overview of the methodology to be used to reduce operating costs based on the required containment levels.

A91647HB

Ignition and explosion characteristics of four kinds of nanopowders

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The diversity and complexity of manufactured nanomaterials is constantly increasing. We are facing a rapid growth of very heterogeneous materials requiring special attention. Their unique characteristics, which are primarily related to their small size, can lead to important scientific and technical innovations in various fields. However, the use of nanomaterials and nanoparticles presents risks that need to be assessed and controlled to enable the emergence and deployment of sustainable technologies that would use them. This work deals with the study of ignition sensitivity and explosion severity characteristics of nanoparticles. It has been carried out on various nanopowders as part of our project (NANOGRA) that aims at a multidisciplinary assessment of the risks related to nanoparticles of economic interest for the Walloon Region. This paper discusses the experimental results of the determination of ignition sensitivity and explosivity characteristics of Carbon Black N990, Corax N550, MWCNT NC 7000 and partially passivated metallic nanoparticles (Aluminum). Key information regarding MIE, Pmax and KSt values was obtained for carbon nanopowders, Corax N550, MWCNT NC 7000, and for carbon black N990 of microscopic size. This allowed to see the influence of the increase of the specific surface. The results of the different tests have led to the conclusion that the carbon nanopowders are capable of generating an ATEX during suspension in the air, with moderate explosion intensity comparable to the ST1 class. They are little and not even sensitive to electrostatic phenomena. Generally, the assessment of explosion parameters of carbon nanopowders has been found to be similar to their microscopic size analogue. The pyrophoric nature of the partially passivated aluminum nanopowder required screening tests (e.g. MIT layer and combustibility) to control the risk of ignition in the steps of the characterization tests. In addition, against expectations, post-test hazards have been highlighted and require somewhat adapt of some tests protocols. The results show that aluminum nanoparticles are very sensitive to the risk of ignition by a phenomenon of electrostatic origin so they could explode more significantly than other particles of microscopic size of the same material.

Session 4
4.4 Risk management

A91834AF

CONTROL OF WORKER EXPOSURE DURING HANDLING OF MANUFACTURED NANOMATERIALS IN FUME HOODS

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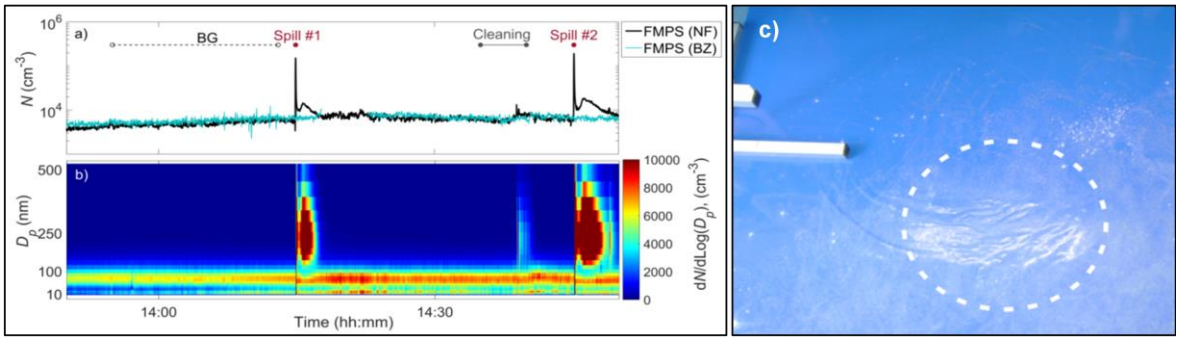
Fume hoods are one of the most common methods of controlling exposure in laboratory environments (Balas et al. 2010). In this research the potential release and the workers' inhalation exposure during synthesis and handling of manufactured nanomaterials (MNMs; CuO, ZnO and TiO2) under a laboratory fume-hood was assessed (Fonseca et al. 2018). In order to increase confidence in worker protection by fume hoods, the capacity of a fume hood to prevent particle release to laboratory air during simulated spillage was also evaluated by varying drop height and mass load (Fonseca et al. 2018). Synthesis, handling and packaging of MNM did not result in detectable particle release to the laboratory air. During simulated spills, notable increase in particle concentrations were rarely detected in the breathing zone of the worker (Figure 1a and b). However, powder spills were sometimes observed to eject into the laboratory room (Figure 1c) and contaminate the workers' laboratory clothing. In contrast to statements in previous scientific publications, this study confirms that an appropriate fume-hood with an adequate sash height of 0.3-0.5 m and face velocities ranging from 0.1 to 0.4 m s-1 provide high exposure control during synthesis and handling of MNMs. Here, preventing on average 98% of particles release into the surrounding environment. Nevertheless, safe approaches for cleaning powder spills should be prepared to prevent exposure via resuspension and inadvertent exposure by secondary routes.



Session 4
4.4 Risk management

A91838AJ

The EU H2020 caLIBRAte project: Developing the Nano Risk Radar Tool

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This paper presents the development of the Nano-Risk Radar in the large EU project caLIBRAte (performance testing, calibration and implementation of a next generation of system-of-systems Risk Governance Framework for nanomaterials). After reviewing the “risk radar like” initiatives worldwide (e.g. in insurance industry), the paper presents the development of caLIBRAte Nano-Risk Radar that is largely based on the method developed in the iNTeg-Risk project (www.integrisk.eu-vri.eu). The Nano-Risk Radar helps to identify and to monitor the emerging risks in the area of nanotechnology by considering the environmental, health/safety, socio-political, economic/financial, regulatory/legal and technological aspects. The indications about the potential risks are being collected from the different sources, such as Expert level: Platform for including experts, opinions / warnings; Scientific publications level, Public and stakeholders’ perception level (conventional sources; reports on surveys, focus groups and similar) as well as the social media/ networks. A special technique for automatic identification of new risks in the internet-based sources, developed for insurance industry and measuring singularity and ubiquity of new information, has been developed and deployed. The results of the identification and monitoring process will also be used for the predictive part based on the agent-based models (previously calibrated on the monitoring results). The caLIBRAte Nano-Risk Radar will be integrated with other tools, within the caLIBRAte System of Systems (SoS). The Risk Governance Framework based on System of Systems (SoS) will be applicable for the assessment and management of human and environmental risks of Manufactured Nanomaterials (MN) and MN-enabled products. The SoS is based on the 10 steps of emerging risks procedure initially specified in CWA 16649:2013 and planned to be included into the new ISO 31050 standard. The Cooper Stage-Gate model will be integrated with the System of Systems.

Session 4
4.4 Risk management

A91845BD

SOME CONSIDERATIONS WHEN EVALUATING PHYSICO-CHEMICAL HAZARDS OF NANOPOWDERS

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The regulatory classification of the physico-chemical hazards of powders is defined in two references, which describe the test methods to be applied, as well as the criteria and the classification thresholds. These two references are respectively the European CLP Regulation and the transport of dangerous goods UN regulation. These two reference systems enable to associate identified hazards with safety rules related to the handling, storage and production of the powders. Traditional microscale powders as well as innovative materials like nanopowders or very fluffy materials need to follow these classification rules. Typically, the properties of interest for nanopowders are related to the reactivity with air and water. The related hazards are defined by the CLP regulation in the following classes: flammability, pyrophoricity, self-heating, water reactivity and oxidizing capability.

The hazardous properties of nanopowders can a priori be routinely determined with the regulatory experimental tests performed in an adequate platform like S-NANO at INERIS. However, several aspects were overlooked so far for innovative materials that show specific properties like very low density and high specific surface area. This presentation deals with a review of the limitations of the current tests as well as detailed considerations related to some tests (powder segregation issues, specific ignition issues, safety issues for the operators…).

These aspects could perhaps be not thoroughly considered for microscale powders but in the case of nanopowders, these parameters are shown to be of importance in order to evaluate physico-chemical hazards. It is then of primary importance to assess carefully these new behaviors in order to prevent the production of misleading information in safety data sheets.

Session 4
4.4 Risk management

A91846BD

INSIGHT IN THE BURNING BEHAVIOR OF ALUMINUM NANOPOWDERS

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Nanomaterials are innovative materials and they sometimes show unexpected behavior that could impact the determination of their safety parameters. In this work, aluminum nanopowder (40 – 60 nm) burning behavior was investigating by considering the influence of coating, pre-heating as well as the preparation procedure. These tests were performed in the INERIS S-NANO platform dedicated to the evaluation of flammability and explosivity of nanopowders. They were focused on the evaluation of the reactivity and the ignition sensitivity of the nanopowder to hot surfaces which constitute one of the main sources of ignition of combustible materials. Once a hot surface has raised the temperature of a portion of powder to its ignition temperature, combustion reaction then self-propagates.

DSC/TGA tests were performed to characterize both the reactivity of the samples and determine the oxide layer thickness of the particles, which has a direct influence on the thermo-kinetics parameters of aluminum. These results were put in perspective with available data in the literature to highlight the unique reactivity of this product whose particle size distribution is close of the theoretical critical diameter inducing pyrophoricity of aluminum.

Layer ignition tests were also performed so that a deposit a dust layer of given size and thickness on a horizontal circular plate was heated to predetermined temperatures until a critical temperature for ignition is reached. Temperature values were ranging between 200 and 450°C. No ignition was observed however the dust layer showed a great ignition sensitivity to burning metal particles (sparks) and a differentiated burning behavior depending on the initial temperature of the powder. It is shown that the initial temperature of the powder has a marked influence on the burning class of the nanopowder as confirmed through VDI 2263-1 combustibility tests: at low temperature (<300°C), the aluminum nanopowder burns in a smoldering mode whereas at higher temperature (>400°C), aluminum burns actively with bright light emission of the burning zone. This type of behavior, which has been observed in the past for some microsized powders (Bartknecht, 1989) may have direct implication on the management of fire risks related to deposits of metallic nanopowders and special attention should be paid on the potential misuse of such test results to implement safety barriers (Agnes, 2018).

Session 4
4.4 Risk management

A91869MS

Nanomaterials as an occupational risk in metal additive manufacturing

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Metal Additive Manufacturing (AM) is a process of joining metallic materials based on 3D model data, aiming the manufacture of three dimensional parts by the successive addition of material, usually layer upon layer. This technology is nowadays seen as an emerging one, showing exceptional perspectives of growth, being able to produce parts in various materials such as precious metals (for example gold, silver and platinum) and several metal alloys, such as aluminium, titanium, nickel, cobalt and magnesium based alloys, among others. However, as the range of feedstock materials, technologies and applications increases, so do the concerns about its impact on health and safety of those who are exposed to the particles emitted during these processes, particularly when AM uses metal powder.

Regarding emissions, studies thus far show that nanomaterials are emitted during AM processes, a fact that rises the concern about its impacts and enhances the complexity of risk management on these processes. When risk management aims nanoscale, it becomes a true challenge as it deals with several different nanomaterials and the lack of systematic and standardized risk assessment methodologies. At this scale, risk management raises many doubts regarding the selection of quantitative or qualitative approaches, the identification, characterization and quantification of nanomaterials, the definition of occupational exposure limits and the outlining of control measures.

Having this conscience, a review was developed to summarize some of the recent developments in the field of risk management of occupational exposure to nanomaterials during metal additive manufacturing. Additionally, this review emphases the need for more investigation about risks regarding nanomaterials in workplaces, which is essential to ensure workers' safety conditions and preserve their health, as well as to make conscious decisions on risk assessment, public health, medical monitoring and control measures, namely personal protective equipment.

Session 4
4.4 Risk management

A91635NS

PROSPECTIVE ENVIRONMENTAL RISK ASSESSMENT OF NANOCELLULOSE

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Nanocellulose (NC), as a renewable material, is drawing increasing attention from research, industry, and governments alike. The material's recyclable and versatile properties make it an attractive contender in achieving sustainability objectives and moving towards a greener economy, by addressing both ecological and waste issues. Nanocellulose is also widely recognized as being non-toxic, adding to its attractiveness. Reviews of nanocellulose toxicity nevertheless show discrepancies and knowledge gaps in study results, likely linked to the lack of uniformity in study design. The nanocellulose market is expected to experience substantial growth in the upcoming years, both through a growth of already commercially available products, as well as new products and applications being developed and entering the market. In order to investigate the potential future environmental implications of nanocellulose, we conducted a prospective environmental risk assessment.

To assess the exposure, we performed a dynamic Material Flow Assessment (MFA) of nanocellulose at the European scale, in order to quantify current and future flows and stocks of the material. This assessment looks at the production, manufacturing, use, and end-of-life stages of the material. Using a dynamic approach allows for long-term projections of these stocks and flows by taking into account market-growth forecasts. Predicted environmental concentrations (PEC) are obtained by converting flows into concentrations.

To assess the hazards, a review of ecotoxicological studies of nanocellulose is conducted and using a species sensitivity distribution the predicted no effect concentration (PNEC) is obtained. The combination of PEC and PNEC allows to quantify the risk surrounding nanocellulose. Results give room for an early identification of areas requiring further study and monitoring. By proactively identifying potential risks at the development stage of nanocellulose-based products, future issues can be foreseen and averted.

Session 4
4.5 Nano responsible development and sustainability

A91673MS

Managing the value chain of nanomedicine

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One of the hot topics in nanomedicine is the use of nanobiomaterials for drug delivery. The nanosize brings new challenges and this especially for small and medium enterprises (SMEs) which usually do not have all the resources to bring this technology on the market as nanomedicine is complex, costly and combines knowledge from different disciplines. For bringing a new nanomedicine on the market and to stay there, it is necessary to have a good management of the value chain. Literature in this domain already exists for more conventional medicine [1], but not yet for nanomedicine. Using different methods such as literature review, online questionnaire and interviews, this study maps the current value chain of nanomedicine in Europe and Switzerland, the different business models currently used, and identifies key interactions among stakeholders. As first result, we could identify that few industries are already developing such products and that there are fears regarding the added technological and/or regulatory challenges of nanotechnology in the medical field blocking its development. Furthermore, SMEs, having not the necessary means (e.g. funds, personal, and knowledge) to completely develop a nanomedicine on their own, will have to collaborate with other stakeholders if they want to have a chance to bring their product on the market. This study aims to help SMEs to better prepare ahead how to establish and manage their value chain and understand the different interactions they will need to have with other stakeholders.

[1] Rees, H. (2011). Supply Chain Management in the Drug Industry. J Wiley &Sons.

[2] This project has received funding from the Horizon 2020 framework program of the European Union, ProSafe Joint Transnational Call 2016; from the CTI (1.1.2018 Innosuisse), under grant agreement Number 19267.1 PFNM-NM

Session 4
4.5 Nano responsible development and sustainability

A91819DP

SOCIETAL ENGAGEMENT IN NANOTECNOLOGIES: EXPERIENCES FOR A DIALOGUE IN THE FOOD, ENERGY AND HEALTH SECTORS

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Societal engagement and co-creation between researchers, companies and the public could stimulate the innovation process and support the alignment of future nanotech products with societal needs and concerns.

Within the GoNano project (2017–2020), an analysis of stakeholders' perspectives and issues for dialogue on nanotechnologies in the sectors of food, energy and healthcare has been performed. A selection of research and innovation priorities and scenarios, social perspectives and challenges for public dialogue in these sectors have been identified.

The analysis has been informed by the available literature and through interviews with a broad panel of stakeholders from research, industry, and policy making and civil society organizations across Europe.

The main needs and concerns emerged are related to the health and safety of nanomaterials and related risk assessment and testing activities, uncertainties in existing regulatory frameworks, user acceptability, risk perception, and communication with citizens and consumers about the impacts (risks and benefits) of nanotech, including aspects related to trust and misleading information.

Several other issues are related to the sector concerned and are not specific to nanotechnologies.

While stakeholder engagement is seen as important for innovation by most stakeholders, the practical way to implement it in research practices in an effective and useful way for all stakeholders concerned is seen by most stakeholders as a real challenge.

A key aspect is a careful design of dialogue initiatives, based on the analysis of stakeholders and societal impacts related to specific applications, as the GoNano methodology (fig 1) aims to do over the course of the project.

This contribution provides insights on ways to organize effective dialogue initiatives, starting from the experiences of GoNano, with a focus on the food, health and energy sectors.

GoNano has received funding from the EU H2020 R&I programme under GA 768622.

Session 4
4.5 Nano responsible development and sustainability

A91848PK

Safety culture and perceptions and practice with nanomaterials in academia and industry

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Introduction: Work and research with manufactured nanomaterials (MN) has primarily focused on innovation, toxicity, governance and safety management tools, and some studies have looked at how the public perceives the benefits and risks of MN. The objective of this presentation is to provide preliminary results of a study of OSH professionals' in academia and industry and their perceptions and actions in attaining and applying knowledge about MN in relation to a safety culture model.

Methods: Interviews were carried out with OSH professionals at five academic institutions and five industrial companies. Relevant interview statements were coded into five topics regarding MN: risk comprehension, information gathering, actions, communication and compliance. The statements were then coded according to a five-step safety culture ladder model reflecting increasing safety maturity from: passive, reactive, active, and proactive to generative.

Results: Approximately 230 relevant interview statements were coded. None of the statements lived up to the highest level of a 'generative' safety culture, whereas the majority reflected an 'active' safety culture. There were a number of similarities and differences in the statements between and within academic institutions and industry in their safety culture maturity, particularly in regards to accepting NM risks as part of the job. The differences are also reflected in structural differences between the two types of institutions, e.g. size, organizational structure, turnover, and cultural and linguistic diversity, which provide challenges in affecting and sustaining cultural change in safety.

Implications: The study reinforces the need for politicians and engineers to collaborate with communication experts and social scientists in effectively framing NM information that allows for flexible deployment of multilevel and integrated safety culture initiatives to support operational excellence. Future studies should include places where nanotechnology is having a growing influence e.g. scientific and technical teaching institutions, manufacturing, construction, cosmetics, etc., and initiatives could also look at strengthening safety education of NM risks (and chemical risk understanding in general) starting in public and trade schools.

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A91238VF

MINERALOGICAL ANALYSIS OF PATIENT PULMONARY LAVAGES: FROM NANO TO MICRON-SIZED PARTICLES DETECTION AND PATHOLOGICAL SIGNIFICANCE

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Mineralogical analyses of clinical samples have been proved useful to identify causal relationship between exposure to airborne particles and pulmonary diseases. However, this type of analyses only considers the micron-sized fraction of the particles, neglecting the specific impact of submicron/nano-sized particles which have been otherwise shown to be reactive and able to induce biological effects. To fill this gap, we specifically developed an innovative protocol to isolate micron-sized particles from submicron/nano-sized particles contained in 100 broncho-alveolar lavages and bronchial washes from patients who suffered from interstitial lung diseases. We then determined qualitatively and quantitatively the metal load in each of these fractions. Results showed significant differences between the three fractions in terms of metal load confirming that the separate analysis of the fractions is relevant. It also means that the assessment of the micro-sized fraction alone, as commonly done in clinical practice, only gives a partial view of the mineralogical analysis. Furthermore, we investigated correlations between these mineralogical analyses and clinical data. This approach towards a better understanding of the development of some respiratory diseases such as sarcoidosis opens new perspectives in the clinical nanotoxicology field.

Session 5
5.1 Toxicology

A91497SL

Deficient macrophage autophagy protects mice from Cerium Oxide nanoparticle-induced alveolar remodeling.

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The emission of cerium oxide nanoparticles (CeO_2NPs), used as diesel fuel catalyst, into the ambient air represents a health concern. Data from the literature suggest that pulmonary exposure to these NP can lead to the development of lung fibrosis, with a concomitant macrophagic infiltration. However, the exact underlying mechanism(s) remain(s) to be fully elucidated. In our study, we hypothesized that autophagy, a physiological self-renewal mechanism, and particularly that of macrophages, could play a role in CeO_2NPs-induced lung fibrosis in mice.

Mice lacking the early autophagy gene Atg5 in their myeloid lineage ($Atg5^{fl/fl}$ $LysM^{Cre+}$ mice - $Atg5^{-/-}$) and their wildtype (WT) counterparts were exposed to CeO_2NPs (5 or 50µg) by a single oropharyngeal administration and sacrificed up to 1 month after. At that time, lung remodeling was thoroughly characterized (inflammatory cells infiltration, expression of fibrotic markers such as αSMA, TGFβ1, total and type I and III collagen deposition).

After 28 days, histological analysis of WT mice revealed a dose-dependent increase in inflammatory cells infiltration (macrophages), increased expression of fibrotic markers, in peribronchial as well as alveolar spaces. On the other hand, $Atg5^{-/-}$ mice were protected from the alveolar phenotype (less alveolar thickening, insignificant total and type I and III collagen deposition, no increased expression of αSMA, TGFβ1 in the alveolar region), whereas no effect of Atg5 deletion could be detected in the bronchi area. Interestingly, although a similar macrophagic infiltration (in terms of total number of macrophages) could be detected in both mice genotypes, WT mice were characterized by the accumulation of M1 subtype of macrophages in response to CeO_2NPs, whereas M2 macrophages were the most represented subtype in $Atg5^{-/-}$ mice. These results were confirmed after in vitro exposure of mouse peritoneal macrophages to CeO_2NPs: expression of M1 markers iNOS and CD68 was increased, whereas no difference was observed for the expression of M2 markers CD206 and CD163. Moreover, blockade of autophagy by Bafilomycin A1, prevented the increased expression of M1 markers in response to CeO_2NPs.

The exact consequences of autophagy interplay with macrophage polarization in response to CeO_2NPs are currently under investigation, but overall these data strongly suggest that downregulation of macrophage autophagy could represent an important approach to protect from NP-induced lung remodeling.

Session 5
5.1 Toxicology

A91558KY

HIGH RESOLUTION MASS SPECTROMETRY BASED SAFETY ASSESSMENT OF MWCNT, ZNO AND MSN NANOPARTICLES VIA *IN VITRO* CULTURE SYSTEM

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The copious existence of nanomaterials (NMs) in modern life enforces the research community to understand their chronic effects; this raises the urgent need to understand the safety of new age materials in biological systems. To comprehend the NMs mediated signaling mechanism, we used the iTRAQ based quantitative proteomic approach using CHO-K1 as a model system. Cells were exposed with three types of NMs (ZnO, MSN and MWCNT) with optimized appropriate concentration (5µg/ml, 15µg/ml, and 5µg/ml respectively) identified using MTT and WST-8 cellular toxicity assay in dose and time dependent manners. Protein samples obtained from the cell lysate after 24h treatment were analyzed using high resolution mass spectrometer. Complementing a series of functional measures, gene network enrichment analysis of proteomic was used to compare quantitatively the biological impact of NMs concentrations. Analysis of proteomics data revealed the identification of more than 6244 proteins in NMs treated CHO-K1 cells with total count of 11 million spectra. The differentially expressed proteins include some key proteins involved in anti-oxidant response, metabolic process, cell adhesion, cytoskeletal dynamics, cell cycle, cell death and cell signaling. We specifically found that MWCNT increases the intracellular Ca2+ which intern expanded the cell size and finally initiated the cellular senescence process. Similarly, ZnO revealed the apoptosis mediated cellular senescence via decreasing in the cell size due to shrinkage which significantly impaired cell symmetry (morphology) and cell migration assay. Finally, we provide evidence for ZnO NPs increased catastrophic DNA damage and apoptosis and MSN15 increase the expression of Clusterin, Prolyl 4-hydroxylase, beta polypeptide, Tripeptidyl peptidase II and Ubiquitin carboxy-terminal hydrolase L1, which function as chaperon to prevent the protein aggregation. The results also suggested that the MSN much safer than MWCNT and ZnO NPs, so it can be used in biomedical application. The used quantitative proteomic approach has definitely increased our understanding of different NMs in biological and physiological aspects.

Keywords: CHO-K1, Enrichment analysis, iTRAQ, Proteomics, Toxicity

Session 5
5.1 Toxicology

A91630YS

Novel toxicity related to nanomaterials? Silica nanoparticles cause pleural and pericardial effusion in workers and in rats

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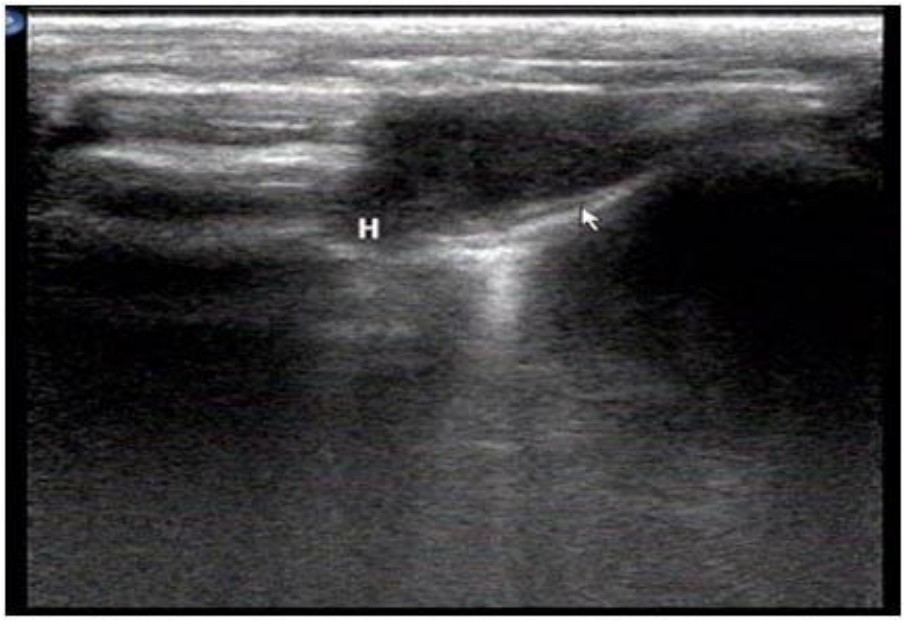
Nanomaterials introduce novel risk factors and potentially lead to novel hazards within the workplace or through environmental contamination. Here we introduce our study in the nanoexposed workers and animal experiments. Further information on the novel toxicity related to the silica nanoparticles was collected and the potential mechanisms were discussed. Our study shows that silica nanoparticles can cause unusual symptoms of pleural effusion and pericardial effusion both in heavy exposed workers and animals. These findings of the novel toxicities highlight the awareness that some nanomaterials like nanosilica may cause unusual toxicity upon heavy exposure, which should be taken seriously in the development of nanoscience and nanotechnology.



Session 5
5.1 Toxicology

A91648PH

Differences in Nuclear Deposition & DNA Methylation in Multi- and Single-Walled Carbon Nanotube exposure in vitro

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Subtle DNA methylation alterations mediated by carbon nanotubes (CNTs) exposure might contribute to pathogenesis and disease susceptibility. In order to understand the epigenetic toxicity, in particular DNA methylation alterations, of single-walled (SW)CNTs and short multiwalled (MW)CNTs, we performed global/genome-wide, gene-specific DNA methylation and RNA-expression analyses after exposing human bronchial epithelial cells (16HBE14o- cell line). In addition, the presence of CNTs on/in the cell nucleus was evaluated in a label-free way using femtosecond pulsed laser microscopy.

Generally, a higher number of SWCNTs, compared to MWCNTs, was deposited at both the cellular and nuclear level after exposure. Nonetheless, both CNT types were in physical contact with the nuclei. No global (5-mC) DNA methylation alteration was observed for both CNTs. After exposure to MWCNTs, 2398 genes were hypomethylated (at gene promoters), and after exposure to SWCNTs, 589 CpG sites (located on 501 genes) were either hypo- (= 493 CpG sites) or hypermethylated (= 96 CpG sites). Cells exposed to MWCNTs exhibited a better correlation between gene promoter methylation and gene expression alterations. Differentially methylated and expressed genes induced changes (MWCNTs > SWCNTs) at different cellular pathways, such as p53 signalling, DNA damage repair and cell cycle. On the other hand, SWCNT exposure showed hypermethylation on functionally important genes, such as SKI proto-oncogene (SKI), glutathione S-transferase pi 1 (GTSP1) and shroom family member 2 (SHROOM2) and neurofibromatosis type I (NF1), which the latter is both hypermethylated and downregulated.After exposure to both types of CNTs, epigenetic alterations may contribute to toxic or repair response.

Moreover, our results suggest that the observed differences in the epigenetic response depend on particle type and differential CNT-nucleus interactions.

Session 5
5.1 Toxicology

A91649US

Intracellular uptake and toxicity of iron oxide nanoparticles

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Introduction: Over the past few decades nanotechnology and materials science has progressed extremely rapidly. The uses of nanoparticles are widely reported in variety of areas including advanced materials, electronics, magnetic, optoelectronics, biomedicine, pharmaceuticals, cosmetics, energy, hyperthermia, environmental detection and monitoring. Since Iron oxide nanoparticles with unique magnetic properties have a high potential for use in several biomedical and bioengineering applications, the present study was aimed to evaluate toxic effects of iron oxide nanoparticles in splenic lymphocytes of male Wistar rats.

Methods: Lymphocytes were isolated from spleen of male Wistar rats and were treated with different concentrations of iron oxide nanoparticles. Cell viability, Reactive oxygen species (ROS) level, anti-oxidative parameters, mitochondrial membrane potential (M.M.P.) and morphological studies were performed after different incubation time. Cell viability was studied by Trypan blue exclusion method. Generation of intracellular reactive oxygen species (ROS) was estimated by DCFHDA staining and other antioxidant parameters like SOD, CAT, and GSH were also measured by spectrophotometer. JC-1 staining was performed to quantify mitochondrial membrane potential. Morphological changes and uptake were seen with Transmission electron microscope (TEM) and Elemental mapping.

Results: Results revealed a significant decrease in the cell viability of lymphocytes treated with higher concentration of IONPs nanoparticles. Similarly a significant increase in ROS production is observed in concentration dependent manner. Mitochondrial membrane potential and antioxidant parameters (SOD, CAT, and GSH) show significant decrease as compared to the control. Moreover morphological changes show intracellular uptake and localization of nanoparticles in cell, which cause cell damage.

Conclusion: Thus, the present study concludes that higher concentration of iron oxide nanoparticles may induce oxidative stress which May leads to cell death. Hence, it is important to consider the concentration of these IONPs before use in biomedical applications.

Session 5
5.1 Toxicology

A91651AC

Effects of maternal Au-NP exposure by ingestion on feto-placental development and placental function, in a rabbit model

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Oral contamination by gold, including gold-nanoparticles (Au-NP) exposure, occurs via food, dental fillings, tobacco and pharmaceuticals. The general population, including pregnant women, is exposed by ingestion, but effects of Au-NP during pregnancy on the feto-placental development remain misunderstood. The aim of this work was to evaluate the effects of an oral maternal sub-chronic exposure to Au-NP throughout the gestation on the feto-placental development and placental function in a rabbit model. Pregnant females were orally exposed (NP, n=9) or not (C, n=9) to uncoated Au-NP (5 nm diameter), at 1.54 µg/kg/day (corresponding to the estimated daily exposure of humans through diet), 5 days/week, from D3 to D27 of gestation (total exposure: 18-20 days). Gestation was monitored by ultrasound, including fetal biometric measurements and fetal blood flows. At D28, effects on maternal and fetal biometry, maternal hematology and biochemistry were analyzed using a linear mixed model taking into account exposure, litter size, sex and duration of exposure as fixed effects, and dams as random effects. To detect DNA lesions, the alkaline comet assay was performed on various maternal and fetal tissues. Au-NP distribution in placental tissue was evaluated by transmission electron microscopy and placental function was explored by transcriptomic approach. Fetal growth was normal throughout the gestation, despite a significant decrease of cerebral diastolic velocity at D21 in NP compared to C. At D28, adrenal glands were heavier in NP dams, whereas maternal hematology and biochemistry, fetal biometry remained unchanged. No DNA lesions were observed in maternal and fetal tissues at D28. The presence of «finger-prints» inclusions was revealed by ultrastructural analysis in the labyrinthine area (exchange area) of the placenta, in the maternal blood space and in the trophoblast of the NP group. Moreover, dense elements were observed in erythrocytes of fetal vessels' suggesting that Au-NP could cross the placental barrier. Placental transcriptomic data were analyzed using GSEA (Gene Set Enrichment Analysis) and revealed that gene set enrichment profiles differed completely between males and females in NP compared to C. In conclusion, in utero exposure to Au-NP by maternal ingestion affected only weakly maternal and fetal biometric phenotypes but Au-NP were present in the placenta and placental gene expression was affected in a sex-specific manner.

Session 5
5.1 Toxicology

A91663SM

IN-VITRO AND IN-VIVO GENOTOXICITY OF TITANIUM-DI-OXIDE NANOMATERIALS INFLUENCED BY ITS DISPERSION STATE

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Titanium-di-oxide nanomaterials (TiO_2 NMs) are one of the most produced nanomaterials and has already been integrated into many commercial products such as cometics, paints etc. Increased production and use of TiO_2 NMs has increased the risk of exposure and raised the concern about their safety. Despite several studies investigated the genotoxic effects of TiO_2 NMs, the results are often contradictory and non-comparable due to variation in experimental parameters. Dispersion state is believed to be an important parameter but its influence on the genotoxicity of TiO2 NMs is poorly understood. Therefore, the aim of this study was to prepare TiO_2 NMs suspensions in well-dispersed state (contain predominantly primary/single particles or small agglomerates) and less well-dispersed state (contain primary particles, small and large agglomerates), and investigate their genotoxicity using in-vitro and in-vivo system. Nano TiO_2 (primary particle size ~17 nm) and non-nano TiO_2 (primary particle size ~117 nm) were selected to compare the size dependent effects. Stock dispersions were prepared for each of these NMs using modified Spalla and Guiot protocol. Human monocytic cells (THP-1) were exposed to non-toxic doses (5, 25, 50 µg/ml) of all these suspensions (diluted in serum free cell culture medium) for 24 hours and the DNA damage was evaluated using alkaline comet assay. Nano TiO_2 in its less well-dispersed state (18-127 nm) induced DNA damage dose dependently while no significant effect was observed in their most dispersed condition (18-34 nm). In contrast to nano-TiO_2, non-nano TiO_2 was genotoxic in its most dispersed state (122 - 155 nm) but not in their less well-dispersed condition (122 - 416 nm). For in-vivo, mice were exposed to 100 µg (aspiration) and 500 µg (gavage) of these suspensions and at day three, whole blood was collected from the sacrificed mice and the comet assay was performed. Similar to in-vitro, the results indicate that the different dispersion state also influences the genotoxicity in-vivo. The dispersions are being characterized for several parameters associated with physico-chemical characteristics (such as size, shape, surface topology, fractal properties) of primary particles and agglomerates, and multiple statistical analysis will be performed to link the particle properties to the observed genotoxic effects.

Session 5
5.1 Toxicology

A91682JO

Development of a microfluidic flow system for nanomaterial toxicity screening

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Reliable, high-throughput screening techniques for toxicity analysis are essential to rapidly identify nanomaterial hazards effectively. An existing electrochemical screening method, whereby cyclic voltammetry is used to assess the interaction of nanomaterials with a lipid-coated electrode, has been established as an effective method of screening nanomaterials. However, wider use of this technique is limited as a high level of operator knowledge and skill is required. To improve this screening procedure, a microfluidic screening device has been designed that significantly reduces the required operator skill level by automating multiple aspects of the screening process. This work presents an overview of the platform design, demonstrates the use of the system and discusses ongoing work to develop the system. The main features of the design include reservoirs to store buffer, lipid and nanomaterial samples used in the screening process; a microfluidic flow cell containing a sensor element on a fabricated electrode for electrochemical analysis and syringe pumps used to control the flow of fluids through the flow cell. Automation of the syringe pumps enabled accurate repeatability of the screening process through precise control of the fluid flow rates, minimizing fluid consumption, and significantly reduced the required skill level of the operator, with the system requiring minimal input on a user-friendly visual control interface to operate. To demonstrate the performance of the system, various nanomaterial samples were screened using the device to assess the interaction with the lipid-coated electrode, showing good agreement with results obtained using existing screening methodologies. Ongoing work aims to improve the screening system by establishing an automated data-processing method to quantify nanomaterial interactions and by integrating a sample auto-loader for screening programmes.

Session 5
5.1 Toxicology

A91714AP

REACTIVITY MEDIATED VARIATION IN BAND GAP OF OXIDE BASED NANOMATERIALS IN BIOLOGICAL FLUIDS AND MAPPING OF ITS TOXIC POTENTIAL

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Dissolution, use of band gap and conduction band energy (as per the theoretical framework: toxicity regime of -4.12 to -4.84eV) in addition to hydration enthalpy (accounts for ionic index) have been explored as the dominant paradigms for the assessment of toxicity. Dissolution translates into the release of ions in the concentrations that may trigger a biological response different from that of the NPs themselves. On the other hand bandgap of a material is associated with direct electron transfer mechanism to the biomolecules. Oxidative stresses generated by chemical species (ROS) in the process inside the cells stimulate inflammatory responses or even lead to cell death.

Bandgap energy of NMs is a function of major physicochemical factors like size (bandgap increases as a material is downsized), morphology and introduction of defects in addition to the composition. Under highly dynamic and time-dependent reactive conditions, dissolution translates into not just release of ionic species but also reduction in size. Hence, the toxicity of a nanomaterial could be a combination of the dynamic bandgap, dissolution and size. In our study, we temporally mapped the variation in the reduction of size as a function of dissolution to variation in the bandgap of oxide-based nanomaterials.

Nickel oxide and copper oxide NPs were chosen as they both are different in composition and uphold different dissolution profiles. The NPs were studied in 1mM $NaNO_3$, simulated body fluid, artificial lysosomal fluid (ALF) and cell culture media (CCM). With 7.4% dissolution of CuO NPs suspended in 1mM $NaNO_3$ reflected in 16.62% increase in the bandgap energy which can be correlated to aggregation behaviour of the nanoparticles over the period of 48 hours demonstrated through TEM results. Similarly, on 96.8% dissolution of CuO NPs in ALF translated in 19.35% increase in the bandgap energy temporally. However, in CCM the increase in the bandgap energy was upto 28.7%. Similar trends were observed for nickel oxide NPs too on aggregation and dissolution under specific media conditions. The particle and ionic components of the nanoparticles were separately tested on A549 cell line for cell viability, intracellular ROS generation and mapping of mitochondrial membrane potential. The study offers an avenue to foster the understanding of intertwined energetic mediated modes of toxicity of the NMs under dynamic conditions in addition to providing a strong feedback towards building nanomaterials.

Session 5
5.1 Toxicology

A91822FP

Positive surface charge: a predictive factor for nanoparticle toxicity?

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Surface charge is considered as a key factor for nanoparticle (NP) toxicity, a positive charge being generally associated with greater undesirable effects. However, by screening a carbon NP library in THP-1-derived macrophages, we found previously that a cationic charge does not suffice to impart NPs with toxicity. To get further insight into this, we carried out a comprehensive study on 5 cationic carbon NPs (zeta potential from 18.6 to 26.9 mV) produced by pyrolysis of citric acid and various passivation reagents, namely branched poly(ethyleneimine) (bPEI) 25k (NP_1), bPEI600 (NP_2), pentaethylene hexamine (PEHA) (NP_3), N,N-dimethylethylene diamine (DMEDA) (NP_4) and DMEDA/poly(ethylene glycol) (PEG)550 (NP_5) leading to NPs with different density of protonatable amino groups at their periphery. A negatively charged and non-cytotoxic NP (NP_6) prepared from ammonium citrate (-40,0 mV) was used as control. NPs had a size ranging from 7.2 to 43.8 nm and exhibited intrinsic fluorescence allowing the study of their cell fate by confocal laser scanning microscopy and FACS. In THP-1-derived macrophages, the viability loss (MTT assay) evoked by the NPs (0-200 µg/mL) at 24 h was as follow: high for NP_1 (EC_{50}=18 µg/mL) and NP_2 (EC_{50}=34 µg/mL), moderate for NP_3 (EC_{80}=124 µg/mL) and NP_4 (EC_{80}=43 µg/mL) and negligible for NP_5 and NP_6 (viability loss<20% at 200 µg/mL). A similar trend was observed in airway epithelial cells (A549 and Calu-3), although less acute than in macrophages (e.g., EC_{50}=62 µg/mL in A549, and 151 µg/mL in Calu-3 for NP_2). NP_1, NP_2, NP_3 and NP_4 were taken up by THP-1 cells at 4 h, but NP_5 and NP_6 were not. As well, among the 6 NPs, only NP_1 and NP_2 induced significant oxidative stress (evidenced by decreases in reduced glutathione levels), release of the pro-inflammatory cytokine IL-8, activation of the NLRP3 inflammasome (IL-1beta release), and mitochondrial dysfunction. Thus, this study clearly confirms that measuring the surface charge of a cationic NP does not suffice for predicting its toxicity, since NP_3 (+18.6 mV), NP_4 (+21.3 mV) and NP_5 (+26.9 mV) displayed no or moderate toxicity, whereas NP_1 (+22.7 mV) and NP_2 (+26.4 mV) exhibited deleterious effects. Our results indicated also that NPs with the highest density of positive charges (NP_1 and NP_2) were the most toxic, whereas NP PEGylation (NP_5 vs NP_4) resulted in reduced cytotoxity. Therefore, the charge together with the surface chemistry are predictive factors of NP toxicity.

Session 5
5.1 Toxicology

A91833?P

COMPARISON OF PBPK MODELS DESCRIBING THE DISTRIBUTION OF NANOPARTICLES IN MAMMALS

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In the presentation, the principles of physiological based pharmacokinetic (PBPK) models will be outlined. Various PBPK models published will be analyzed from the point of views of their reasonability and mathematical treatment. Some recommendations for PBPK modelling will be suggested.

Session 5
5.1 Toxicology

A91849VF

IN VITRO AND IN VIVO INVESTIGATION ON THE BEHAVIOR AND THE TOXICITY OF ALUMINUM NANOPARTCLES BY INGESTION

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Aluminum nanoparticles (Al NPs) are increasingly used in several goods including food additives, medication, and beverage and water treatment. If EFSA has established a tolerable weekly intake (TWI) of 1 mg/kg bw for human oral exposure (EFSA 2008), the behavior of Al NPs and their potential effects on human health have been scarcely investigated. Nevertheless, aluminum was depicted to cross epithelial barriers and to include neurotoxicity and embryotoxicity.

Using both in vitro and in vivo (3 and 28 days by gavage) studies, we investigated the behavior and the toxic effects of Al0 and Al2O3 NPs in comparison with the ionic form AlCl3. Intestinal and hepatic human cells showed an uptake of the two NPs although the detection by IBM highlighted a higher amount for Al0 NPs. No toxic effects (cytotoxicity, apoptosis and oxidative stress) as well as no genotoxicity with the micronucleus and the H2Ax assays were observed (exposure from 0.6 to 256 µg/cm2). While inconclusive results were obtained with Al0 NPs due to interference, Al2O3 NPs induced oxidative DNA damage visualized by the Fpg-modified comet assay. The two Al NPs did not cross the in vitro intestinal cell models and a low solubility was reported in the two cell media. In vivo, following oral exposure (3 gavages, 6, 12.5 and 25 mg/kg), Al was detected in several organs including liver and spleen with higher Al amounts for rats treated with Al2O3 NPs than for the ones treated with Al0 NMs. No induction of chromosomal mutations was detected by the micronucleus assay both on bone marrow and on colon. With the comet assay, an effect was reported only in bone marrow for Al2O3 NPs. In the 28 days study, no genotoxic effect was observed with the micronucleus and the comet assay except in spleen with the intermediate dose of Al0 NPs. The presence of Al2O3 NPs was observed by TEM in intestinal tissue while no Al0 NPs was detected.

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Session 5
5.1 Toxicology

A91868CM

A clinical approach to determine whether exhaled breath condensate is representative of deep lung for nanoparticle biomonitoring

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There is now general agreement that the most health-damaging particles are those which can penetrate and lodge deep inside the lungs. That is why there is a special concern about nanoparticle exposure, especially in some occupational fields where nanoparticle inhalation is prone to occur. Assessment of external exposure must be addressed but this approach should be completed by biomonitoring which is the only way to take into account the use of protective devices and individual variability. Exhaled breath condensate (EBC) is more and more described as a useful matrix to assess biomarkers of exposure and effect of the respiratory tract in a non-invasive way. However, the question arises to what extent EBC is representative of deep lung.

We have evaluated this issue in a clinical collaborative study where EBCs were compared to bronchoalveolar lavages (BALs) and bronchial washes (BWs) for their metal and particle loads in the same patients. EBCs were collected with the RTube device in 100 patients and characterized by their volume, total proteins and Na contents. The EBC particle load was assessed with dynamic light scattering and electronic microscopy, and the EBC metal composition for 12 metals was determined with ICP-MS. A size-fractionation procedure was used for the evaluation of the particle and metal loads of BALs and BWs.

The results indicate that in terms of particulate content, EBC might be representative of both the sub-micrometric and nanometric/dissolved size fractions of BAL and BW. All metals were found in EBC at lower levels of one or two orders of magnitude than in BAL and BW, at the exception of Si and Zn that were found at similar levels. While all biological matrices presented their own specificity in terms of elemental profiles, some general trends were found, such as Si being a main component. The correlations between the different biological matrices were assessed as well.

This study brought the unique opportunity to compare EBC to invasive respiratory samples in the same persons, which is only possible in a clinical context. In the future, EBC profiles determined in patients might be compared to other types of population and further characterized using innovative technics such as single particle ICP-MS.

Session 5
5.1 Toxicology

A92118HS

A DAILY GESTATIONAL EXPOSURE TO DIESEL EXHAUST PARTICLES IMPAIRED THE BRAIN AND OLFACTORY DOPAMINERGIC PATHWAYS OF RABBIT PUPS

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Previous results obtained at gestational day (GD) 28 from rabbit fetuses daily exposed to diesel exhaust (DE) particles from GD3 to GD27 showed the presence of nanosized particles (20-48nm) in the olfactory sensory neurons and the glomerular layer of the olfactory bulb (OB), along with cellular and axonal hypertrophy. Concomitant bulbar monoaminergic homeostasis disturbances, especially affecting the dopaminergic system, were also observed (Bernal Melendez et al., Toxicology Letters, 2016, 259S, S201-S202). However, the neurotransmission pathways potentially affected by this gestational exposure and their long-term consequences have yet to be further explored. To further investigate the effects of DE exposure with a focus on the dopaminergic system, the OB and brain of GD28 (8 controls; 8 exposed) and adult (8 controls; 10 exposed) rabbits were analyzed using histochemistry, immunohistochemistry and chromatography analysis in order to assess the anatomical and functional continuum between the olfactory system and other central structures of the brain at these two states. At GD28, increases in the content of dopamine and the tyrosine hydroxylase (TH) -labeling intensity per cell were observed in OB of exposed fetuses without any increase in the number of dopaminergic neurons. At the adult stage, OB of exposed animals exhibited higher levels of dopamine and its metabolites (DOPAC and HVA). Within the brain of the same rabbits, the cytochrome oxidase activity, a marker of energetic metabolism, and the TH-labeling intensity were increased in the ventral tegmental area, a key area which is implicated in the reward circuitry of the brain, whereas both markers remained unchanged in the dopaminergic pars compacta of the substantia nigra which plays a role in the regulation of the fine motor control. All these findings suggest that the imbalance in the dopaminergic system observed in OB of the exposed fetuses at the end of the gestation seems to persist in adulthood, and is associated to alteration in more central structures. Because of the known anatomical and functional continuum between the olfactory system and the rest of the brain, and the importance of dopamine homeostasis in the plasticity of neural circuits, such alterations could participate to disturbances in higher integrative structures, with possible long-term behavioral consequences.

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Session 5
5.1 Toxicology

A90586AR

STANDARDIZING IN-VIVO ANALYSIS METHODS FOR TOXICOLOGICAL EFFECTS WITHIN FRESHWATER ORGANISMS FROM NANO-POLYSTYRENE EXPOSURE

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Modern industry is moving into the use of various new technological and chemical techniques, amongst which is a growing interest in developing the application of “nano-carriers”. These are nanoparticles designed to contain certain chemicals in a manner that reduces the overall concentration of the various chemicals used. Also specialised compounds and capsules are used to control the mechanisms behind chemical release to ensure optimal application of the active ingredients. However despite the peaking interest on these novel products, there is a noted lack of research in the potential toxicological effects related to the nano-carriers. The purpose of this research is to determine if a consistent and non-invasive testing method of analysis may be produced for determining morphologic complications and toxicity/mortality effects of specific nano-carriers within freshwater organisms to act as a realistic but controlled in-vivo comparative assessment to the potential results from nano-carriers present in effluent wastewater products. The current testing was focused on nano-polystyrene, as these are commonly existing substances that are already found in residual effluence & waste water due to the everyday use and disposal of bulk polystyrene. Four test organisms were chosen to provide a mixture of relatively transparent anatomy that will permit numerous visual analytical techniques to be conducted, along with organisms that can be processed using known biochemical assays to determine the biological impacts. The visually analysed test species also have well-documented growth pattern which permit easy identification of morphological malformations during early stages development.

Initially specialised fluorescent nano-carriers would be used in combination with fluorescence and light microscopy to analyse general nanoparticle flow patterns within the organisms. Also general comparisons with set controls to determine forms and degrees of morphology & toxicological alterations. Later, non-fluorescent compounds were utilized for detection analysis would be conducted by a combination of compound-detecting spectral techniques such as Raman and UV-Vis spectroscopy. These would be combined with other methods as final confirmation for the presence and causation of impact on these organisms from the nano-particles. The resulting information determined whether these nano-plastics are inherently toxic, or incur toxicological effects following release to the environment.

Session 5
5.2 Environmental interactions of nanomaterials

A91249Md

N-Acetylcysteine as antidote for silver nanoparticles intoxication

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The use of silver nanoparticles (AgNP) in consumer products is growing exponentially. Consequently, increases the human exposure to AgNP significantly when handling during manufacturing, using and disposing of AgNP-containing products. In cases of AgNP poisoning, the medical procedure is not established yet. We found that thiol-containing antioxidants N-Acetylcysteine (NAC) could act as chelating agent in vitro for AgNP, reverting their cytotoxic effects. Here, we hypothesized that NAC could act as an antidote for AgNP intoxication in vivo. AgNP (5 mg/kg) led o increase in serum biochemical parameters of the hepatic function (aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP)) in adult male Wistar rats compared to control. All biochemical parameters showed physiological values after a single administration of NAC (1g/kg) one hour after injection of AgNP. In accordance with liver biochemistry results, the hepatic tissue of AgNP group exhibited inflammatory cell infiltration at the hepatic portal system, while no visible alteration was observed in hepatic parenchyma of the AgNP+NAC group. Immediately after AgNP injection, the hind paws exhibited a dark bluish color suggesting inadequate oxygenation of the blood. Compared to the control group, AgNP group showed a decrease in many blood parameters such as red blood cells, hemoglobin, hematocrit levels, and platelet count. No alterations in hematological parameters were found in the animals treated with AgNP+NAC. The white blood cells (WBC) count was higher in the AgNP group when compared to control, NAC and AgNO3 groups. Typically, an increased number of WBC is associated with inflammation, whose was shown above at the liver portal system of AgNP-treated animals. A significant density of Kupffer cells was found nearby the portal area; although, in animals treated with AgNP+NAC, the population of Kupffer cells was more rarefied. The treatment with NAC led to an altered silver biodistribution, which would avoid their accumulation in the liver while increasing their renal excretion. Overall, we conclude that NAC reversed toxic effects of AgNP, and could to be a potential candidate for early intervention in cases of AgNP intoxication.

Session 5
5.2 Environmental interactions of nanomaterials

A91250Md

Thiol-antioxidants binding to silver nanoparticles interfering with cytotoxicity assessment

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Cytotoxicity of chemically and biologically synthesized silver nanoparticle (AgNP) have been broadly investigated, and the oxidative stress is generally presumed as the primary mechanism of cell death. Most of these studies rely on antioxidants to establish this cause-and-effect relationship; however, details on how these antioxidants interact with AgNP are often neglected. Therefore, we decided to study interferences of interaction between thiol-antioxidants (N-acetyl-L-cysteine, L-cysteine, and glutathione) or non-thiol-antioxidants (Trolox and ascorbic acid) with AgNP. Our results showed that both antioxidants families mitigated the production of ROS in Huh7 hepatocarcinoma cells upon AgNP treatment. However, thiol-antioxidants can reverse the cytotoxic effect, whereas non-thiol-antioxidants are unable to reverse the cytotoxic effect. Further, we found that the mitigation of cytotoxicity correlates with the chelation capacity of the antioxidant, demonstrated through the aggregation assays using dynamic light scattering technique and silver-thiol bonding confirmed by X-ray photoelectron. Our findings show that the care should be taken in the interpretation of cytotoxicity when studying metallic nanoparticles with thiol-antioxidants. Determining the correct mechanisms underlying the cytotoxic effects of nanoparticles is critical to promote the progress of nanotechnology.

Session 5
5.2 Environmental interactions of nanomaterials

A91485AN

Binary interactions of aluminium oxide and copper oxide nanoparticles mixture in freshwater systems

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Commercial production and use of engineered nanoparticles (ENPs) in industrial applications and consumer products are increasing rapidly due to their novel properties. For example, aluminium oxide (nAl_2O_3) and copper oxide (nCuO) nanoparticles are extensively used in cosmetics, paints, textiles, etc.; hence, are found to co-exist in the aquatic systems. To date, data is available on environmental processes (e.g. aggregation, dissolution, dispersion, etc.) of individual nAl_2O_3 and nCuO transformation in the aquatic systems. However, only handful studies have reported environmental processes of ENPs mixtures. Understanding the interactions of ENPs mixtures is essential due to likely implications to their bioaccessibility or effects to aquatic biota through: alteration of ENPs stability, control on bioavailable metallic ionic species, and influence on the nature of interactions with organisms. Herein, we show that aggregation and dissolution of nAl_2O_3 and nCuO mixtures in freshwater sourced from two river systems were influenced by the resultant interactions between the ENPs, and the characteristic composition of the freshwater. Results of transmission electron microscopy (TEM) confirmed the heteroaggregation between the ENPs. Moreover, aggregation of nAl_2O_3/nCuO mixtures under variant ratios increased as the concentration of nCuO decreased. This was attributed to the adsorption of nCuO onto the nAl_2O_3 surfaces. The aggregate sizes in the mixtures tended to be larger when compared with those for individual ENPs. Overall, this study illustrates that environmental transformation of ENPs mixtures may be unique, and could not be deduced from fate data for individual components. Therefore, interactions of ENPs mixtures in the aquatic systems will influence their stability and dissolution, and in turn, determine the consequent ENP bioaccessibility, bioavailability, or effects potential following interaction with aquatic biota.

Session 5
5.2 Environmental interactions of nanomaterials

A91496CC

Investigations of the hazard assessment of selected nano-objects used as additives for EVA matrix nanocoposites

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Waste management is a challenge for any developed country, especially since economic development and technical progress causes a general increase in waste volume and complexity. The main purpose of waste management systems is to reduce and control the effect of waste on the environment. This can be done in numerous ways, but the three most common waste management processes are recycling, incineration and landfilling. Products containing nanomaterials are generally not labelled specifically, so there is no easy way to identify nanomaterials in waste treatment processes. Hence, many nanomaterials may end their life cycles in waste treatment facility.

Information and literature about the end-of-life of nanocomposites often remains partial and does not address the overall fate and transformations of nanoparticles that may affect biological responses.

This presentation underlines that the physico-chemical features of nanoparticles can be modified by the incineration process and the available toxicological data on pristine nanofillers might not be relevant to assess the modified nanoparticles included in soot. Combustion tests have been performed at lab-scale using a cone calorimeter modified to collect fumes (particulate matter and gas phase) and have been characterized using various techniques. Nanocomposites selected were Poly (ethylene vinylacetate) (EVA) containing nanoparticles, boehmites or alumina. Evaluations of cytotoxicity responses on pristine nanofillers, soot and residual ash, show that safe boehmite nanoparticles, become toxic due to a chemical modification after incineration process.

A91542JH

IMPORTANCE OF ELECTROCHEMICAL AND SURFACE CHARACTERISTICS OF A RANGE OF METAL NANOPARTICLES FOR ENVIRONMENTAL FATE

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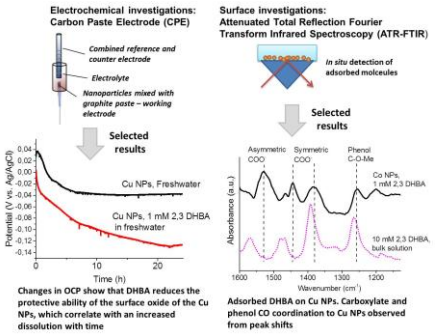
Environmental risk assessment of the diffuse dispersion of metal nanoparticles (NPs) requires knowledge on their environmental fate in terms of changes in particle characteristics and their transformation in contact with freshwater and similar media. This work describes how surface interactions with natural organic matter (NOM) and the electrochemical properties of metal NPs influence their dissolution and characteristics. Investigated NPs include copper (Cu), manganese (Mn), aluminum (Al), tungsten carbide (WC), tungsten carbide cobalt (WC-Co), and cobalt (Co). NOM interactions were studied by means of dihydroxy benzoic acid (DHBA) and Suwannee River humic acid.

DHBA and humic acid readily adsorbed on Cu, Co, WC-Co, Al, and Mn NPs (<1 min) via multiple surface coordinations. DHBA adsorbed via covalent bonding with NPs of Cu and Al, which enhanced their degree of dissolution through weakening of the metal-oxygen bonds of the surface oxide. The adsorption of DHBA was initially observed to reduce the open circuit potential (OCP) of the same NPs, indicative of a less protective oxide/adsorbed organic surface layer. For the Al NPs, the OCP recovered over time, showing improved barrier characteristics (passivity) of the surface oxide with time at these conditions. For the WC NPs, no surface interactions were taking place either with humic acid or with the DHBA monomers, possibly due to lattice structure effects (mismatch between adsorbent and surface oxide). The OCP of the WC NPs initially decreased followed by an increase as a result of development and formation of a surface oxide of improved protective properties (WO_3).

In all, this study shows that the comparison of NPs of different surface characteristics is a way to increase the knowledge on the environmental fate of NPs, useful in terms of improved understanding of dissolution mechanisms and an aid for grouping of NPs within the framework of environmental hazard and risk assessment.



Changes in OCP show that DHBA reduces the protective ability of the surface oxide of the Cu NPs, which correlate with an increased dissolution with time

Adsorbed DHBA on Cu NPs. Carboxylate and phenol CO coordination to Cu NPs observed from peak shifts

Session 5
5.2 Environmental interactions of nanomaterials

A91824BE

IN VIVO TOXICITY PROFILING OF CARBON AND CLAY BASED NANOMATERIALS USING THE ZEBRAFISH EMBRYOTOXICITY ASSAY

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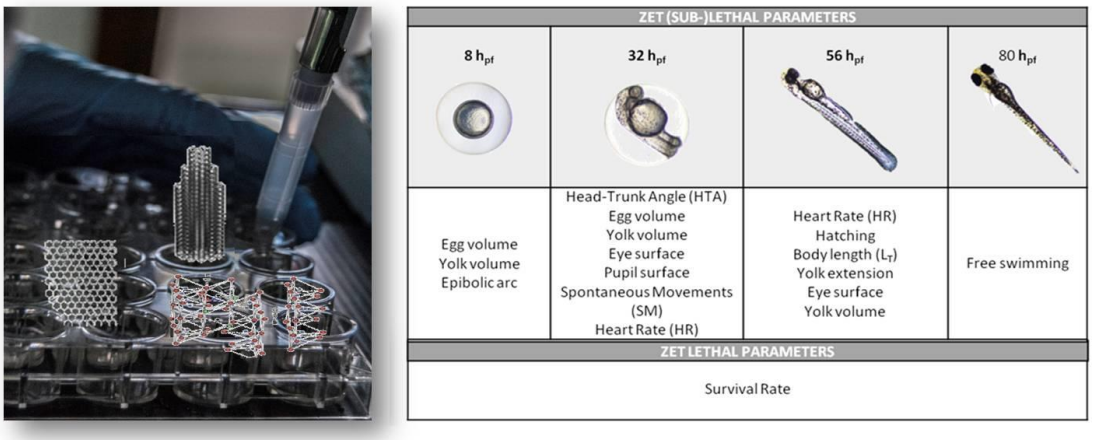
International awareness towards safe and sustainable nanostructured materials have conducted to the development of pioneering and novel green and smart nanosolutions, and have boosted a remarkable expansion potential for multiple industry sectors. Yet, current uncertainty in the regulatory framework, the limited literature available on their potential effects towards human health and environmental safety, and the scarce information on their specific properties have limited their use in the industry.

Our research group has detailed screened in vivo the nanosafety profile of two carbon and two clay based nanomaterials via in vivo zebrafish embryo toxicity (ZET) protocol (Figure 1): multi-walled carbon nanotubes (MWCNTs) and graphene, and cloisite-5 and -20, respectively. This research is being developed in the framework of the funded project Interreg SUDOE-NanoDESK (http://sudoenanodesk.europeanprojects.net/).

Newly fertilized zebrafish zygotes were monitored via continuous waterborne exposure to nominal concentrations of 0.025-25, 0.01-100 and 0.01-10 mg.mL-1 for 80 hours post-fertilization (hpf), for MWCNTs, graphene and both nanoclays, respectively. Mortality, developmental delay signals, phenotypical malformations, spontaneous movements and free-swimming patterns, heart rate and hatching were assessed. Although some sub-lethal nanotoxicity associated with MWCNTs and graphene exposure was recorded, particularly affecting spontaneous movements and cardiovascular system, zebrafish embryonic survival rate was shown to be above 80 %. Both organoclays were demonstrated to be non-nanotoxic, and despite zebrafish embryos cardiotoxicity was registered for test concentrations superior to 0.01 mg/L at 32 and 56 hpf, it cannot be assigned to the nanoclays as the solvent at the highest concentration tested gave the same cardiotoxic level.



Session 5
5.2 Environmental interactions of nanomaterials

A91826SL

Binary mixture toxicity of metal oxides nanoparticles and triclosan on Bacillus subtilis in freshwater systems

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Metal oxide engineered nanoparticles (ENPs) such as zinc oxide (nZnO) and iron oxide (nFe_2O_3) are commercially widely used, and are therefore continuously being emitted into the environment. However, their associated ecological impacts are yet to be fully quantified either as single, or mixtures of ENPs. In addition, once in the environment, ENPs also interact with other contaminants such as organics e.g. triclosan (TCS) – an antimicrobial agent used in personal care and household products, and widely detected in wastewater, freshwater, sludge, and sediments. However, to date, there is scarcity of information on ENP-ENP-, or ENP-ENP-organic-interactions, and their concomitant toxicity in freshwater systems. To address some of the information gaps, herein, we report findings on the toxicity of binary mixtures of nZnO, nFe_2O_3 and TCS on Bacillus subtilis. The B. subtilis was used as model organism as is widely ubiquitous in ecological systems like freshwater and soils. Dose response curves for single chemicals were used to establish 2 h EC_x values under visible light exposure in freshwater sourced from two river systems. Concentration addition (CA) and independent action (IA), and toxic unit (TU) approach models were used to establish the toxicity of the binary mixture of nZnO and TCS in different river water samples; whereas nFe_2O_3 was not used due to its low toxicity (where no EC_{50} was found even concertation of 1000 mg/L). Secondly, following single mixture exposure tests, concentration ratios of nZnO and TCS were also examined experimentally using crosswise concentrations (EC_x values), while ternary mixtures were experimentally examined using the derived binary results at two fixed concentrations of nFe_2O_3 (1 and 5 mg/L). Results showed that nZnO toxicity was dependent on water chemistry of exposure media; hence a significant difference in 2 h EC_{50} values in the two river systems was observed. The toxicity of TCS was not water chemistry dependent, with 2 h EC_{50} values being in the mg/L range in both river water samples. The findings on the measured and predicted effects of the mixtures as well as microscopic analysis to account for the interactions with bacteria will be presented.

Session 5
5.2 Environmental interactions of nanomaterials

A91864TM

MULTIMODAL TOXIC MECHANISM OF GRAPHENE OXIDE TO ALGAE AND CYANOBACTERIA – THE ROLE OF SURFACE OXIDATION

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Algae and cyanobacteria are primary producers in aquatic ecosystem and will get in contact with GO, when disposed in environment. We evaluated interaction between three GOs with different rates of oxidation (HO-GO, HU-GO and TO-GO) and Raphidocelis subcapitata and Synechococcus elongatus representing algae and cyanobacteria, respectively. Relevant growth inhibition occurred even at low concentrations of GOs (6, 25 µg/ml) after 96 h for both organisms. With Synechococcus there was almost no difference between the three GOs and inhibition effect was probably mainly due to indirect mechanisms. These involved shading/aggregation of GOs with dominant effect on photosynthesis and nutrients depletion and sorption on GOs with subsequence influence on the growth and cell division. In the case of Raphidocelis on the other hand, there was significantly higher inhibition effect for HO-GO then for higher oxidized HU-GO and TO-GO suggesting additional mechanism of action. Therefore, we studied direct interaction between three GOs and algal cells with flow cytometry and microscopy imaging. We discovered that GOs can act as “nanoblades” with the ability to cause mechanical or oxidative damage to algal cells depending on the number of functionalization groups on its surface. Interestingly, we observed the highest effect after shortest incubation time (2 h), but after longer period of time (24 and 48 h) algal cells were able to develop defensive mechanisms, regenerate and generally get accustomed to the GO presence, what prove a million years of algae and cyanobacteria experience with nanocarbon species in the real ecosystems.

Session 5
5.2 Environmental interactions of nanomaterials

A91866SB

THERMAL TRANSFORMATIONS OF MANUFACTURED NANOMATERIALS AS A PROPOSED PROXY FOR AGEING

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Ageing is an important part of a manufactured nanomaterial's (NM) lifecycle and can be considered as a transformation over time. Most NMs react in ways that change their behaviour and properties over time upon exposure to environmental conditions, e.g. temperature, humidity and redox. In experimental simulations, time has to be substituted by a proxy to make timescales more realistic. Thermal ageing accelerates the normal ageing processes and thus elevated temperatures can be used to simulate prolonged ageing, allowing access to information on the long-term effects of NM ageing within a shorter time. We will be presenting data from time and temperature dependent experiments on a fully characterised library of laboratory synthesised comparable polyvinylpyrrolidone (PVP) capped NMs (with core compositions of ceria, copper oxide and zinc oxide) and a commercially available uncoated ceria NMs, to assess their transformations. Results generally show a decrease in NM stability, changes in NM size and changes in core oxidation state with increasing temperature/time. These changes varied depending on the NM core composition. Additionally the PVP capping, despite stabilising the NM dispersion, still allowed the NM core to be influenced by external factors. This indicates likely ageing-related reduction in efficiency, though to a lesser extent than the uncapped NMs. Overall the experiments emphasised the complex features influencing the lifecycle of NMs.Numerous physical and chemical changes occurred in parallel or sequentially resulting in no linear correlations between transformations, temperature and time. In the hope of extracting correlations between time/temperature and induced changes of NM properties additional work involving similar temperature ageing studies is being carried out. This involves ageing of commercially available 20 and 100 nm gold NMs characterised at various time points by DLS, UV-VIS, TEM and single-particle ICP-MS. The latter aims to elucidate the dissolution behaviour in aquatic environments.

Session 5
5.2 Environmental interactions of nanomaterials

A91883DM

Nanoecotoxicity of GO@AgNPs nanohybrid on Zebrafish embryos: Influence of natural organic matter and chorion membrane removal

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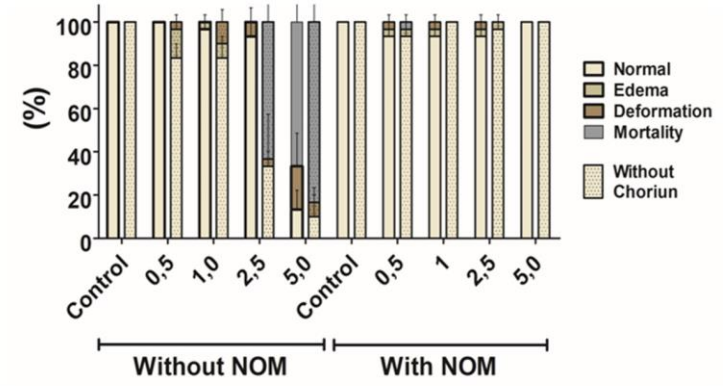
Single-layer graphene oxide decorated with silver nanoparticles (GO@AgNPs) nanohybrid is an emerging material to applications in nanotechnology such as catalysis, biosensors, composites, and antimicrobial materials. However, it is necessary to assess the potential risks of this nanohybrid material to environmental health. In aquatic environment, the nanomaterials can interact with natural organic matter (NOM), modifying their colloidal stability and consequently, change their effects on organisms. Here, we evaluated the nanoecotoxicity of GO@AgNPs on Zebrafish (Danio rerio) embryos in presence and absence of NOM. The GO@AgNPs nanohybrid material was synthetized by reducing AgNO3 with Na3C6H5O7 (sodium citrate) in the presence of GO. The nanohybrid was characterized by TEM, AFM, TGA, and XPS techniques. The colloidal stability of nanohybrid in zebrafish medium was monitored by UV-vis spectroscopy. The 24 hours post-fertilization (hpf) embryos were exposed during 96 hours to 0.5, 1.0, 2.5, 5.0 mg.L-1 GO@AgNPs, in presence or absence of NOM (Suwannee River NOM, 20 mg.L-1), with and without chorion barrier membrane. The positive and negative control groups' exposure were also performed. The fish embryo toxicity (FET) test showed the increase of deleterious effects on embryos with increase in concentration of nanohybrid material. This toxic effect was more severe in the embryos exposed without chorion. Its removal usually started the exposition of embryos to toxic materials in early phase. However, the presence of NOM mitigates the deleterious effects, revealing the antidotal proprieties of NOM for GO@AgNPs (Figure 1). These findings showed the critical influence of chorion membrane and NOM in the modulation of the adverse effects of GO@AgNP nanohybrid material on zebrafish model.



Session 5
5.2 Environmental interactions of nanomaterials

A90683AS

CYTOTOXICITY OF NITRIC OXIDE RELEASING CHITOSAN NANOPARTICLES COATED WITH HYALURONIC ACID TO TUMOR CELL LINES

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Nitric oxide (NO) has been involved in a wide range of biological roles, including anti-tumor properties. Although several advances have been achieved in the treatment of cancer, the mortality remains high. In this context, several studies described the promising employment of NO donors in cancer chemotherapy, particularly in combination with chemo/radiotherapy sensitizers. However, NO use is limited by its concentration, short life time, and delivery to the application site. Due to its instability (*ca*. 0.5 seconds), more stable species have been used to carry and delivery NO, e.g., S-nitrosothiols (RSNOs), which are biological produced as metabolites of NO. In order to enhance the sustained NO release, RSNOs have been incorporated into nanomaterials. Considering that CD44 is a glycoprotein overexpressed in cancer cells, hyaluronic acid (HA), which has high affinity to CD44, has been used to target nanomaterials toward cancer cells. Thus, the aim of this study was to synthesize, characterize, and evaluate the cytotoxicity of NO-releasing chitosan nanoparticles coated with hyaluronic acid (HA-CS NPs) against tumor cells. First, the thiol-containing molecule, mercaptosuccinic acid (MSA), was encapsulated (encapsulation efficiency higher than 90%) in HA-CS NPs. The obtained nanoparticles showed an average hydrodynamic size of 55.9 ± 3.1 nm, polydispersity index (PDI) of 0.37 ± 0.04 and a zeta potential of 15.6 ± 0.15 mV, indicating the stability of HA-CS NPs in aqueous suspension. Free thiol groups of MSA-containing HA-CS NPs were nitrosated leading to the formation of S-nitroso-MSA-CS NPs, which act as spontaneous NO donor (NO-NP). Kinetics of NO release from the CS NPs revealed a spontaneous and sustained release of NO at the millimolar range for at least 10 hours under physiological temperature. The cytotoxicity of NO-NP was evaluated against human melanoma cells (Skmel19) and the results showed that NO-NP exhibited a concentration-dependent cytotoxicity (0.2 – 10.0 μg·mL-1). Interestingly, at the concentration of 0.2 $\mu g \cdot mL^{-1}$, the NO-NP were 60% more cytotoxic than the control group without the HA coat. The half-maximal effective concentration (EC50) were found to be 1.48 and 5.62 $\mu g \cdot mL^{-1}$ to NO-NP with and without the HA coat, respectively. Therefore, the result shows the successful formation of a nanoparticle with high affinity for cancer cells which highlight the potential uses of NO-NP for anti-cancer therapy.

Session 5
5.3 Safe use of nano objects for medicine applications

A90687WR

GREEN SYNTHESIS OF SILVER NANOPARTICLES USING GREEN TEA EXTRACT, CHARACTERIZATION, ANTIBACTERIAL ACTIVITY AND BIOCOMPATIBILITY

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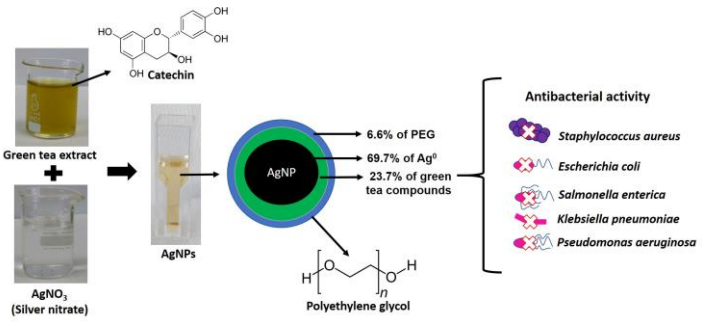
Silver nanoparticles (AgNPs) have extensively explored in the field of nanotechnology due their potential applications in cancer treatment, drug delivery and their well-known effectiveness as potent antimicrobial agent. This work describes a biogenic synthesis of AgNPs with a commercial green tea extract (Camellia sinensis). The tea polyphenols acted as reducing and stabilizing agents for the nanoparticles. The surface of the biogenic AgNPs was further coated with polyethylene glycol (PEG) to enhance their dispersion and biocompatibility. The obtained nanoparticles were characterized by ultraviolet-visible spectroscopy (UV-vis), X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FT-IR), thermogravimetric analysis (TGA), electronic and atomic force microscopy (AFM), X-ray photoelectron spectroscopy (XPS) and dynamic light scattering (DLS). The results demonstrated the formation of spherical nanoparticles of pure Ag° coated with tea polyphenols, at the nanoscale with moderate polydispersity and a high stability in aqueous suspension. The nanoparticles did not exhibit significant toxicity to human keratinocyte (HaCaT) cells. The antimicrobial efficacy of the biogenic nanoparticles was demonstrated against gram-positive Staphylococcus aureus (ATCC 29213), gram-negative Pseudomonas aeruginosa (ATCC 27853), Klebsiella pneumoniae (ATCC 700603), Escherichia coli (ATCC 25922) and Salmonella enterica (ATCC 14028) bacterial strains. Salmonella enterica was found to be the most sensitive strain to the nanoparticles, with a minimum inhibitory concentration and minimum bactericidal concentration of 7 and 15 µg/mL, respectively. Interestingly, at the concentration range in which the AgNPs showed an antibacterial effect, they were not toxic to HaCaT mammalian cells. Thus, green tea synthesized AgNPs could find important biomedical applications in the combat of pathogenic bacteria with low cytotoxicity to normal cells (Figure 1).



Session 5
5.3 Safe use of nano objects for medicine applications

A91499GV

IN VIVO TRANSFORMATIONS OF INDIUM PHOSPHIDE QUANTUM DOTS IN A MODEL ORGANISM

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Due to their size-tunable and bright photoluminescence in the UV/VIS range, Quantum Dots (QDs) are promising fluorescent probes for theranostics and FRET-based biosensing *in vivo* [1-3]. InP QDs recently emerged as the best candidates for biomedical applications, being less toxic and more stable than Cd-based QDs, considered in a first time [3, 4]. Therefore, prior to any medical application, the biocompatibility and the stability of InP QDs *in vivo* must be thoroughly assessed.

We investigated the biodistribution and transformations of two different InP QDs formulations, InPZnS core and InPZnS/ZnSe/ZnS core-shell QD [5], in a model animal system, the invertebrate *Hydra vulgaris*. The polyps were exposed to sub-toxic doses of QDs that do not alter morphology nor reproduction. Although the QDs show no measurable optical activity after 3 h in the animal, synchrotron micro-beam X-ray Fluorescence (µXRF) imaging detected the presence of indium in several compartments of *Hydra* transversal sections. Micro-beam X-ray Absorption Spectroscopy (µXAS) revealed the absence of InP species after 3 h *in vivo*, but rather the presence of oxidized indium species, indicating a degradation of the QD material. This shows that the unexpectedly quick loss of optical properties is not due to clearance but to the transformation into optically-inactive indium species in the animal. Surprisingly, *in vitro* assays showed no degradation of the QDs, even after 24 h at pH 4.5. This highlights the importance of *in vivo* models to assess the biotransformations of nanotechnologies.

All synchrotron analysis were carried out on the beamline ID21 of the ESRF [6], on sections of the animals in the frozen hydrated state, in order to preserve the ionic content and elemental speciation. Our work demonstrates that *Hydra vulgaris* is an ideal model to assess the stability of nanomaterials *in vivo*, yet reducing vertebrate experimentation. Synchrotron µXRF imaging and µXAS proved to provide unique information about the fate of photoluminescent nanotechnologies *in vivo*, especially in case of loss of the optical properties, and can help design future biocompatible fluorescent probes.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91598UV

Cardiovascular disease as a (nano) particle-induced occupational disease

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Epidemiological studies link inhalation of particles to increased risk of cardiovascular disease. Inhaled particles may induce cardiovascular disease by several different mechanisms including translocation of particles to systemic circulation, activation of airway sensory nerves resulting in autonomic imbalance and particle-induced pulmonary inflammation and acute phase response.

The acute phase response is the systemic response to acute and chronic inflammatory states caused by for example bacterial infection, virus infection, trauma and infarction. It is characterized by differential expression of ca. 50 different acute phase proteins including C-reactive protein (CRP) and Serum amyloid A (SAA). Blood levels of CRP and SAA are closely associated with risk of cardiovascular disease in epidemiological studies. The acute phase protein SAA is causally related to atherosclerosis and cardiovascular disease. Overexpression of SAA leads to increased plaque progression and inhibition of SAA synthesis leads to lowered plaque progression in APOE -/-mouse models [1].

We have shown that inhalation and airway exposure to different particles induce pulmonary acute phase response in mice [2]. The pulmonary acute phase response correlates with the total surface area of the deposited particles, neutrophil influx into the lung and with blood concentrations of acute phase proteins.

In a recent controlled human exposure study, inhalation of ZnO particles induced systemic acute phase response in a dose-dependent manner at exposure levels well below the current occupational exposure limit in many countries [3]. This calls for re-evaluation of the current occupational exposure limits taking risk of cardiovascular disease into account and underscores cardiovascular disease as an occupational disease [4].

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Session 5
5.3 Safe use of nano objects for medicine applications

A91622ND

OncoTherad: A New Nanobiological Response Modifier, its Toxicological and Anticancer Activities

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OncoTherad: A New Nanobiological Response Modifier, its Toxicological and Anticancer Activities

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This study reports the effects of a new therapeutic option for non-muscle invasive bladder cancer (NMIBC) based on OncoTherad [1] intravesical immunotherapy in an appropriated animal model. OncoTherad is a nanostructured inorganic phosphate complex associated to glycoside protein, which exhibits immunomodulatory and antitumor properties. Serum levels of ALT, AST, alkaline phosphatase, urea and creatinine in rats, mice and rabbits treated intravesically with OncoTherad at doses of 20-100 mg/kg, did not differed statistically from their respective controls, indicating the absence of systemic toxic effects. The urinary bladder, ureter, spleen, stomach, pancreas and kidneys of rats, mice and rabbits of the Control group did not present inflammation and histopathological changes. NMIBC was induced by treating female Fischer 344 rats with N-methyl-N-nitrosourea (MNU). Bacillus Calmette-Guérin (BCG) were used as positive control in the animal model (approved by Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 4536-1/2017)). Posterior to the MNU treatment, the animals were distributed into four experimental groups: Control group, MNU (Cancer) group, MNU+BCG group and MNU+OncoTherad. Our results demonstrated that animals treated with OncoTherad distinctly showed a significant histopathological recovery from the cancer state and diminish the urothelial neoplastic lesions progression in 80% of animals when compared to BCG treatment. In addition, BCG and OncoTherad intravesical immunotherapies were able to restore TLR2 levels. However, OncoTherad treatment led to increase of TLR4 levels when compared to BCG. Thus, the activation of TLR4 by Oncotherad was efficient in reducing urothelial neoplastic lesions progression. All data showed OncoTherad as a feasible candidate for the bladder cancer treatment.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91658AD

The exposure to non-toxic concentrations of silver nanoparticles impairs crucial nuclear hepatocyte functions

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The widespread use of silver nanoparticles (AgNP) in consumer goods raises concerns about their toxicity to humans and their impact on environment[1]. AgNP toxicity in cells and animals has been extensively studied and is at least due to oxidative stress and metal homeostasis disruption, two processes strongly interconnected in cells. However, the impact on human health of the increasing use of AgNPs in medical devices remains understudied, even though AgNP-containing dressings are known to release silver in the bloodstream. In this context, we analyzed metal content in liver biopsies and detected widespread and sometimes significant silver accumulation both in healthy and sick livers, levels being statistically higher in patients with various hepatic pathologies[2]. These data strongly suggest that AgNP-containing medical devices lead to Ag exposure followed by storage in the liver of patients under hospital care, which raises interest about the impact of AgNPs on this organ.

We have previously shown in hepatocytes, the intracellular dissolution of AgNPs within endo-lysosomes[3] followed by Ag (I) binding to biomolecular thiols[3]. However, the precise subcellular distribution of Ag (I) and the nature of the disrupted physiological pathways remained unknown. The development of a correlative electron microscopy – synchrotron nanoprobe X-ray fluorescence imaging approach performed on the same cell section enabled the determination of the subcellular distribution of Ag (I) species under long-term AgNP exposure to non toxic concentration[2]. We thus observed a significant amount of Ag (I) species accumulating in specific regions in the nucleus. Furthermore, the use of 3D electron microscopy and confocal reflectance microscopy enabled us to visualize a direct nuclear transfer of Ag (I) species from lysosomes but not of AgNPs. At very low AgNP concentrations, these Ag (I) species impaired nuclear receptor activity, disrupting critical mechanisms of liver physiology in clinically-relevant exposure scenarios, and justifying further research into defining a framework for the safe use of AgNPs in medical devices.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91676CT

IN VITRO TOXICITY ASSESSMENT OF FOOD ADDITIVES E171 (TiO2) AND E551 (SiO2) ON A HUMAN INTESTINAL MODEL

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Titanium dioxide (TiO_2, E171) and silica (SiO_2, E551) are part of the most used mineral particles in food, pharmaceutical and cosmetic industries, respectively as whitening and anti-caking agents. While E171 is not considered nanomaterials by the EU definition, it can contain up to 40% nanoparticles (NPs) in the number size distribution. Conversely, E551 is a nanomaterial, composed of particles with primary diameter 15-20 nm, aggregated as chaplets. This, combined with their widespread use, has raised concern about their potential effects on health, especially about their impact on the intestine which is poorly documented.

For a more accurate investigation of titanium dioxide toxicity, we compared the impact of E171 on a coculture of Caco-2/HT29-MTX cells with that of two model TiO_2 NPs: A12 (anatase, 12 nm) and NM105 from the Joint Research Center at the European Commission (anatase/rutile, 24 nm). In the same way, we compared E551 with two SiO_2 NPs: Fumed silica (pyrogenic synthetic amorphous silica, 252 nm, aggregated NPs) and LS30 (colloidal synthetic amorphous silica, 21 nm). We first assessed the overall toxicity of those NPs (cytotoxicity, genotoxicity, oxidative stress), and then focused on the intestinal barrier function (epithelial characteristics, mucus secretion, cellular ability to exclude toxicants).

Our results show the absence of cytotoxicity of E171, TiO_2 NPs, E551 and SiO_2 NPs, as well as the absence of DNA strand breaks formation. However, the exposure to E171 and TiO_2 NPs induced a significant increase in intracellular reactive oxygen species production. E171 was also shown to alter mRNA expression of efflux pumps genes and genes involved in mucus secretion. The exposure to E171 and TiO_2 NPs also influenced the expression of inflammation markers as well as cytokine release; slightly different levels of expression were detected after E551 exposure as well, but only at low concentrations; and cytokine levels were unchanged.

Overall, these results suggest that, even though not cytotoxic nor genotoxic, both E171 and E551 may mildly alter the intestinal barrier function. E171 might also trigger inflammation, which could lead to the development or the aggravation of inflammatory diseases, such as inflammatory bowel disease (IBD).

Session 5
5.3 Safe use of nano objects for medicine applications

A91688WF

Association of Graphene Oxide Derivatives for Non-Muscle Invasive Bladder Cancer (NMIBC) Treatment.

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The most widely used therapy modality for the treatment of bladder cancer (BC) is based on the intravesical administration ofBacillus Calmette-Guérin (BCG) associated with transurethral resection. Despite the anticancer activity of BCG, a significant number of patients exhibited intolerance, besides potentially fatal complications, such as systemic BCG infection. Furthermore, 50% of non-muscle invasive bladder cancer (NMIBC) tumors have recurrence within 4 years after treatment. Doxorubicin (DOX) is a chemotherapeutic agent in transitional cell carcinoma of the urinary bladder, but when this drug is administered systemically in certain doses it can induce cardiac toxicity and myelosuppression. Besides DOX, after the recent discovery of interference RNA (siRNA), these substances started to be studied by silencing genes associated with cancer. In this work, we developed graphene oxide (GO) hybrids for administration of DOX and siRNA for VEGF (vascular endothelial growth factor). Furthermore, we associated GO hybrids containing DOX and siRNA. For the transport of DOX, GO was initially carboxylated in order to bind DOX through amide bond formation. For the delivery of siRNA for VEGF, GO was covalently bonded to polyethylene glycol (PEG), and also to the cationic polyethyleneimine (PEI) for allowing complexation. Ultimately, the hybrids were administered in vivo (Fischer 344 rats) in order to investigate the antitumor effect against NMIBC. The ultrasonography of the rat´s bladder revealed that 60% of the animals treated with GO carboxylated and DOX did not show apparent signs of lesions, while 100% of the animals treated with free DOX showed those signs. Concerning the animals which were treated with GO-PEG-PEI-siRNA, only 20% of them showed signs of lesions. Finally, the association compound GO-PEG-PEI-siRNA-DOX resulted in the absence of lesions. Histopathological analyzes showed that GO derivatives containing DOX or siRNA reduced the aggressiveness of NMIBC. It is worth to mention that the association between GO-COOH-DOX and GO-PEG-PEI / siRNA potentiated the action on the reduction of the aggressiveness of the tumors, since 60% of the animals treated with this association showed no signs of lesions. Therefore, the GO derivatives represent a promising strategy for NMIBC.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91700FD

TOWARDS LESS TOXIC QUANTUM DOTS

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Semiconductor nanocrystals also known as quantum dots (QDs) possess unique optical properties, which make them attractive for their utilization in optoelectronic devices and for biomedical applications. During their life cycle, the aging of quantum dots can lead to dissolution and induce high toxicity due to the release of toxic chemical compounds. In this context InP-based QDs show a lower intrinsic toxicity in comparison to the more popular heavy metal containing Cd-based QDs. However, toxicity studies focusing on the InP core material and the influence of different shell designs on the cytotoxicity potential are still limited. Our laboratory synthetizes different indium-based QDs following a safer by design approach with the aim of producing QDs that are less toxic. These QDs are composed of a core of In, P and Zn, which is covered with a single or a double shell.

In this study, we investigated biocompatible InZnP QDs covered with a single shell composed of ZnSe/ZnS, and QDs with double shells, where this first shell was further covered with a layer of ZnS. Primary human keratinocytes were exposed to these QDs, either pristine or after aging in a weathering chamber. First, the kinetics of QD physico-chemical transformations during the aging process were studied by photophysical characterization over 64h. Important transformation products were identified. Second, the toxicity of QDs was evaluated. Therefore, a lactate dehydrogenase assay (LDH) (probing plasma membrane integrity), BrdU assay (probing the cell proliferation), and WST-1 assay (probing the mitochondrial activity) were used to assess the cytotoxic potential. Trypan blue and Hoechst staining were also used, followed by a counting of cell nuclei. To assess the genotoxicity of the new designed QDs, we used 53BP1 staining, which probes double strand breaks to DNA, and micronucleus assay, which probes chromosomal damage. Both assays were analysed via high content analysis (HCA). Finally, the oxidative stress was assessed, also using HCA.

Our results show that the physico-chemical transformation of QDs is very rapid, with a total dissolution occurring during the first two hours of ageing. Transformed QDs are much more toxic than pristine QDs.

Conclusively, these results confirm that a careful shell design of QDs can reduce their toxicity but does not totally prevent them from dissolving and releasing potentially toxic In ions.

Session 5
5.3 Safe use of nano objects for medicine applications

A91495NR

GRAPHENE OXIDE NANOPLATELETS POTENTIATE ANTICANCER EFFECT OF CISPLATIN IN HUMAN LUNG CANCER CELLS

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Graphene oxide (GO) has been widely explored by many in drug delivery strategies and toxicity assays. The toxicity of graphene oxide depends on the size of the sheets. Smaller sheets show lower toxicity; quality which is essential for utilization in biomedical applications. However, despite vast research on GO, anticancer properties and drug carrier capabilities of graphene oxide nanoplatelets have yet to be fully explored. Herein, we have uniquely prepared graphene oxide nanoplatelets (GONPs) from well-defined stacked graphite nanofibers (SGNF) with base of 100x100 nm for toxicity and drug potentiation studies when co-administered with chemotherapeutic drug, cisplatin (CP) in human lung cancer cells, A549. Results obtained from our studies have found that not only was GONPs able to act as drug carriers, but GONP can also significantly potentiate anticancer effect of CP in A549.

Session 5
5.3 Safe use of nano objects for medicine applications

A91501MM

RELIABILITY OF DETECTION OF NANOMATERIALS UNDER THE TOXIC SUBSTANCES CONTROL ACT (TSCA) AND THE REACH

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Risk assessment that has regulatory applicability has to be based on legally binding norms. The approaches taken by the regulatory bodies in the US and EU to implement those norms, i.e., regulative risk assessment processes, were studied in this work through empirical analysis.[1] The data consisted of notifications/dossiers for the nanomaterials or the substances that contain also nanoform under the Toxic Substances Control Act (TSCA) and Regulation (EC) No 1907/2006 of the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) received by the Environmental Protection Agency (EPA) and the European Chemicals Agency (ECHA), respectively, and decisions of the Agencies. The analysis focused on the challenges in detection of nanomaterials and information collection that are the core functions of risk-based regulation and may create dissimilar compliance requirements for the companies. Orders, restrictions, and information and test requirements set during the processes were compared to find possible differences. The data was analyzed using descriptive statistics and classification. In addition, two case studies from the EU and three from the US were selected for more detailed qualitative examination of information and test requirements.

The results revealed that a loophole in detection of nanomaterials and information collection on them exists in the EU under the REACH. Furthremore, regulative risk assessment processes performed by the ECHA and EPA under the REACH and the TSCA, respectively, may result in different compliance requirements for the companies, which may lead to increased compliance costs. The differences arise partly from the legal provisions that determine the authority and obligations of the Agencies, but also from the decision-making practices adopted by the ECHA and the EPA. The future will show whether the upcoming amendment of the REACH annexes changes the situation. However, more intense regulatory cooperation between policy makers (including regulatory officials) in the US and the EU is encouraged to create consistent and publically legitimate regulatory risk assessment framework for nanomaterials under the TSCA and the REACH.

[1] M. Miettinen, *Empirical Analysis of Regulative Risk Assessment Processes of Nanomaterials under the Toxic Substances Control Act (TSCA) and European Union Regulation Concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH)*, submitted to Jurimetrics J. (2018).

Session 6
6. Regulation / Standardization

A91683PT

A problem with ISO 16890: ratings can depend on test aerosol choice

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ISO Standard 16890 provides HVAC system designers an improved way to estimate the particulate air quality supplied by filtered outdoor air. It does this first by defining two bimodal particle-size distributions, one typical of urban locations, the other typical of rural locations. Each filter is tested for its efficiency as a function of particle size over the diameter range 0.3 µm to 10 µm.

The overall particle mass efficiency is then calculated for the filter as if it were to operate on the assumed urban and rural size distributions. This is done for three upper size limits, 10 µm, 2.5 µm, and 1 µm, which yields three ratings called ePM10, ePM2.5 and ePM1. System designers can use local data (often supplied by government agencies) for the mass concentrations of particles smaller than the three sizes to estimate the mass concentrations in the filtered air entering the building. The impact of prefilter/filter combinations can be accounted for.

ISO 16890 uses two different test aerosols - liquid DEHS and dry, solid KCl. Normal testing by the standard uses KCl aerosol for the size range 1 to 10 µm, to show the effects of particle adhesion. However, the standard allows either aerosol to be used over the entire range, if the laboratory first shows that all fractional efficiencies measured on a "reference filter" do not differ by more than 2%.

Nanoparticles can be included in the calculations if efficiency tests include the nanoparticle range, for there is no lower limit on the typical particle size distributions, and the local PM values are measured gravimetrically, using the mass captured by high efficiency sampling media. Our study was intended to evaluate the effects of filter fiber electrical charge on ePMX ratings for two filters, one a pocket design having charged polymer fibers, the other having uncharged glass fiber media in multiple mini-pleated panels. Both filters were tested before and after exposure to isopropyl alcohol (IPA) vapors, which eliminates electrical charges on filter fibers.

As expected, the filter with no charge on its media showed essentially the same efficiency at each particle size regardless of aerosol type or IPA treatment. For the intentionally charged filter, efficiency differed noticeably for the two aerosols. If a laboratory chooses the "reference filter" option, its filter ePMX values will depend on whether DEHS or KCl is chosen as a test aerosol.

Session 6
6. Regulation / Standardization

A91817OW

DUSTINESS OF NANOMATERIAL IN POWDER: OUTCOMES OF THE PRENORMATIVE RESEARCH PROJECT CARRIED OUT UNDER THE M461 EUROPEAN MANDATE

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In recent years, dustiness has become an input parameter for control banding tools developed for nanomaterials. In Europe, dustiness is also considered relevant, as in the context of REACH registration dossiers. In addition, some recently developed strategies to measure exposure by inhalation require that information on dustiness be provided. In this context, considering that it was important that validated and harmonized methods should be proposed in the near future a pre-normative research program was set up with the ultimate objective of proposing standards. In this project involving six European reference institutes in occupational health, a harmonized approach was elaborated and applied to four dustiness methods that coexist in Europe, that is the RD, the CD, the small rotating drum (SRD) and the vortex shaker (VS) methods. The harmonization concerned the conditioning and preparation of the powder test samples, the aerosol sampling line, the measurement strategy, the sequence of the tests and the data processing. The strategy makes it possible to determine, in addition to the classical respirable dustiness mass fraction (mg/kg), two new pertinent dustiness indices based on the number (particle/mg) and surface metrics (m^2/kg). In addition, it qualifies the size distribution of the emitted aerosol as well as the morphology and chemical characterization of the particles. To test the four dustiness methods, ten candidate powders manufactured and used on an industrial scale have been selected. These powders have different chemical natures (TiO_2, SiO_2, $CaCO_3$ and $BaSO_4$) and are characterized by properties covering wide ranges. For example, their volume-specific surface area ranges from 15 m^2/cm^3 to about 1850 m^2/cm^3. As a result, a database consisting of approximately 250 values for each metric (mass, surface and number) was generated. The results obtained were repeatable, with CV of the order of 20%. For each of the metrics, the indices obtained typically extend over several orders of magnitude, which clearly make it possible to differentiate the powders between them. Despite the great diversity of the tested powders, the number size distributions were relatively close to each other with modes that range from 0.9 µm to 2.4 µm. This project has led to draft standards, currently under revision: prEN 17199 (2018) Workplace exposure - Measurement of dustiness of bulk materials that contain or release nano-objects or submicrometer particles, Part 1 to 5.

Session 6
6. Regulation / Standardization

A91827AS

The European Union Observatory for Nanomaterials as a tool for increased transparency on the safety and markets of nanomaterials

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Nanomaterials on the EU market are regulated under the REACH and CLP regulations. In addition, over the past years significant research work has been done to examine the safety of nanomaterials and to develop tools that enable researchers and regulators to examine the safety of these chemicals. Nevertheless, there continues to be a perception that insufficient information is available on the safety of these chemicals.

Consequently, the European Commission has entrusted the European Chemicals Agency (ECHA) with the creation and management of a European Union Observatory for Nanomaterials (EUON). The aims of the Observatory are to increase the availability and transparency of information on the safety and markets of nanomaterials in the European Union. The Observatory should achieve this aim by collecting publically available information on nanomaterials, launching studies to address specific knowledge gaps, and making the collected information available to the public.

To this end, ECHA launched the Observatory in June 2017, and updated the database in June 2018. The Observatory provides a variety of information on nanomaterials to the public, including information on their safety, uses, and relevant regulations. The Observatory will continue to expand over the coming years to provide further information to the public. The presentation will provide an overview of the Observatory, including recent developments and future directions.

Session 6
6. Regulation / Standardization

A91844JL

APPLICATION OF STANDARDIZATION FOR THE DESIGN OF CNT-BASED PRODUCT PILOT LINES IN COMPLIANCE WITH EU REGULATION ON MACHINERY

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The “PLATFORM” manufacturing platform for the pilot production of pre-commercial CNT-based nano-enabled products, consists of three pilot lines (PPLs) for the manufacture of buckypapers, doped prepregs and doped veils. PPLs have been constructed with the ultimate goal to commercialize these products in the European market in 2020; and this goal requires having PPLs in compliance with the applicable product safety regulation by that date (CE marking).

The main EU regulation for new machinery (as the PPLs) is the Directive 2006/42/EC on Machinery. This Directive sets out the general mandatory Essential Health and Safety Requirements (EHSRs) relating to the design and construction of machinery, while particular technical specifications for fulfilling them are provided in European harmonized standards. Application of harmonized standards is voluntary, but confers a presumption of conformity with the EHSRs they cover.

PPLs are unique machines for their own use and must comply with this Directive before they are put into service in 2020. But the Directive does not provide specific EHSRs for nanosafety and, consequently, no harmonized standards are available in this field for the safe design of PPLs.

In this context, this paper shows the standardization strategy followed by project PLATFORM (GA 646307) for the design of PPLs, to comply with the mandatory EHSR referred to the risks to health due to the emissions of hazardous materials and substances produced by machinery (Directive 2006/42/EC, Annex I, 1.5.13). In the absence of nanosafety harmonized standards to satisfy the aforementioned EHSR, the design and design verification of PPLs were carried out through A & B - type harmonized standards (e.g. EN ISO 12100, EN ISO 14123-1/2), as well as other European standards such as EN 689 and EN 17058.

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Session 6
6. Regulation / Standardization

A91873AM

Mesocosm Testing as a Standard for Non Occupational and Exposure Driven Risk Assessment of Engineered Nanomaterials?

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The recent years have witnessed an increased interest in developing (pre)-standardized procedures and guidance documents for a harmonized determination of parameters utilized in the risk assessment of nanomaterials. This consists in a variety of exposure- and hazard measurements, including "simple" physical-chemical values (e.g. size, charge) as well as biological end-points. Usually, these are standalone tests developed independently of one another. As a result, these parameters, that often are at the node of risk assessment trees, are determined under a number of experimental conditions. Nevertheless, one might wonder to which extent the non-occupational section of the life cycle of a nanomaterial can be accounted for by a sequence of tests. Indeed in an actual environment, the fate of a nanomaterial is under the control of a multiplicity of simultaneously interacting parameters, and does not necessarily obey the dichotomic process of usual risk assessment schemes. Mesocosm testing is an interesting alternative to performing separate determination of a collection of parameters. Indeed, mesocosms provide exposure and hazard data in a single experiment. The systems are allowed (and even expected) to evolve, as opposed to strictly controlled standards. Robustness of this method for monitoring the environmental effects of nanomaterials has been demonstrated. The critical factor over which the operator has a control, is the exposure scenario (e.g. pulse vs. chronic contamination, applied dose). Here we show how guidance on how to carefully design this exposure, could translate into a standardized procedure for using mesocosm testing as risk assessment tool.

Session 6
6. Regulation / Standardization

A92066MM

Overview of proposed indoor air quality standard ISO16000-34: Strategies for the measurement of airborne particles

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Particulate matter air quality is estimated to be one of the most significant sources of adverse health effects and even very significant direct cause of death. The Global Burden of Disease (GBD) study estimated that 2.9 million deaths in 2015 were associated with household air pollution, whereas WHO estimated 4.3 million related deaths in 2012 (Lancet Commission of Pollution and Health). Epidemiological studies indicate that the health effects of air quality are especially related to the sub-micron particles (Pope and Dockery 2006). People in industrialized countries spend most of the day indoors exposed to diverse conditions of particulate matter of varied concentration and size distribution. Ultrafine particles are either transported into indoor air from outdoor environments or the particles directly result from indoor sources like smoking, residential wood burning, cooking etc. including wide variety of sources for nanoparticles.

The concentration, composition, and size distribution of airborne particulate matter in indoor environments can be challenging to measure reliably. Measurement strongly depend on parameters such as the room size, relative humidity, air exchange rate, air flow conditions, and sink effects on different surfaces (e.g., walls, ceilings, floor coverings, furnishings). Depending on the indoor air conditions this can result in highly variable levels of indoor ultrafine/nanoparticle pollution that are not easily determined or measured in terms of their impact on health.

Increased need for reliable and comparable measurements has brought up a requirement for the standardisation of measurement of fine and ultrafine (PM10, PM2.5 and UFP) particles in indoor air. This work has been underway in ISO Technical Committee ISO/TC 146, Air quality, Subcommittee SC 6, Indoor air. As a result, the upcoming ISO 16000-34 standard will include for the first time a comprehensive overview and guidance on indoor air ultrafine and nanoparticle measurement methods and protocols together with recommendations for the instrumentation, uncertainty evaluation, quality assurance and typical cases of reference studies.

This presentation will review and evaluate the upcoming and proposed ISO 16000-34 and 37 standards, their meaning for the nanoparticle indoor air exposure studies and some insights and notes from the work of the working group 23 for ISO/TC146/SC6.

Session 6
6. Regulation / Standardization

A91377YH

APPLICATIONS AND PROSPECTS OF NANOMATERIAL-BASED PHOTOCATALYSIS TECHNOLOGY FOR AIR PURIFICATION

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Nanomaterial-based photocatalysis, a promising strategy for atmospheric air purification, has attracted more and more attentions in recent years. Scientists are anticipating a new breach to prepare functional nanomaterials in large-scale for eliminating gas pollutants such as NOx?VOCs and HCHO with high efficiency. Moreover, the development and fabrication of air purification units and devices based on photocatalysis technology are highly emphasized. These efforts can contribute to the sustainable development of the whole society. In this study, the new challenges and prospects for nanomaterial- based photocatalysis technology are discussed in detail, aiming to give implications to researchers in the field of air pollution control and environmental catalysis study.

Session 7
7. Urban particles and emerging pollutants

A91445JC

Hybrid Solar-Assisted Large Scale Cleaning System (HSALSCS) for Urban Air

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To combat the urban smog, a Hybrid Solar-Assisted Large-Scale Cleaning System (HSALSCS) has been designed and constructed in Xi'an, China. The HSALSCS consists of a large-scale glass shelter coated with photocatalytic materials (solar collector), a chimney and a particle filtration system. An air flow is driven exclusively by buoyancy generated in the collector-chimney system, and particulate matters (PM) and nitrogen oxides (NOx) in polluted urban air are removed by the filtration system and photocatalytic materials, respectively. The dimension of the glass shelter is 60 m in length and 43 m in width, and the height of the chimney is 60 m. The HSALSCS system is capable of processing atmospheric air with a volume of 5-8 million m3 per day in winter, while the processing volume can reach to 20 million m3 in summer. Ten monitoring stations across a 10 km2 area around the tower were set up to evaluate its efficiency on reduction of air pollutants. The PM2.5 concentration had a decline of 11-19% as compared with that at outside this region. The result of this study demonstrates that the HSALSCS can serve as a guaranteed tool for improving air quality in urban areas.

Session 7
7. Urban particles and emerging pollutants

A91506CC

Early-life Exposure to Ultrafine and Fine Atmospheric Particulates Exacerbates Asthma Development in Mature Mice

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Epidemiological studies have suggested that elevated levels of air pollution contribute to an increased incidence or severity of asthma. Although late-onset adult asthma seems to be more attributable to environmental risk factors, limited data is available on the impact of early-life exposure to size-fractionated ambient particulate matter (PM) on asthma in adults. We aimed to determine the effect on the development and exacerbation of asthma in the adult after the mice were exposed as juveniles to three size-fractionated ambient particulates collected from Beijing.

PM with different granularities can induce oxidative stress; in particular, F1, with the smallest size (< 0.49 μm), decreased the mRNA expression of DNMTs in vitro and in vivo the most significantly. In an asthma model of adult mice, pre-exposure as juveniles to size-fractionated PM caused increased peribronchiolar inflammation, increased airway mucus secretion, and increased production of Th2 cytokines and chemokines. In general, F1 and F2 (aerodynamic diameter < 0.95 μm) particulates affected murine adult asthma development more seriously than F3 (0.95-1.5 μm). Moreover, F1 led to airway inflammation in the form of both increased neutrophils and eosinophils in BALF. The activation of the TGF-β1/Smad2 and Smad3/Stat3 signaling pathways leading to airway fibrosis was more profoundly induced by F1.

This study demonstrated that exposure to ambient PM in juvenile mice enhanced adult asthma development, as shown by increased Th2 responses, which might be associated with the persistent effects resulting from the oxidative stress and decreased gene expression of DNMTs induced by PM exposure. The observed differences between the effects of three size-fractionated particulates were attributed to particle sizes and chemical constituents, including heavy metals and also PAHs, since the amounts of PAH associated with more severe toxicity were enriched equivalently in the F1 and F2 fractions. Relative to the often mentioned PM2.5, PM with an aerodynamic diameter smaller than 0.95 μm had a more aggravating effect on asthma development.

Session 7
7. Urban particles and emerging pollutants

A91524JM

Source apportionment of Submicron particles and its associated trace metals in indoor and outdoor air in the western part India

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PM0.5-1 and PM0.25-0.50 samples were collected from Nov 2015 to Jan 2016 in indoor and outdoor air of domestic home of Mumbai, India. Twenty four hour samples were collected on 25-mm PTFE filter paper using Sioutas Impactor with SKC Leland Legacy Sample Pump operated at 9 L/min. The sampled filters were digested in 6–8 ml HNO3 and kept on a hot plate at the temperature of 40–60 °C for 90 min, the solution was diluted with a known volume and analyzed on ICP-AES. The range of the Particulate matter concentration at urban site was 28,65 µg/m3 to 35.23 µg/m3, 24.31 µg/m3 to 32.86 µg/m3 in indoor and at outdoor it ranged from 25.43 µg/m3 to 37.89 µg/m3, 22.32 µg/m3 to 44.30 µg/m3 in PM0.50-1.0; PM0.25-0.50 respectively. The concentration trends of trace metals in indoor and outdoor was in the order Zn>Al>Fe>Cu>Cr>Mn and Ni. The Zn, Al and Fe was found to be dominant and higher in indoor and outdoor air. The probable reason of being the higher Zn concentration in indoor and outdoor was due to automobiles such as lubricating oils and tires, while Al and Fe may arise from ressuspended dust. The sources of analyzed metals are house dust and anthropogenic activities indoors and another from infiltration from outdoors. The results of the present study are of practical importance in identifying sources and processes that control levels of fine particulate matter in a reparable size range. Further, the elemental constituents of reparable size range particulate matter are of public health interest, as it determines human susceptibility to pollution processes. The above study is further under processes and the detailed results of the study will be published and presented in the conference proceeding.

Session 7
7. Urban particles and emerging pollutants

A91555SY

Ventilation in a four-bed ward equipped with air cleaner and system air-conditioner

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Effective ventilation is very important to protect patients from being infected by airborne viruses. This study examined the effects of an air cleaner and a system air-conditioner on local air quality in a four-bed hospital ward. The ventilation efficiency was evaluated in terms of mean air age and decay rate for the cases where the air cleaner and the system air-conditioner were turned on or turned off while the ventilation system was always turned on. In addition, the influence of the patients' curtains on the ventilation efficiency was examined. The mean air age was estimated by numerically solving concentration transport equation in addition to the continuity, momentum, and energy equations. The decay rate was experimentally obtained by measuring particle number concentrations at seven locations in a laboratory simulating a four-bed hospital ward. The use of all patients' privacy curtains could deteriorate the air quality to some extent, because the air circulation indoors was disturbed by these curtains. The use of the air cleaner was found to be helpful for the improvement of overall air quality in the ward. Depending on the local position in the ward, the airflows from the air cleaner and the system air-conditioner could improve the local air quality by contributing to the introduction of fresh air or could lower the local air quality by interfering with each other.

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Session 7
7. Urban particles and emerging pollutants

A91634SL

Atmospheric simulation chamber: a versatile tool to comprehensively understand air Quality impacts on Health in preclinical models

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Introduction: The World Health Organization estimated that there were 3.7 million of premature deaths due to air pollution in 2014, confirming that air pollution represents the largest environmental risk for health. Despite these evidences, a strong limitation of our knowledge relies on the complexity of the atmospheric mixture: at any point in space, thousands of pollutants with important chemical diversity coexist, producing an instantaneous chemical reactivity that cannot be estimated with conventional methods of organic chemistry. In order to realistically simulate atmospheric mixtures in all their complexity in the laboratory, environmental chemists have developed photoreactors that are conceived to reproduce and control atmospheric processes: simulation chambers. Using such a chamber (CESAM atmospheric simulation chamber - cesam.cnrs.fr), we developed an innovative platform to analyze the health effects of realistic model atmospheres at the preclinical level. Here, we report the first results of the feasibility study.

Methods: A realistic atmosphere, mimicking a 2017 pollution event in Paris, was generated inside CESAM chamber and photostationnary maintained for 48 hours. The chamber was connected to stalling cabinets where mice were exposed (whole body) and sacrificed after 6 or 48 hours. Lungs, spleen, adipose tissue, heart, mesenteric ganglions were then harvested to address the expression of detoxification and antioxidant genes, as well as total cell count (TCC) and inflammatory cytokines expression in BAL fluid.

Results: The atmosphere contained 57.3 µg/m3 particulate matter, 114±11 ppb NO2 and 242±101 ppb O3. No mortality nor weight loss were observed. In the lungs, no modification could be detected after 6 hours. However, after a 48 hours exposure, increased expression of Ahr, Cyp1a1, Hmox1 and NQO1 was detected, as well as increased TCC and KC concentrations in the BAL. Extra-pulmonary modifications were also detected: increased expression of Ahr, Cyp1a1, Hmox1 and NQO1 in the spleen, Hmox1, Cyp1a1 and Cyp1b1 in ganglions, and Hmox1 in the adipose tissue and heart. Interestingly, modifications in adipose tissue and heart could already be observed after 6 hours of exposure.

Conclusion: These preliminary results demonstrate the feasibility of our innovative experimental approach, which represents a versatile tool to get a better comprehensive understanding of air pollution impacts on health.

Session 7
7. Urban particles and emerging pollutants

A91639DS

Separate characterization of adsorption and radical formation in Titania-based hybrids for air cleaning via photocatalysis

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For the time being, air pollution is one of the most pressing issues in China but recently started to raise more and more concerns in Europe as well. Therefore, beyond the need of reducing release, the degradation of volatile organic compounds (VOCs) both indoor and outdoor has become an important aspect. Two challenges do occur: the first one is the formation of new materials with enhanced photocatalytic activity compared to the gold standard P25. The second one is to understand and tailor the highly complex photocatalytic reaction pathway which includes transport of the pollutant to the vicinity of the catalytically active material, adsorption of the VOC on the surface of the photocatalyst and finally the degradation reaction itself. While the former is already addressed [1, 2], for the latter new methods have to be developed.

In this study, our techniques developed for the quantification of particle surface properties with respect to adsorption of different pollutants and photoluminescence (PL) will be presented. First it will be discussed how standardized Hansen parameters derived by analytical centrifugation (AC) [3] can be used to tune the surface properties of hybrids, i.e., composites of TiO_2 as well as carbon-based materials like reduced graphene oxide (rGO), for optimum pollutant adsorption. Second, it will be shown how the PL quench of the semiconducting oxide core in the presence of chemisorbing species, e.g., functionalizing ligands, carbon materials, can be related with molecular properties of the latter, e.g., electronegativity [4].

In conclusion, our work reveals how surface characterization of nanomaterials can be used to get a better understanding of the various influencing factors on the photocatalytic performance of advanced materials. The derived data will allow a holistic consideration of hybridization and thus pave the way towards rationally designed photocatalysts.

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Session 7
7. Urban particles and emerging pollutants

A91652PS

Modification of physicochemical parameters of diesel fumes allowing the use of nonwoven filters for the removal of solid particles

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Exhaust gases emitted by Diesel engines are a mixture of numerous chemical compounds created as a result of incomplete combustion of fuel oil, engine oil and additives.

Diesel fumes are dangerous for the natural environment as well as humans. Their harmful effect on human's health manifests itself by irritation of mucous membrane of the respiratory tract and eyes, headaches as well as diseases of the cardiovascular, hematopoietic, lymphatic and respiratory systems and etc. Agency for Research on Cancer and World Health Organization has classified Diesel engine exhaust gases as a human carcinogen (Group 1).

The biggest problem with the purification of Diesel engines exhaust is connected to a removal of solid particles and nitrogen oxides. At the present moment, the most efficient way to reduce the emission of solid particles from Diesel engines is the filtration of exhaust gases. This is done by Diesel Particulate Filters (DPF). Such filters can be either disposable or regenerable, wherein regeneration can take place during engine operation or during its maintenance. The most often used types of filters include ceramic filters (cordierite, made of silicon carbide), ceramic fabric filters, sintered metal filters, ceramic or metal foam filters and corrugated metal film filters. These filters can be made without or with the addition of catalytic material. However, the use of such metallic catalysts increases the price of the filters.

In the present study, a new method for the modification of physicochemical parameters of diesel exhaust which allows the use of nonwoven filters to remove Diesel exhaust particles is presented.

This method relies on cooling the Diesel fumes with a heat exchanger, diluting with cold air or introducing water mist into the fumes. The cooled exhaust gases are filtered on nonwoven filters and the condensate is removed from the system. The method is mainly intended for the purification of exhaust gases from off-road machines such as power generators.

Session 7
7. Urban particles and emerging pollutants

A91689JS

TITANIA-BASED NANOCOMPOSITES FOR TYPICAL VOCS DEGRADATION

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Volatile organic chemicals (VOCs), which are detrimental to air quality and human health, have attracted increasing attention in recent years. Long-term exposure to VOCs will cause respiratory diseases, such as lung cancer. In addition, VOCs can under oxidized conditions through complex heterogeneous reactions. It is particularly urgent to develop both technology and new materials to decompose VOCs efficiently. In this presentation, two titania-based nanocomposites, the hybrids of graphene with titania and quantum dots with titania have been synthesized and evaluated in gaseous photocatalysis process. Two types of volatile organic chemicals (VOCs), acetaldehyde and o-xylene, were selected to probe the different adsorption and photodegradation mechanism. Experimental results showed that the removal efficiencies of the acetaldehyde and o-xylene with reduced graphene oxide (rGO)-TiO2 nanocomposites was superior to P25. The enhanced adsorption properties and efficient electron-hole separation both contributed to the results. While for the coupling of TiO2 with carbon quantum dots, similar enhanced photocatalytic performance achieved, the generation of Ti3+ ions helps to improve carriers' separation efficiency and absorb parts of visible light.

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Session 7
7. Urban particles and emerging pollutants

A91706JT

Direct detection of airborne bioaerosol on filter with immunoassay

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Airborne bioaerosol monitoring is of great significance to guarantee air quality and to reduce risks of infection. However, it is still a challenge to detect the airborne bioaerosol due to its relatively low concentration and tedious sample treatment process. In this work, the direct detection of airborne bioaerosol on filter was proposed. E. coli droplet was generated by the humidifier as the model bioaerosol and then filtrated via filter and vacuum system. After that, an enzyme-linked immunoassay was adopted. The accumulated E. coli can contribute to the enhancement of detection signal and the detection duration can be shortened due to the direct immunoassay on filter.

Session 7
7. Urban particles and emerging pollutants

A91721ZY

Health effects of ambient ultrafine (nano) particles in haze

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Research results have shown clear associations between short-term or long-term exposure to ambient fine particles (FPs, PM2.5) and the increased incidence and mortality of cardiovascular or respiratory diseases. However, the ambient ultrafine particles (UFPs, PM0.1) are dominant contributors to particle number in haze weather. Exposure to nanoparticles in the workplace is also a health concern to occupational workers with increased risk of developing respiratory, cardiovascular, and neurological disorders. Real time production of particle concentration and size distribution in the range from 5.52 to 98.2 nm were recorded in a wire-cut electrical discharge machine shop (WEDM) during a typical working day. Under the realistic exposure condition, human inhalation simulations were performed in a physiologically realistic nasal and upper airway replica. Particle size distribution carries very important information in determining human airway dosimetry. It was found out that human inhalation dosimetry was extremely sensitive to real time particle concentration and size distribution. A pure number or mass concentration recommendation on the exposure limit at workplace is insufficient. A particle size distribution, together with the deposition equations, is critical to recognize the actual exposure risks. The close collaborations among atmospheric researchers, environmental protection department staff working on atmospheric monitoring and health science researchers are of most importance.

Session 7
7. Urban particles and emerging pollutants

A91784FP

State of art: Characterization of braking particles from car emissions

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The problem of particles emitted by car brakes is a new challenge. However, estimations show that emissions of car brakes account for 10% to 30% of the traffic-related pollution. Recent developments of particle filters on engines significantly reduced exhaust pollution; consequently, the proportionate contribution to pollution from brake wear particles is destined to increase, and this source of pollution will probably be blamed as engine emissions are today. Thus, the potential health risk associated with braking particles could lead to a specific regulation.

Braking converts a vehicle's kinetic energy into thermal energy as a result of the friction between disc and pads. The friction between a composite pad made of a polymer matrix loaded with abrasive and lubricant compounds and a metallic disc causes wear on both parts. This wear, or matter loss, occurs via a complex tribological process, often with the creation of a transformed layer on the surface, before being released by the pad and disc. The nature and the number of fine particles emitted from the contact, potentially airborne, not only depend on the pad and disc composition, but also on conditions of tribological solicitations. In order to reduce aerosol particles emission, a better understanding of particle generation mechanisms is essential. This will enable the optimization of the sampling process, the material choice, and the braking protocol.

To anticipate any future regulation requirements, automobile field needs a world methodological consensus on the topic. This communication aims to specify the reliable approach to characterize emitted particles during a dynamometric test. Several stakeholders have already developed measurement equipment adapted to braking emissions. However, the current poor consensus on the required testing protocol raises questions. Olofsson et al. focus on understanding emission mechanisms while presenting an interest on on-road tests. Other authors approach the challenge with a more applicative research of dynamometer and their instrumentations.

Previous investigations enable identifying bottlenecks and their solution. The first approach to these questions consists of improving knowledge of particles emitted by braking. By precisely characterizing those particles, authors study their behavior towards their environment and during sampling. Thus, authors attempt to adapt specific metrology according to size and compositions of detected particles.

Session 7
7. Urban particles and emerging pollutants

A91842SA

POTENTIAL EXPOSURE ASSESSMENTS OF AIRPORT'S WORKERS TO COMBUSTION NANOAEROSOLS AND CHARACTERISATION OF EMISSIONS

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People working in airports are exposed to combustion nanoaerosols produced by aircrafts, trucks, or generators. A first study was conducted, in 2012, in two French airports, Marignane, near Marseille, and Roissy, near Paris. The aim was to assess the characteristics of nanoparticles potentially inhaled by workers directly or not-directly exposed to these sources of ultrafine particles (UFP). As a part of a longitudinal approach, a second study is conducted in 2018.

These results are included in a larger study conducted by clinicians and researchers from Aix-Marseille and Montpellier Universities, and the occupational health service of Air France that aims to evaluate the effect of worker's exposure on their respiratory function.

The characterization of aerosols includes measurements of the concentration using condensation particle counters and measurements of the size distribution using fast mobility particle sizer (FMPS), scanning mobility particle sizer (SMPS), and electrical low pressure impactor (ELPI). Particles are sampled using collection membranes placed on the ELPI's stages. Measurements are performed on the tarmac near aircrafts and near specific sources like an exhaust of jet aircraft engines and a push.

In addition, compared to the 2012 campaign, personal field measurements (Sioutas® and Particlever Sampler®) are realised on sixteen workers of four professional categories. The samples are analyzed by SEM–EDS to provide information including size, shape, agglomeration state, chemical composition of the particles, total mass carbon concentration.

The goal is to evaluate the different levels of exposure to combustion aerosols as a function of workers categories.

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Session 7
7. Urban particles and emerging pollutants

POSTER PRESENTATIONS

A90831CD

COMPARISON BETWEEN A 5KV BENCHTOP ELECTRON MICROSCOPE AND CONVENTIONAL TEM FOR NUMBER SIZE DISTRIBUTION OF POWDERS AND COLLOIDS

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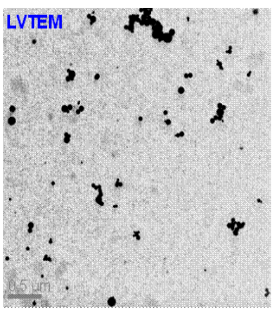
Nanomaterial powders and colloids are already a large industry and are expected to continue to growth rapidly. In the context of risk assessment associated to nanomaterials, the characterization of nanoparticle size and morphology are required.

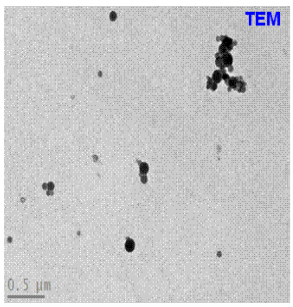
Until now, the reference method giving a direct access to these parameters is Electron Microscopy (EM), notably TEM, HRTEM, SEM or STEM. Although these methods are widely harnessed, the main issues that are highlighted are the high cost of the devices, heavy maintenance, high qualification for manipulating the microscope, and the damage caused by the electron beam on the most sensitive samples (biological or polymer materials).

Since about ten years, low voltage transmission electron microscopes (LVTEM) have been evaluated in order to solve these issues. Indeed, they could reveal more advantageous than conventional TEM.

Such microscopes have an extremely compact design and low resource requirements, (benchtop setup) and they can combine several imaging modes (SEM, STEM, ED) in one single device.

Here, we present a first comparison of a 5 kV TEM (LVEM5 Delong Instrument) with a conventional TEM operating at 200 kV (CM200, Philips) to determine the number size distribution of primary particles of two industrial powders (TiO2 and SiO2) and two colloidal reference suspensions for particle size (SiO2 FD 304 and NM 300K). The samples were prepared with an optimized deposition protocol involving glowing and Alcian blue solution pre-treatment on the EM grids. For the number size distributions, the projected equivalent surface diameter was measured. In order to avoid any operator artifacts, the same operator analyzed the LVEM and CM200 microphotographs taken at 5 kV and 200 kV for all the samples respectively. Between 100 and 400 primary particles were counted to determine the number size distributions. The LVTEM revealed a good resolution (figure 1) and the biases obtained on the median diameters d50 are generally under 15%.





Session 1
1. Measurement and characterization of nano objects

A91367MK

Analysis and Optimization of nanoscale InxGa1−xN heterojunction solar cells design

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The success of the Ternary indium-gallium-nitride (InxGa1−xN) heterojunction technology in the field of optoelectronics; light-emitting diodes (LEDs) and laser diodes. Its inherent properties such as their direct band gap, polarization charges, high absorption coefficient and radiation resistance has made this material an excellent candidate for photovoltaic applications.

We report on two-dimensional numerical simulations of InxGa1−xN hetero interface solar cells where all the important device parameters have been defined, the insulator thickness above the cells and InN mole fraction are an important design parameters to attain highest energy convertion efficiency for space based PV applications.

Session 1
1. Measurement and characterization of nano objects

A91404JK

GROUPING NANOMATERIALS BY BIODISSOLUTION AND TRANSFORMATION – COMPARING ABIOTIC, IN-VITRO, IN-VIVO

KELLER Johannes [1], KOLTERMANN-JÜLLY Johanna [1,3], VENNEMANN Antje [2], MA-HOCK Lan [1], WERLE Kai [1], LANDSIEDEL Robert [1], WIEMANN Martin [1], WOHLLEBEN Wendel [1]

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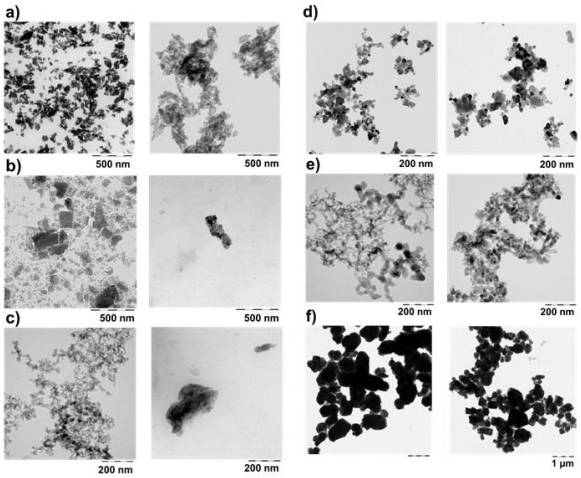
Engineered nanomaterials (ENM) of different composition differ immensely in their pulmonary clearance behavior in vivo. It is unknown to which extent the pulmonary clearance of a given composition is modulated by different sizes, shapes and coatings of the ENM. For some ENM, unexpectedly fast clearance from the lungs was observed [Konduru et al]. Clearance rates faster than 40 days cannot be explained by mucociliary and macrophage-mediated (physical) clearance mechanisms. We therefore investigated the biodissolution (chemical clearance) of several ENM under physiologically relevant conditions, as the underlying mechanism of fast pulmonary clearance. However, methods that screen for biodissolution and transformation need to be validated against bioprocessing and clearance data in vivo. Here we apply a previously optimized abiotic flow-through method to 24 (nano) forms of 6 substances and compare selected cases against macrophage-assisted biodissolution in vitro and against short-term inhalation results in vivo. The TEM images in Figure 1 show the transformation of nanomaterials through dissolution. We find that the relevance of results is not enhanced by macrophage-assisted biodissolution in vitro. We propose the abiotic flow-through screening as Tier 2 methodology for grouping and read-across purposes, and integrate the assessment of transformations by TEM analysis in a unified protocol. Additionally, Tier 3 in vivo clearance is consistent with the group limits that we derive for biodissolution and transformation. The similarity is high for families of Fe2O3 (nano) forms, SiO2 nanoforms, CeO2 nanoforms, ZnO nanoforms, thus primarily determined by the substance. However, the family of Cu-based nanoforms is very heterogeneous and requires testing of dissolution and transformation for each CAS number separately.



Session 1
1. Measurement and characterization of nano objects

A91570AL

YTTRIA INFLUENCE OF STRUCTURE AND BIOACTIVITY OF ZIRCONIA NANOPOWDERS

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Zirconia is an important material that features in many applications in industry and also in biomedical field. The bioactivity of zirconia-based material has been studied by several researchers in recent years, however, it is not yet clear what structure of zirconia/yttria stabilized zirconia nanoparticles is favourable for inducing apatite nucleation in biological fluids. It is believed that determining the nanoparticulated zirconia structural dependence on apatite formation could provide valuable insights for the preparation of nanozirconia-based bioactive materials.

The materials used in the present work were commercials nanopodwers purchased from PlasmChem with the following description provided by the manufacturer: (1).ZrO2 - Nanopowder, monoclinic, further referred to as 0YZr; (2) ZrO2 - Nanopowder, tetragonal Stabilized with 3 mol% Y2O3 further referred to as 3YZr; (3) ZrO2 - Nanopowder, tetragonal Stabilized with 6 mol% Y2O3further referred to as 6YZr.

This study investigates the influence of yttria concentration on the structure and consequently on the behaviour of zirconia nanopowders in simulated body environment. The samples were characterized by means of X-ray diffractometry (XRD), Transmission electron microscopy (TEM), Scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR) Raman Spectroscopy, X-Ray Phoptoelectron Spectroscopy (XPS), specific surface area and pore volume. The bioactivity was evaluated after incubation of the samples in Simulated body Fluid (SBF) for 14 respectively 28 days.

The obtained results reveal that samples 0YZr and 3YZr are relatively fine grained powders while 6YZr is a very fine powder (SEM, TEM). The 0YZr sample only presents the monoclinic ZrO2 crystaline phase, the 3YZr sample presents the tetragonal ZrO2 as and the monoclinic ZrO2 phase in a smaller proportion, while the 6YZr sample presents only the tetragonal ZrO2 crystaline phase (XRD, Raman). Vibrational spectroscopies (FTIR, Raman) evidence a degree of bioactivity revealing HA specific bands, the intense in the spectra of 0YZr sample immersed in SBF for 28 days, there intensity decreasing with the increase of yttrium content but not enough to be ignored. The presence of P after SBF on the sample's surface is confirmed by XPS.

Session 1
1. Measurement and characterization of nano objects

A91636TC

Improved light scattering measurement with microscopy data for nanoparticle number-based size distribution

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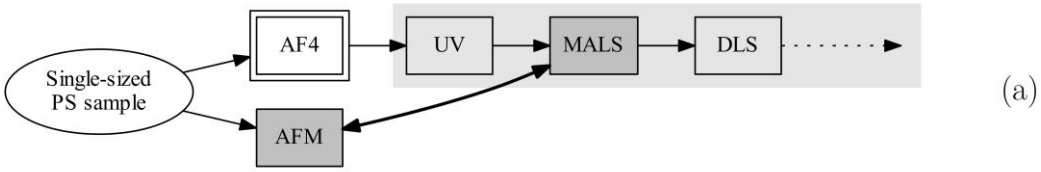
Nanomaterials market is continuously growing thanks to enhanced features and the novel properties of nanomaterials, compared to their macroscopic equivalent. Novel properties and risks essentially come together from the small size of these objects. Products containing nanomaterials fall under the scope of EU regulations 1223/2009, 1169/2011 and 528/2012. They all share in the definition of "nanomaterial" the assessment of the size distribution and number-based concentration. This requires the combination of several techniques.

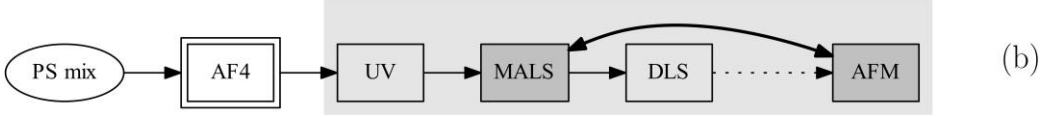
So far, dimensions of nanoparticles (NP) are well assessed by microscopy. Efforts are concentrated on the measurement of concentration. Several methods have been developed to measure the concentration as a function of size, according to the NP interactions with light (absorption for UV, scattering for MALS, time correlation for DLS). They suffer from poor resolution when dealing with polydisperse sample. With separation techniques like Asymmetrical Field-Flow Fractionation (AF4), this drawback is mitigated by separating according to hydrodynamical size for further inline measurements, improving the resolution of these ensemble techniques.

The present work first assesses the comparability of size from light scattering techniques (AF4-UV-MALS-DLS) with microscopy technique (AFM) of polystyrene particles. A sample preparation is developed in order to fit for both techniques, microscopy and AF4- UV-MALS-DLS. Accounting for the response of the light scattering as a function of size, the light scattering model now compares to microscopy techniques, as sketched in figure (a).

Aliquots from mixture of the previously measured samples are analyzed by UV-MALS-DLS online after AF4 separation, and are collected and analyzed with AFM (see figure (b)). Despite dilution from the separation process, quality of the separation is assessed and comparability is still achieved, aiming at better concentration and size measurements at the same time.



(a)



(b)

Session 1
1. Measurement and characterization of nano objects

A91637SB

INTERCOMPARISON IN THE LABORATORY OF VARIOUS CONDENSATION PARTICLE COUNTERS CHALLENGED BY NANOAEROSOLS IN THE RANGE 6 – 460 NM

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Number concentration is commonly used for airborne nanoparticle monitoring, task emission classification, or protective equipment performance evaluation against nanoparticles. The use of Condensation Particle Counters or their implementation as part of a strategy to assess exposure to airborne nanomaterials have been recently described in European standards (prEN 16897, 2017, and prEN 17058, 2016, respectively).

This study aim is to compare the number concentration of airborne nanoparticles reported by 8 different models of CPC with regards to a reference CPC, for a set of aerosols of interest. Among the models investigated, 3 are handheld CPC (TSI model 3007, 2 TSI model 8525 P-Trak), while the 5 others are stationary CPC. The latter include butanol-based CPC (TSI models 3776 and 3772-CEN) as well as water-based CPC (TSI model 3786, 2 TSI model 3787).

Polydisperse test aerosols with modal diameters between 6 and 460 nm were produced in the CAIMAN experimental facility. Non-hydrophobic aerosols consisted of metal-based particles (Ti, C, Al, Cu, Ag), as well as nebulized suspensions (SiO2). Hydrophobic particles consisted of DEHS as well as alkanes (n-C13 to n-C20). Overall, 375 different conditions were investigated to represent a wide range of aerosols potentially encountered in workplaces. The range of number concentrations provided by the reference CPC was 500 – 400 000 cm-3.

To highlight the possible effect of particle counting efficiency on the total concentration reported by the different CPC, 40% of the test aerosols presented a modal diameter below 40 nm. Besides, the influence of particle hydrophobicity for water-based CPC was investigated through the generation of ~100 hydrophobic test aerosols.

CPC response was found to be sensitive to the mode of the aerosols measured, depending on the counting efficiency curve of the CPC investigated. A significant effect of particle hydrophobicity on the response of CPC TSI model 3787 was also demonstrated.

Session 1
1. Measurement and characterization of nano objects

A91655EM

RENOVATION AND OTHER SOURCES OF INDOOR 1.1 – 4.0 nm AND ULTRAFINE PARTICLES

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Indoor air aerosol is a combination of aerosol from outdoor and indoor sources (Hussein et al. 2004). Single digit (diameter) nano aerosol particles are often considered to have indoor origin, due to high losses when transported through HVAC systems or infiltration. Recent studies report high outdoor concentrations of traffic-originated sub-3 nm particles (Rönkkö et al. 2017), some of which might be detected indoors despite the losses. Possible indoor sources of sub-3 nm particles can bevarious, e.g. primary sources like combustion (e.g. candles), or SOA formation, and we anticipated that also renovation work may be a source.

We measured particle number size distributions in the size range of 1.1-4 nm and number of 4-1000 nm particles using an Airmodus A11 nano Condensation Nucleus Counter (nCNC), from laboratory air under normal operation and during HVAC ductwork renovation in the adjacent room. The laboratory was in lower pressure than adjacent rooms. Air came in via air supply units and through the doors, moving past the instruments to local ventilation exhaust units. When the air supply was cut off during renovation ~9am–3pm, all sampled air came from adjacent rooms; exhaust units remained on. The reno work included cutting metal and draining and water vacuuming ducts of chilled beams system.

Night-time concentrations of sub-4 nm particles were of the same order of magnitude as reported for outdoor measurements and what has been reported for indoor ion concentrations, indicating either similar formation mechanisms, e.g. ion induced nucleation (Wagner et al. 2017, Kolarz et al. 2009, Hirsikko et al. 2011), or clusters having higher penetration trough the HVAC system than >1.5 nm particles. Night-time particle concentrations were lower after the renovation. Renovation work generated high concentrations of <1000 nm particles, and a lot of sub-4 nm particles. We also observed a likely SOA event, or the effect of nearby traffic, in the morning before renovation. Except during the renovation, the number of <4 nm particles was higher than >4 nm. Cutting metal ducts is a likely source of nanocluster aerosol. Renovation work can expose both the workers and people in the vicinity to nano particles in high concentrations.

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Session 1
1. Measurement and characterization of nano objects

A91671JN

Single Particle ICP-MS: metrological needs for detecting, counting and sizing nanoparticles

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The single particle measurement by ICPMS or sp-ICPMS is a technique able to detect, count and size metallic and metalloids nanoparticles. It is a very sensitive technique that allows target nanoparticles to be searched for even in complex matrixes such as food, biological tissues, or environmental samples potentially containing mixtures of particles of different chemical natures. Sp ICPMS has therefore a great potential to be used for nanosafety issues.

However, as this technique is relatively new, some metrological challenges remain to be solved in order to achieve robust and reproducible measurements in all laboratories. For example, an inter-laboratory comparison aimed at measuring Ag particles in chicken meat resulted in median diameters measured by the participants ranging from 32nm to 85nm (Weigel et al., 2017).

As the French National Metrology Institute, LNE is currently organizing an interlaboratory comparison with several different measurement techniques including sp ICP-MS for the determination of the size of gold and titanium nanoparticles in aqueous matrix. We will present the latest results of this comparison and compare them with the results of the other measurement techniques (e.g SEM) to improve if necessary the practices in terms of sample preparation, data acquisition and data treatment.

In addition, an example of application of sp ICP-MS in food analysis currently developed at LNE with the aim of comparing different kind of ICP-MS geometry will be presented

Session 1
1. Measurement and characterization of nano objects

A91685WL

Interaction of silver nanoparticles with metalloproteins: corona formation, NPs dissolution and protein conformation changes

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Silver nanoparticles (AgNPs) are widely used owing to their antimicrobial properties and included in about 30% of nanotechnology based consumer or medical products. The release of AgNPs unintentionally spread in the environment but also direct exposure is suspected to impair some key biological functions, leading to toxicity. In this study, in depth investigations were carried out into the interaction of citrate-coated AgNPs (20 nm) and three metalloproteins: Catalase, Cytrochrome C and Superoxyde dismutase, all involved in the cell protection against oxidative stress but varying from their structure and native metals cofactors.

The behavior of the AgNPs and the related consequences for the proteins in terms of structural changes and metal displacement were studied by a multi-technique approach combining dynamic light scattering (DLS), UV-vis spectroscopy, fluorescence spectroscopy and circular dichroism (CD) spectroscopies. The separation of the different size populations formed, together with on-line quantifications of their metal content were performed by asymmetrical flow field-flow fractionation (AF4) linked to inductively coupled plasma mass spectrometry (ICP-MS). The “protein corona” and the conformation change of three protein will be discussed, taking into account the structure characteristics of the protein.

Session 1
1. Measurement and characterization of nano objects

A91695YM

Measurement and observation of particles generated during abrasion of CNT composite resin

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In recent years, development of products using CNT composite materials has been proceeding actively, but carcinogenicity of CNT is suggested by animal experiments.

Therefore, it is necessary to evaluate the human health risk of CNT composite materials including CNTs. The purpose of this research is to clarify the dynamics of CNT in CNT composite resin at the time of abrasion of CNT composite resin.

In this study, we conducted abrasion of CNT composite resin and resin without CNT as controls and measured particle size distribution and the number concentration of the particles produced at that time. We collected particles generated during abrasion of the CNT composite resin using a nuclepore filter and observed that filter with an electron microscope.

As a result, it was confirmed that the particle size distribution and particle number change depending on the presence or absence of CNT. We didn't observe single scattered CNT by observation of the nuclepore filter used for collection.

We conclude that the CNT contained in the CNT composite resin scatters in a state attached to the resin fragments, not as a single body, when the CNT composite resin is abraded.

It is suggested that clarify the dynamics of CNTs detached from CNT composite resin by tracing trace metal elements contained in CNT.

Session 1
1. Measurement and characterization of nano objects

A91853KJ

Data-rich OECD WPMN test materials - suitable for establishment and testing of grouping, read-across and risk assessment models?

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About a decade ago, the OECD Working Party on Manufactured Nanomaterials (WPMN) launched its so-called sponsorship program in which a number of industrially relevant MN and a few non-MNs were characterized and tested in a number of national and internationally supporting research projects. Usually these characterization data were collated in local project data libraries, but never really assessed and collected in validated and accessible data bases. A major attempt was made in the e.g., the NANOGENOTOX and NANoREG projects to establish physicochemical characterization data on many of the OECD WPMN test materials using mutually (within project) accepted protocols. In NANoREG data were compiled in ISA TAB-like data templates or uploaded to the NANoREG data base. However, this endeavor was not fully successful. In current work in the EU H2020 caLIBRAte and NanoReg2 projects, the uploaded and additional hard-copy-filed NANoREG data, as well as published and other accessible data generated by other projects are being procured and important data gaps covered.

In this paper, we critically map the historical data development on the OECD WPMN test materials considering data sources, abundance, variability, and protocol developments. Second, considering that the OECD WPMN test materials are some of the most studied industrially produced MN, we discuss how representative the OECD WPMNM test materials are for grouping and model development considering ranges in key physicochemical properties and use multiparametric statistical analysis to assess how the OECD WPMN test materials group alone and across a larger suite of different MN. This study brings important elements into the current in silico hazard model developments and the expressed regulatory need to establish and demonstrate read-across and grouping principles.

We demonstrate that focusing on the OECD WPMN test material is not sufficient to demonstrate grouping principles. However, the data may be suitable for testing and demonstrating elements of risk assessment tools. However, the ranges in some parameters, such as shapes and higher generation NMs with different surface chemical modifications are by far inadequate for model demonstration and to establish grouping principles.

Acknowledgement: The research leading to these results has received funding from the European Union's Horizon 2020 research and innovation program under Grant Agreement No.686239 ‘caLIBRAte’.

Session 1
1. Measurement and characterization of nano objects

A91880SC

DESIGN AND EVALUATION OF AN AIRBORNE FIBER SELECTION MODULE

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Asbestos-like fibrous morphologies together with bio-persistent material properties have raised concerns about possible lung carcinogenicity of nanofibres. Fibre exposure assessment currently fully relies on filter sample analysis and requires laborious EM-based morphological characterization and quantification. Fibrous selective detection principles could be used to provide real-time fibre exposure information. Those principles could have high potential for dusty environment were morphological characteristics could be used to discriminate high aspect ratio objects from spherical particles.

The determination of fiber number concentration in real time, with portable devices, can provide an immediate response onsite and must lead to significant savings compared to conventional methods. However, it is known that these direct-reading devices have weaknesses in terms of reliability for various reasons, which considerably limits their potential for use.

The main challenge of the SelFi project is to develop a device which, simply placed upstream of the direct reading devices, would let pass only the fibers while collecting the non-fibrous particles. This paper will present the concept of a novel device combining the action of gravity or inertia with electric fields. The action of these field forces allowing a selection of fibrous particles compared to non-fibrous particles has been demonstrated analytically. Simulation using COMSOL multiphysics (finite element analysis) were used to optimize the different parts of the device (unipolar charger, selection stage). The performance of the device using different types of particles such as monodispersed standard polystyrene latex aerosols generated in controlled environment and various counters and granulometers (CPC, SMPS, Fidas Mobile) will be presented.

The research leading to these results has received funding from the French *Plan Recherche et Développement Amiante* (SelFi project) of the *Ministère de la Transition Ecologique et Solidaire*.

Session 1
1. Measurement and characterization of nano objects

A92201VK

HOW TO MEET NEW CHALLENGES IN ADVANCED NANOPARTICLE ANALYTICS

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Three current research projects performed at BAM's Division for Surface Analysis and Interfacial Chemistry are presented that tackle important challenges with regard to the characterization of nanomaterials: 1) The characterization at ambient pressure, 2) the investigation of core-shell nanoparticles, and 3) the characterization of non-spherical particles by electron microscopy.

1) Surface analytical techniques such as Photoelectron Spectroscopy (XPS) or Secondary Ion Mass Spectrometry (SIMS) typically require measurements in ultra-high vacuum. However, for many applications (e.g. catalysis) it is important to know the surface chemical properties of nanomaterials at ambient conditions. Therefore, near-ambient pressure X-ray photoelectron spectroscopy (NAP-XPS) was used to investigate nanoparticles in suspension. The used instrumental set-up allows to directly insert nanoparticle suspensions into the analysis chamber and to measure without prior sample preparation. Compared to dry reference samples measured under high-vacuum, a shift towards higher binding energies was observed for silver nanoparticles in water, indicating a change of surface potential at the water-nanoparticle interface.

2) To determine the dimensions of core-shell nanoparticles (shell thickness, core and total diameter), scanning transmission X-ray microscopy (STXM) was used. The analyzed model system consists of a polytetrafluorethylene (PTFE) core surrounded by a polystyrene (PS) shell, providing a strong X-ray absorption contrast and a well-defined interface. The introduced STXM?based methodology yields particle dimensions in agreement with scanning electron microscopy (SEM) results and provides additional information such as the position of the particle core, which cannot be extracted from a SEM micrograph.

3) The accurate measurement of size distributions of non-spherically shaped nanoparticles (representing most of the industrial nanoparticulate materials) is a challenging analytical task. High-resolution electron microscopy (TEM and SEM) is best suited to access the shape of individual nanoparticles. To fill the gap between ideal, monodisperse particles of spherical shape and complex real-world samples, BAM has started the work to develop reference nanoparticles of controlled shape, such as TiO2 platelets, bipyramids, and elongated particles. Results of a recent ISO inter-laboratory comparison will be shown with emphasis on the measurement parameters, descriptors and data analysis.

Session 1
1. Measurement and characterization of nano objects

A92381df

LESSONS LEARNED FROM THE SAFERNANO DESIGN AND LAW AND NANOTEXNOLOGY INFORMATICS TRAINING (COMPARISON OF EU & USA INTERDISCIPLINARY

FEITSHANS JD AND SCM AND DIR (CONTACT AUTHOR) Dr ilise L [1], FIGUEIREDO, Eduardo [1], CRUZELLES RODRIGUES, Prof. Ms. Ivandick [1]

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Applying Nanotechnology to real life lab to market business strategies for consumer use requires keen understanding of nanoinformatics. Training in Europe for students across disciplines using nanoinformatics offers key information from programs regarding Nanotechnology applications and commercialization: Safernano Design and Law in France, and 15 years of Nanotexnology in Thessaloniki Greece provide interesting models for training when developing the next generation of Nanotechnology products and its large-scale commercialization. These two summer programs offer a multidisciplinary approach that has synthesized nanotechnology applications with law and policy. Each therefore represents a breakthrough for all training schools across several professions. The European approach is compared to the American perspective. noting however that many alternative programs do not mix business and pleasure as effectively as the European summer programs discussed here, In the IDEA League, a consortium of five universities in Europe including ETH Zurich, the model touches upon the USA model's concern for complexity, fast-paced results in a pressured setting where an immediately useful deliverable is required. By contrast, the Emeritus program at MIT is a fast-paced and deliberately intensive program. Online participants who are students are expected to use the information gleaned in the training program right away at the jobs in industry government or other parts of commerce. European training programs therefore offer important insights for developing nanotechnology for consumers because training addresses issues of health and safety from "Lab to Market". Forethought in design therefore includes safety concerns and risk assessment in compliance with regulations and laws. This presentation reflects comments from students and faculties from several nations on both sides of the Atlantic, including both North and South America.

Session 1
1. Measurement and characterization of nano objects

A92656AG

VORTEX SHAKER DUSTINESS METHOD: PRELIMINARY RESULTS OF INTERCOMPARISON

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The so-called dustiness methods are increasingly recognized as relevant in the *a priori* evaluation of the exposures of workers handling nanomaterials in powder form.

Dustiness is defined as the propensity of a powder to generate an aerosol during its handling.

In this work, the recent standardized Vortex Shaker dustiness method was implemented on eight representative industrial nanopowders through an intercomparison study.

The purpose was to have initial feedback on the repeatability and reproducibility of the method.

In this view, identical experimental setups in two distinct institutes (INRS and CEA) were used.

The nanopowders were compared in terms of, number-based and mass-based dustiness indexes and number-based size distributions of the airborne particles generated.

Here, we discuss the variability of the results obtained.

Session 1
1. Measurement and characterization of nano objects

A91691YM

Dose dependence of Alveolar Epithelial Cellular Uptake on Endophilin-mediated Endocytosis

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In recent years, it was discovered that uptake of proteins occurs in 10 seconds, and endophilin-mediated endocytosis involves in the uptake. The purpose of my work was to evaluate whether the particle size and the surface modification could contribute to the uptake of nanoparticles in endophilin-mediated endocytosis.

Using confocal laser microscopy and 3 type nanoparticles (P-25(particle size: 25nm, non-modified), C-25(particle size: 25 nm, carboxyl modified), and C-250(particle size: 250 nm, carboxyl modified)), we observed cells immunostained clathrin or endophilin. Similarly, using IL-2 (), P-25, C-25, C-250, C-250® (different emission wavelength from C-250), we observed cells immunostained with IL-2 receptor.

The correlation coefficient from the scatter plot from fluorescence intensity of coatomer protein and nanoparticles in a cell was calculated. As the result, there were positive correlations between 3min and 5min, and between C-25 andC-250. Conversely, there was no correlations between P-25 and C-25.

It was concluded from the result that the amount of uptake in endophilin-mediated endocytosis reached maximum at 3 minutes. Similarly, it is more difficult to uptake 250 nm nanoparticles than 25 nm particles, and it was concluded that the uptake by IL-2 receptors in endophilin-mediated endocytosis hardly occurs.

In this work, we examined by using a fluorescence microscope, and there are few findings about the uptake in endophilin-mediated endocytosis. Therefore, it is suggested to examine again in different way.

Session 2
2. Exposure

A91749BH

Exposure to nanometric titanium dioxide in the construction and public works sector

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This study has allowed us to assess levels of exposure to nanometric titanium dioxide among workers in the construction and public works industry and to establish an inventory of prevention measures linked to this activity. Sampling campaigns were carried out on workers exposed to titanium dioxide during preparation of “photocatalytic” cement and during “self-cleaning” wood-stain spraying operations.

The sampling campaigns were conducted using classic measurement techniques: sampling on filters connected to a pump and subsequent post-sampling chemical analysis. Sampling focused on the respirable aerosol fractions by means of a GKC 269 cyclonic separator, and was associated with determination of the aerosol particle-size distribution by means of a Marple impactor stage.

The grain size analysis from the impactors, however, revealed that whatever the form of the nanomaterial - solid in the case of the cement or liquid in the case of spraying – the nanometric titanium dioxide was distributed across all of the impactor stages. Thus, all fractions of the aerosol - respirable, thoracic and inhalable - were concerned. This distribution indicates that the concentration of nanometric titanium dioxide is under-estimated when only the respirable fraction of the aerosol is taken into account at the time of sample collection. At this stage, it is important to determine a sampling strategy that takes into account not only titanium dioxide in its nano-object (NO) form, as when collecting the respirable fraction, but also titanium dioxide in its aggregate and agglomerate (NOAA) forms, which are distributed throughout the respirable, thoracic and inhalable fractions.

Furthermore, the introduction of nanometric-form titanium dioxide to industrial processes employed in the construction sector has not been associated with any specific consideration of the risks linked to its use. Nanometric titanium dioxide is regarded as an ordinary chemical agent and a large majority of the prevention measures linked to its use are only personal protection measures.

A91559IO

A practical method for managing exposure to airborne carbon nanotubes released from their composites

When carbon nanotubes (CNTs) are used as filler material in composites, the release of CNTs may occur during the mechanical and abrasion processes of CNT composites. Since it is difficult to separately quantify free CNTs and CNTs embedded in the matrix, one of the practical methods for managing exposure to CNTs released from their composites involves controlling exposure to respirable CNTs, including both free CNTs and CNTs embedded in the matrix, to a level below the occupational exposure limit (OEL) of the CNTs. The outline of the method we used is as follows:

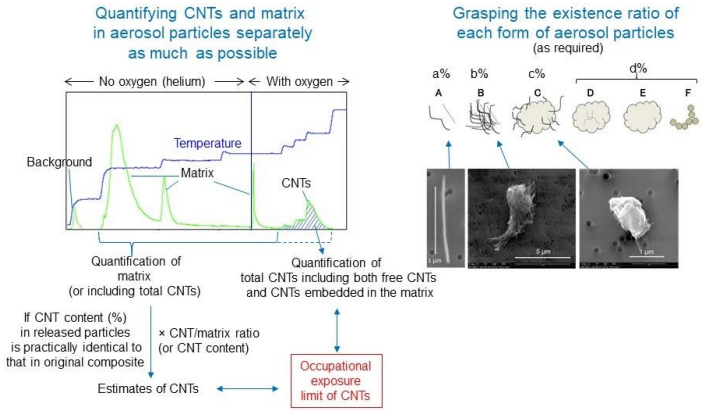
(1) Respirable particles released from CNT composites are collected on a quartz fiber filter. Using carbon analysis, the CNTs on the filter are quantified separately, to the extent possible, from the matrix. Any exposure to respirable CNTs, including both free CNTs and CNTs embedded in the matrix, is controlled to a level below the OEL of the CNTs.

(2) If complete separation and quantification of the CNTs and matrix is not possible, exposure to respirable CNTs is evaluated using a value that includes a part of the contribution of the matrix to the total amount of the CNTs.

(3) As an alternative to (1) and (2) or for their verification, if the percentage of CNT content in the released particles is practically identical to that in the original composite (e.g., if free CNTs are scarcely released), the amount of CNTs can be estimated from the amount of the matrix (or matrix + CNTs), quantified through carbon analysis or gravimetric analysis.

(4) As the case requires, the form of the released particles can be observed via electron microscopy, and, subsequently, the existence ratio of each form can be confirmed.

For details and case studies, please refer to the *Guide to Evaluating Emission and Exposure of Carbon Nanomaterials* published in April 2018 (https://doi.org/10.13140/RG.2.2.30715.41762).



Session 3
3.1 Nano-objects release from nano-enabled products

A91619ER

ARTIFICIAL AGING OF COMMERCIAL PLASTICS TO EVALUATE ENVIRONMENTAL NANOFILLER RELEASE

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Advancements in the fields of nanoscience and nanotechnology has increased the production and incorporation of engineered nanomaterials (ENMs) in commercial goods. One of the most appealing class of products for ENMs is plastic materials. Nowadays, the majority of the plastic used in our products are combination of basic polymers with different nanoadditives which improve the polymer performance. These organic or inorganic nanoparticles can impact different aspects of the polymer: the mechanical characteristics (strength, abrasion resistance, and flexibility), the electrical properties (conductibility), the optical effects (color, UV protection), the permeability capacities (food product shelf life), the functionalities (antimicrobial and self-cleaning activity). [1]

However, nanomaterials, since their dimensions, can display considerable toxicological and ecotoxicological consequences. So nowadays, exhaustive studies on the release of nanomaterials from plastic are required.

Here we apply a previously optimized NanoRelease method [2] to investigate the different emission of ENMs embed in commercial polymers. These materials were artificially aged (Fig. 1) and their ENMs emission were evaluated and compared to determine the mechanistic release pathways.

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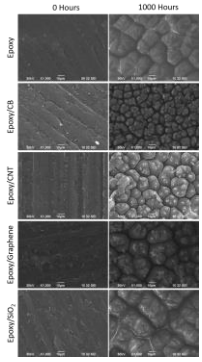

Session 3
3.1 Nano-objects release from nano-enabled products

A91621ER

NANORELEASE FROM AUTOMOTIVE COATINGS HIGHLIGHTS SIMILARITY OF (NANO) PIGMENT EMISSION DESPITE THEIR DIFFERENT CHARACTERISTICS.

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Nowadays, automotive coating often requires the incorporation of nanomaterials (NMs) in their matrix to improve their performance (e.g. mechanical, electrical, optical, functional properties). So, it is no surprise that commercial polymers employ pigments, which are now identified [1, 2] and registered [3] as nanomaterials.

On the other hand, this nanotechnological progress may also be associated with risks related the uncontrolled release of NMs from the products into environments and on humans. Since raising NM quantitates in circulation, their release behavior and causes must be assessed to monitor and to prevent hazards.

In this work, we investigated the induced fragment release of two different polymer matrices incorporating organic, metallo-organic and inorganic (nano) pigments before and after simulated sunlight degradation (Fig. 1). The NM emission outcome helped to highlight how the NM physicochemical properties and its incorporation in the polymer matrix may influence their release.

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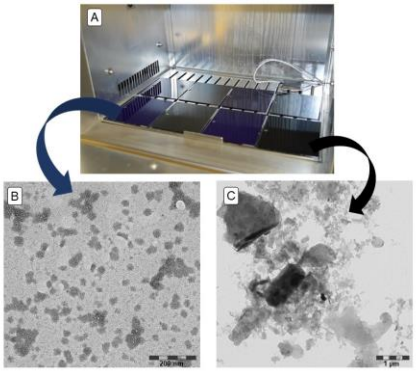

Session 3
3.1 Nano-objects release from nano-enabled products

A91703KA

ABRASION NANO-PARTICLE RELEASE TESTING METHOD FOR NANO-PARTICLE CONTAINING COMPOSITE MATERIALS USING A CHAMBER SYSTEM

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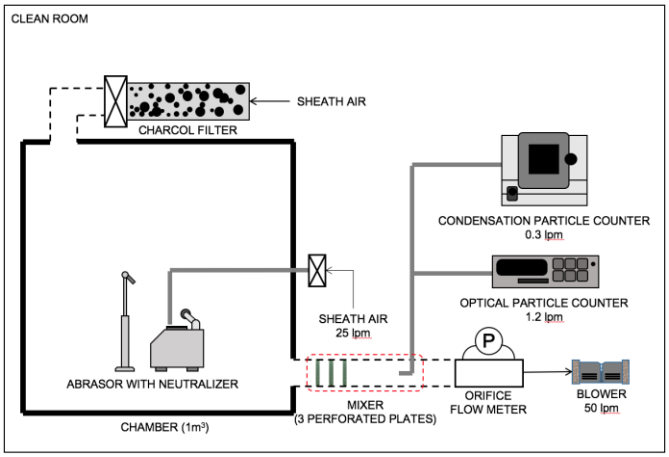
Nano-particle release testing method by abrasion process has been developed using a chamber system. Evaluation of the nanomaterial release from products containing nanomaterials is a crucial step in assessing the safety of these products, and has resulted in several international efforts to develop consistent and reliable technics for standardizing the evaluation of nanomaterial release. A chamber with Taber abrasion system inside was developed. This system consists of particle dispersion and collection parts with abrader and disc-type nanocomposite material specimens. The abraded particles are measured with a condensation particle counter (CPC), optical particle counter (OPC), and a filter for electron microscopy analysis. The performance of this system has been tested using a disc type nano-composite material specimen to determine whether the nanomaterial release is repeatable and consistent within the acceptable range. The test results showed that the total number of particles abraded in each test is within 20% from the average after several repeated test. The released particle number concentration was very similar and the repeatability was very good when a neutralizer was used. However, if a neutralizer was not used the total number of particle release from the sample was not consistent because of high electrical charge of particle. The highly charged particles are easily deposited on the chamber was or in the sampling line.



Session 3
3.1 Nano-objects release from nano-enabled products

A92546SJ

AEROSOLIZED (NANO) PARTICLES RELEASES DURING ACCIDENTAL DEGRADATION OF LI/ION BATTERIES

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Aerosolized (Nano) particles releases during accidental Thermal Degradation of Li/Ion Batteries

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In order to consider nanosafety aspects on the use of nano-enhanced batteries, a potential accidental scenario by calcination (mimicking a defective device) is implemented. The impact of Safe-by-Design (SbD) formulation and aging process of a type of Li/ion button cell is assessed.

The aerosol signature (granulometry, concentration, duration and composition) during the action of thermal degradation is determined and compared for difference between unused/used batteries with or without SbD pattern.

Only the anode of the Li/ion battery is studied. It is composed of a Cu substrate covered by an active layer of graphite with two types of nanoparticles (a “classic Nano” formulation and a SbD formulation). The aging process consists in cycling the batteries to simulate their normal use.

The accidental calcination is performed in conditions derived from a waste industrial incineration process ((2010/75/EU – art. 50): the furnace is set at 850 °C in air flow with a residence time of “at least two seconds” at this temperature. The released plume of particles is measured online by particle counters and granulometers, and collected on a filter for further analysis by SEM. Thermogravimetric analyses (TGA) are also performed to evaluate the thermal behaviour of the samples during calcination in air.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grand agreement no. 646221 NanoReg2.

Session 3
3.1 Nano-objects release from nano-enabled products

A91870JC

Barriers and Facilitators to Using Safe by Design

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The Nanoreg2 Safe by Design (SbD) concept aims at creating safer nanomaterials (NMs), products and industrial processes to reduce the risks to humans and the environment during the product life cycle. SbD goes beyond legislation and can be a valuable tool to prepare companies for future regulatory requirements. Within the project, the barriers to implementing SbD were examined during the progression of industry based Value Chain Demonstrator cases. A variety of methods were used to obtain information during the project including focus groups and interviews with both industrial partners and those project partners involved in the cases. By taking a longitudinal approach, as barriers were identified, solutions to some of those barriers were also identified at a later point. For example, in the earlier stages the following barriers were identified; misunderstanding of the implications of SbD, lack of information on toxicity to carry out the preliminary risk assessment, confusion of which tools are more appropriate for the risk assessment, costs involved and trust. As the project progressed a number of solutions were identified including having technical support from project partners for the implementation of SbD, and the need to avoid future problems from potential legislation. The possibility of obtaining a form of accreditation for using SbD has also been proposed as a means of encouraging its use in the nano industry; but it is not clear whether this would create a new barrier to future innovation. What is unclear is if companies will continue to implement SbD without legislative requirements or without technical support.

Session 3
3.2 Safe-by-design nano-enabled products and process

A92221FP

Testing the applicability of the safe-by-design concept: an Austrian case study on nanoclay-containing coffee capsules

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Food contact materials are diverse and omnipresent, for instance in the form of cutlery, storage and packaging containers, as well coffee capsules. Nanotechnological methods can improve the characteristics of food packaging made of plastic. However, there are concerns regarding the use of engineered nanomaterials (ENMs) for such applications. Within this context, the project “SafeNanoKap” tested the applicability of the safe-by-design (SbD) concept to the specific business case of nanoclay-containing plastic coffee capsules. The main purpose of the SbD approach is to identify possible risks along the entire value chain of ENM-containing products at an early stage and, if necessary, to minimize them. For this reason, potential exposure pathways of nanoclay from coffee capsules along the entire product life cycle were quantitatively mapped by a material flow analysis (MFA). The market potential of nanoclays in coffee capsules was estimated at 5 to 62 tons per year in order to serve the Austrian market. The MFA showed that, after proper waste collection, around 96% of the nanoclay will end up in bottom ashes after waste incineration and thus will be landfilled. Only 4% of it could be recycled annually. However, Austria does not currently carry out a single-sort collection of old coffee capsules made of plastics, and since reuse as food contact material is unlikely due to high hygienic requirements, this would lead to downcycling of nanoclay and to its unwanted transfer to other recycling materials. As MFAs are suitable methods to obtain quantitative information about potential exposure pathways, they are an essential complement to the SbD concept.

Additionally, a SWOT analysis was conducted on the SbD concept based on literature research and stakeholder round tables. For this, authorities, scientists and companies – which are potential “gate keepers” – were invited. In their perspective, the SbD concept is generally welcomed but the practical implementation is currently very time-consuming and expensive, meaning that, particularly, small and medium-sized enterprises (SMEs) are kept off applying this approach on a voluntary basis. Another challenge is to consult expensive external experts that are essential in terms of nanotechnology, which demands maximum anonymity to protect intellectual property, such as innovative nanoformulations or processing methods. Therefore, it remains questionable whether this concept is implemented voluntarily.

A92238GM

SYSTEM INTEGRATION OF CELLULOSE BASED MATERIALS INTO FINAL FORMULATIONS

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Recent advancements towards commercial production and scale up of nano-fibrillated cellulose (NFC) have increased the opportunities for using these unique biomaterials to improve the performance and sustainability of many existing materials. The presentation will summarize recent activities of Performance BioFilaments toward the commercial development of nano-fibrillated cellulose and its use as a functional additive in thermoplastics and wet laid filtration media. For thermoplastics used in the automotive sector, improvements in strength and stiffness of polypropylene and polyamide were found. For filtration media, the extremely high aspect ratio and surface area of nano-fibrillated cellulose allows for network formation of the nano-fibrils amongst other larger fibers. This enables the tailoring of pore sizes in the media, as well as increases in the bond strength between the larger fibers in the network.

A91502TK

Acquiring exposure data and contextual information for demonstration of system-of-systems nano risk governance platform

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Currently, none of the existing REACH compliance models are suited or validated for risk assessment of manufactured nanomaterials, and many existing exposure limits are not suitable for nanomaterials. In EU H2020-funded project caLIBRAte this will be address by developing a 'system of systems', based on a suite of tested and calibrated manufactured nano-specific risk prioritisation and control banding tools. The overall objective of the caLIBRAte project is to establish a state-of-the-art versatile Risk Governance framework for assessment and management of human and environmental risks of MN and MN-enabled products.

To achieve the goals, case studies in industrial sites are needed to generate new occupational exposure and environmental release data with high quality conceptual information for demonstration/verification of the modelling tools.

In this study multi-instrumental occupational and environmental exposure assessment combined with NECID-based data gathering was performed in a paint factory by collaboration of research groups. In the field study comprehensive exposure measurements of the production activities of three different paint batches, using e.g. TiO2, were performed. The activity-based measurements consisted of personal measurement of one worker in two different working stations, and associated nearfield, farfield and background measurements. Online monitoring and mass sampling for particles from 6 nm upward was conducted for whole day shifts during three days. Contextual information was collected for NECID database, for use in later stages with modelling tools.

This paper will describe the occupational exposure assessment and contextual data gathering of the activities in the workplace. Suitability of the gathered data for risk assessment with different modelling tools is discussed.

Session 4
4.1 Occupational risk assessment

A91814RF

Assessment of exposure to amorphous silica nanoparticles: preliminary measurements and laboratory simulations

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Amorphous silica nanoparticles (SiO2 NPs) are widely used in various industrial fields, e.g. in pharmaceutical, cosmetic and food packaging applications. Several studies reported that SiO2 NPs may induce potential toxic effects on human health and there is the need to assess the risk for exposed workers since they are involved in all stages of NPs life cycle. The manufacturing process of SiO2 NPs includes different phases: synthesis, cleaning and characterization in liquid phase and liofilization to obtain powder for the following pouring and partitioning of final materials produced in different sizes. The present study reports the preliminary results of exposure measurements and laboratory simulations conducted on manufactured SiO2 NPs with a mean diameter of 25nm. A multimetric and tiered approach was applied according to the OECD harmonized methodology. First of all, information about materials, processes and exposure scenario have been gathered. Furthermore preliminary real time measurements of particle number concentration (PNC) and lung deposition surface area (LDSA), compared to the corresponding reference background values, have been conducted in the workplace during the synthesis and partitioning phases, using handheld Condensation Particle Counters (mod. 3007, TSI) and DiSCmini (mod. TESTO). At the same time personal samplings in the workers' personal breathing zone (PBZ) have been conducted using a cascade impactor Sioutas (SKC). Simulations of pouring and partitioning of SiO2 NPs powders were also conducted in a laboratory set up: a glove box was used to reduce background levels and different instruments probes were connected to simultaneously measure particle size distribution (PSD), PNC and LDSA, integrated with sampling of airborne materialsf or the following morphological analysis. The workplace preliminary measurements showed PNC values higher than the corresponding background level during the synthesis and pouring phases. Laboratory simulations confirmed the potential emission of airborne SiO2 NPs during the pouring and partitioning phases, since the characteristic diameter of 25nm has been recognized by the PSD analysis. In conclusion such approach allowed to identify the potential of exposure for workers involved in SiO2 NPs production process; an extensive measurement campaign and further chemical-physical and morphological off-line analyses are needed to obtain integrated data for a complete exposure characterization.

Session 4
4.1 Occupational risk assessment

A91840vs

PREDICTION OF EMISSIONS DURING NANOPARTICLE HANDLING

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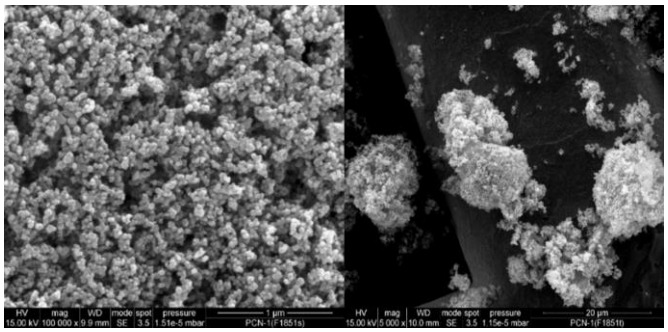
The use of nanoparticles (NP) has grown exponentially in the last years and, therefore, NP exposure can be considered a current emerging risk in workplaces.

A parameter of great interest is dustiness (tendency of powdered materials to generate dust when they are handled). Standard EN 15051 establishes two methods (rotatory drum and continuous drop) to determine inhalable, thoracic and respirable mass fractions of dust.

The aim of this work was to study the dustiness of different nanomaterials which are widely used, including: TiO2, Al2O3, SiO2, black carbon and other oxides (SbSnO and SnO2). To this end, the rotatory drum method was modified to (1) control temperature and relative humidity, (2) measure micro- and nanoparticle concentrations (in mass and number), (3) determine dust particle size distributions and (4) collect samples for morphological assessment. A climatic chamber and online and offline instrumentation (CPC3775, Mini-Las, Mini-Wras and TEM grids) for particle size ranges 4 nm-35 µm were used. HEPA filters were installed in the inlet and exhaust ducts to avoid outdoor interferences and minimize nanoparticle release.

Results did not show any statistically significant increase in NP concentrations (particle number) during the dustiness tests. Conversely to what might intuitively have been expected, statistically significant increases in inhalable, thoracic and respirable mass fractions were detected for all the materials tested. In fact, 80% of the samples showed moderate or high inhalable dustiness, as observed in the micrography showing formation of NP agglomerates. Therefore, although NP concentrations in terms of particle number did not increase significantly during the tests, potential NP exposure risks should be expected during the handling of nanopowders.



Session 4
4.1 Occupational risk assessment

A91633MD

DAILY PATTERNS OF OUTDOOR NANOPARTICLE CONCENTRATIONS IN DIFFERENT ENVIRONMENTS OF A COASTAL REGION OF THE WESTERN MEDITERRANEAN

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In the framework of the LIFE Project NanoMONITOR (LIFE14 ENV/ES/000662), we have used a new monitoring prototype to measure outdoor PM0.1 airborne concentrations. This prototype is based on a diffusion charging device and it was deployed in the Air Quality Surveillance Network of the Valencia region (on eastern side of Spain) throughout 2018.

This study shows the results of eight 15-day field campaigns in which airborne nanoparticles were measured in four different environments and under two different meteorological conditions (summer and winter) typical of the coastal regions of the western Mediterranean.

The results presented show how oudoor temporal patterns of airborne nanoparticule concentrations are strongly dependent on both, the typology of the environment of the measuring site (urban, suburban, industrial and rural) and the prevailing atmospheric dispersive conditions (summer versus winter).

Session 4
4.2 Environmental risk assessment

A91812AS

POLY (VINYL ALCHOOL) AND CALCIUM ALGINATE FILMS FOR LEAD NANOPARTICLES ADSORPTION IN WATER EFFLUENTS

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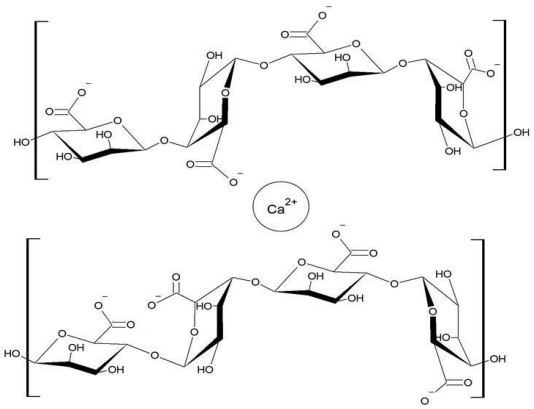
Sodium alginate is the neutralized form of alginic acid, a polysaccharide extracted from algae. It is a biodegradable polymer and can crosslink with bivalent and trivalent cations as lead. The greater the Lewis acidity, the stronger is the crosslinking. This type of crosslinking is called ionotropic gelation. Calcium is the most used ion as a crosslinker agent because it is the less toxic. This work explores the ability of alginate to exchange weak Lewis acid, as calcium, for strong ones, as lead. This can be used as an application for polluted water treatments, since the strongest crosslinkers are heavy metals which are usually present in most polluted rivers. To decrease the water solubility of alginate it was used poly (vinyl alcool) (PVA) crosslinked with poly (ethylene glycol) (PEG), two biodegradable polymers. Different amounts of calcium alginate as a gel were added to PVA solutions. After stirring at high temperatures to solubilize the PVA, PEG was added. The hot gels were put into molds and left for dry at ambient temperature. A volume of 10 mL of 500 µg/L solution of lead nitrate was prepared for each of the films which were put in the solution and left for 6 hours. The choice of this concentration of lead was based on real polluted water rivers. Past the hours, the films were left for dry again and digested in hot nitric acid. The samples of solutions and digested films were analyzed at Inductively Coupled Plasma (ICP) – Optical Emission Spectroscopy (OES). The films were also characterized by Fourier Transform Infrared (FTIR). Preliminary results have shown that the lead can be adsorbed by the films. The adsorption was expressed in terms of mass of film. On average the adsorption was 5.56 µg of lead per gram of dried film. Therefore, it was proven that calcium alginate can exchange the calcium ions for stronger Lewis acid as lead. This have important environmental applications as it can be used as heavy metal remover.



Session 4
4.2 Environmental risk assessment

A91447PD

TOXICITY REMOVAL BY DAPHNIA SIMILIS ASSAY IN BTEX CONTAMINATED GROUNDWATER USING NANOMETRIC TiO2/ZrO2 FILM AND BLACK LIGHT

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TOXICITY REMOVAL BY DAPHNIA SIMILIS ASSAY IN BTEX CONTAMINATED GROUNDWATER USING NANOMETRIC TiO_2/ZrO_2 FILM AND BLACK LIGHT

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A nanometric TiO_2/ ZrO_2 film deals with the development of a photocatalytic tubular reactor to treat superficial and groundwater contaminated with organic volatile compounds, more specifically benzene, toluene, ethylbenzene and xylene (BTEX). The reactor was operated with sample recirculation and it was constituted by two semiconductors catalysts, the titanium dioxide (20 nm) and the zirconium dioxide (60 nm) (TiO_2/ZrO_2). These catalysts were deposited over glass substrate in the form of mixed film and activated with artificial light originated from two 15 W black light lamps representing an average light intensity of 3.6 mW cm^{-2}. The results showed the viability of heterogeneous photocatalysis using a deposition of 15 mixed film layers over the glass matrix. The photodegradation of deionized water contaminated with 10 mg L^{-1} of BTEX gave a 95.9% of BTEX removal at pH 6.6 with a recirculation flow of 280 mL min^{-1}. Among the other components of BTEX, only the benzene did not reach the permitted limit by legislation. The analytes were quantified by solid phase microextraction (SPME). The kinetic of pseudo-first order was observed and being the initial concentration a limiting factor in the degradation rate. The acetophenone was the intermediate species detected during photocatalytic process. In the toxicity experiment using Daphnia similis as organism test, the toxicity removal was reached after 30 min of treatment of contaminated water with gasoline where the initial average CE50-48 h was 14.1% and reaching a final average CE50-48 h of the 84.3 %.

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Session 4
4.3 Tools and commercial equipment

A91859OD

CLEAN AIR DELIVERY RATE OF HOME AIR CLEANERS: WHY NOT MEASURE A SIZE-DEPENDENT DISTRIBUTION? AN ATTEMPT IN THE SUBMICRON RANGE.

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Several national Norms (China, France, US…) characterise the performance of home air cleaners by the Clean Air Delivery Rate (CADR). This quantity is the product of the flow rate by the efficiency of the filter with respect to a given pollutant. It describes how fast and how efficiently the pollutant will be removed from a room in given conditions.

As far as particulate pollution is concerned, the norms consider up to three types of populations. For instance, the French norm demands that a CADR be measured independently in the 0.3 to 0.5 µm, 1 to 2 µm and 3 to 5 µm ranges.

The CADRs of four commercial air cleaners were measured using NaCl particles (diameters 10 to 400 nm, modal diameter 35 nm) as test aerosol. The measurement technique was inspired by the Chinese norm: injection of the test aerosol in a test room, switching on the air cleaner and monitoring the decay of concentration in the room. Total concentrations were measured with a Condensation Particle Counter (CPC) and a scanning mobility particle sizer (SMPS, TSI model 3936) was also installed. CADRs could readily be calculated from the CPC data, but the spectra from the SMPS also proved helpful in two respects:

- The Chinese norm imposes stringent conditions on baseline aerosol count that were not met in our test room. The aerosol concentration therefore did not decay to zero as postulated in the CADR calculations. The size distributions of the ambient and injected aerosols were fortunately quite different; this allowed to determine the moment when the particle size spectrum was back to ambient conditions and made baseline corrections more effective.

- Using the same procedure as with the CPC data, it was possible to calculate a CADR for each particle size class. The idea was to identify, if any, a “least captured particle size”. The “size-dependent” CADRs did not vary by more than 30% for each air cleaner, at their maximum flow rate, and did not exhibit any clear minimum in the investigated range. Three air cleaners had classical fibre-based HEPA filters. The last one was mainly equipped of an electrostatic precipitator and had a clearly different CADR distribution from the other ones (again at maximum flow rate). This is only an isolated result obtained with a few air cleaners among many hundreds, but it encourages further investigation. The size dependency of the CADR may indeed give additional insight into the complex interplay of the elements of air cleaners.

Session 4
4.3 Tools and commercial equipment

A91603CM

DaNa2.0 – Adapting a Concept Based Search Approach to the Nanotoxicology field

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The risk assessment of current and future nanomaterials is facing many different challenges, one of them being the retrieval of relevant information from the continuously increasing collection of nanotoxicology related publications. However, a fast and effective information retrieval for the evaluation of nanosafety related data is a first and very important step for activities such as the DaNa knowledge base.

Traditional approaches to extract information and to maintain an overview over such a rich information resource are query engines, which allow for the formulation of so-called “free text” queries typically consisting of single words or small phrases. The returned and ranked documents will contain the search terms. However, when querying literature databases such as PubMed or even the DaNa knowledge base, users typically want to extract documents containing one or more concepts and not just single words or phrases. Challenges in this context are the ambiguous nature of certain terms as well as the uncertainty of the actual appearance of the used words within the text due to the usage of synonyms or hypernyms.

To overcome these problems, new approaches are extracting more semantic information from the text thereby shifting the search from the word-level to the concept-level. An additional disambiguation step here helps in identifying the concepts that are described in the documents. By means of this, the user will now apply words describing the concepts and not just the search terms he is looking for. An appropriate auto-completion system facilitates this process and improves the quality of search-result considerably.

Such an approach is currently being developed within the DaNa2.0 project not only to support and facilitate ongoing activities but also to help moving forward the field of nano risk assessment and information provision for the public. DaNa2.0 is a national project funded by the German Federal Ministry of Education and Research (FKZ 03X0131).

A91681CS

NANOCOMMONS - A KNOWLEDGE INFRASTRUCTURE FOR RISK ASSESSMENT OF NOVEL AND EMERGING MATERIALS

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Nanotechnology represents an enabling technology with the potential for major breakthroughs in diverse industrial sectors. However, processes at the nanoscale, where novel material properties occur, have also been linked to new or different potential risks, that are still not fully understood [1]. While recent advances provided new insights on what constitutes toxicity of novel and emerging materials (NEMs) in relation to health and environmental hazards, the nanotechnology and nanosafety communities remain disparate and unconnected, whilst knowledge and data remain fragmented and inaccessible.

To address this gap, the project NanoCommons will create an openly accessible e-infrastructure serving the current and future needs of the key research communities, pivotal industrial users and regulators. NanoCommons brings all stakeholders (academia, industry and regulators) together to facilitate pooling and harmonising of methods and data for modelling, *safe-by-design* product development and regulatory approval purposes, thereby driving best practice [2,3] and ensuring maximum access to data and tools and promote data interoperability and translational research.

NanoCommons combines:

- **Networking Activities** (NA) to span community needs assessment through development of demonstration case studies (e.g. exemplar regulatory dossiers),
- **Joint Research Activities** (JRA) to integrate existing resources and embed efficient data management process from the data generation step (facilitated using online laboratory notebooks), to (efficient and harmonised) data curation, preservation and provision of Open and FAIR access to data/models and,
- **Transnational Access** (TA) to provide users with funded access to the data, methods and tools generated or developed under the project. NanoCommons also offers expert guidance along the entire data lifecycle (experimental workflows, data acquisition/analysis/storage, metadata generation, publications etc.) ensuring data quality, completeness and harmonization into the future.

NanoCommons has the unique potential to deliver a step-changing impact for the emerging nanoinformatics in nanosafety community. It will remove barriers from nanosafety-related regulatory and industry processes by revolutionising data capture, management and sharing (FAIR data). [1]Valsami-Jones, E., and I. Lynch. *Science 350.6259* (2015), [2] Robinson, R. L. M. et al. *Nanoscale 8.19* (2016), [3] Hastings, J. et al. *Journal of biomedical semantics 6.1* (2015).

Session 4
4.5 Nano responsible development and sustainability

A91810KJ

The EU H2020 caLIBRAte project – Towards a Nano-Risk (Innovation) Governance Platform

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The caLIBRAte project is establishing a web-based portal connecting a series of thoroughly tested tools, data and guidance to enable trustworthy safety assessment and risk governance of MN and MN-enabled products during innovation and use. The framework will contain tools for: 1) horizon scanning with screening of targeted news and trends in nanotechnology; 2) control banding, qualitative and fully integrated predictive quantitative risk assessment operational at different information levels; 3) safety-by-design and multi-criteria decision support methods; 4) guidance for risk surveillance, -management, and -communication. Linking tools to eNANOMAPPER-caLIBRAte databases is a key objective.

Ending October 2019, the project starts to deliver key results. Suitable human and environmental risk assessment tools have been identified and are being further developed considering stakeholder input on their data availability and competences as well as data from model sensitivity analysis. Data on MN properties, MN hazards, and MN exposure case studies are being gathered and analyzed to identify suitable data sets and needs for closing data gaps for forthcoming model testing. A nano-specific Horizon scanning tool has been developed. Next generation risk assessment methods are under development and will include use of high-throughput testing and genomics data. Experimental studies investigating the role of the surface area paradigm on hazard as well as effects of doping, coating and functionalization has advanced well and results will be used for model revisions. First comprehensive industrial case-studies have also been established, including a completed unique indoor and outdoor measurement field campaign at a paint producer. Case-studies will be used to demonstrate the risk governance framework at the end of the project.

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caLIBRAte
nano risk governance

Session 4
4.5 Nano responsible development and sustainability

A92449ED

SWENANOSAFE – TOWARDS A MULTI-STAKEHOLDER DIALOGUE IN NANOSAFETY

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The increased use and production of various types of nanomaterials in consumer and industrial products raises health, safety and environmental concerns as uncertainties regarding potential risks of nanomaterials still exist.

The Swedish National Platform for Nanosafety, SweNanoSafe, was established in 2016 to promote safe use and handling of nanomaterials in Sweden. The platform is a governmental assignment by the Ministry of the Environment and Energy. It is a communication and cooperation platform bringing together stakeholders from academia, industry, authorities and the civil society. It promotes knowledge exchange and also aims to contribute to integrating safety and sustainability aspects early in the innovation processes.

The main goals of the platform are to:

-ensure knowledge building and knowledge exchange;

-increase knowledge on hindrances to safe use and handling of nanomaterials and how to address the hindrances;

-strengthen education and training in nanosafety

Information needs, knowledge gaps as well as potential actions for addressing the current hurdles have been identified in collaboration with stakeholders e.g. via various meetings, a major conference and three workshops in 2017 and 2018. A Cooperation Council with representatives from the stakeholder groups has played a key role in ensuring that the benefits of the platform are maximised for the actors involved. An Expert Panel and a network of researchers has been established pooling together expertise from different fields of nanosafety. In addition, a Swedish web portal, swenanosafe.se, facilitates timely communication and dissemination of knowledge (mostly in Swedish).

Currently, SweNanoSafe is continuing the process of identifying hindrances and proposing actions to promote safe use and handling of nanomaterials. In this process, the following four areas are in focus: 1) regulations and guidance, 2) research and development, 3) education and skills supply, and 4) knowledge and information exchange.

The multi-stakeholder dialogue and science-to-policy interface play a key role in SweNanoSafe's approach in building trust and support for ongoing and future activities. The multi-stakeholder approach will likely help leveraging the impact of proposed actions towards a more coordinated and sustainable nanotechnology governance in Sweden in the future.

Session 4
4.5 Nano responsible development and sustainability

A91739nw

Novel electrochemical method for assessing nanomaterial influence on biological membrane structure and activity

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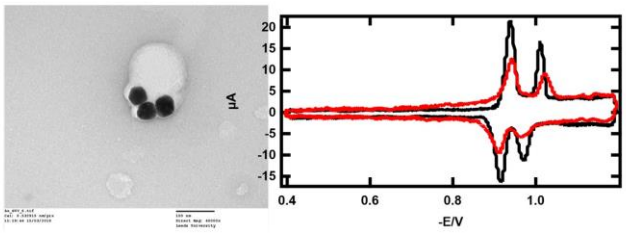
The worldwide use of nanomaterials is an acquainted topic; existing in medicine, electronic devices, consumer products and various laboratory chemical pathways. As such, there are concerns about the release of nanomaterials into the environment. Studying nanomaterial behaviour can prove challenging especially in larger organisms as sometimes accumulation of time presents the potential toxic discourse. Do nanomaterials aggregate around, bypass or modify membranes leading to toxicity or chronic diseases? Herein I introduce an innovative high throughput screening platform being developed into a multi-modular screening system which will incorporate selective in-built targets that mimic tissues and organs all integrated using a microfluidics network. The unique electrochemical biomembrane model has an extensive application in nanomaterials and pharmaceutical screening due to the flexible modifications of the screening platform. The technology provides a reliable means of measuring the biomembrane activity of a variety of materials and identifying activity earlier in the drug or nanomaterial development and will act as a complimentary screen to existing in-vitro and non-animal tests as a first stage screen, filtering those that are not required for further analysis. The comparable in vitro and in silico toxicity testing systems currently available (Log P, IAM, PAMPA) only measure membrane partitioning or do not present any further complexity of the compounds or nanomaterials as well as being time consuming. The platform utilises a DOPC layer sensing element incorporated onto a fabricated electrode chip in a flow cell, connected to a potentiostat where current vs potential profiles are monitored using CV. This platform is currently being developed into a multi-modular selective targeting system mimicking tissues and organs which is the heart of a new H2020 funded project HISENTS.



Session 5
5.1 Toxicology

A91471AS

CYTOTOXICITY OF IRON OXIDE NANOPARTICLES COATED WITH CHITOSAN CONTAINING ASCORBIC ACID TO HUMAN HEPATOCARCINOMA TUMOR CELLS

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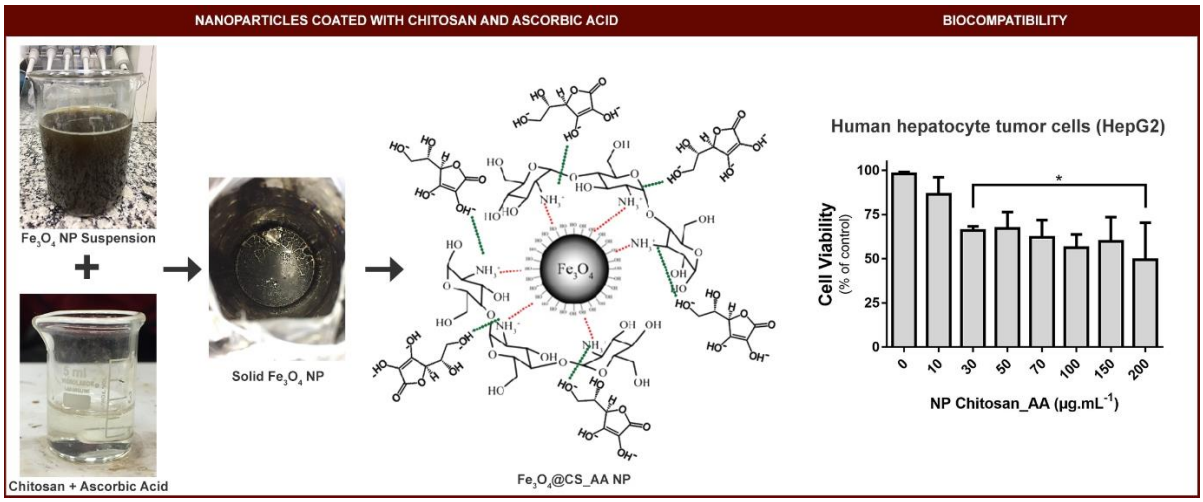
Iron oxide nanoparticles (Fe_3O_4NPs) have extensively explored in the field of nanotechnology due to their potential applications in drug delivery, and cancer treatment due to their well-known magnetic properties. This work describes the chemical synthesis of Fe_3O_4NPs by the co-precipitation method. The surface of the Fe_3O_4NPs was coated with chitosan (CS) to increase their dispersion and biocompatibility, avoiding aggregation. Ascorbic acid (AA), as a model drug, was incorporated into CS layer, leading to the formation of Fe_3O_4@CS-AA. The obtained nanoparticles were characterized by X-ray diffraction (XRD), dynamic light scattering (DLS), Fourier transform infrared spectroscopy (FT-IR) and atomic force microscopy (AFM) and X-ray photoelectron spectroscopy (XPS). Results by AFM showed the formation of spherical Fe_3O_4@CS-AA nanoparticles with an average size of 67.22 + 0.82 nm. DLS analyses revealed that the nanoparticles have a hydrodynamic size of 463.07 + 33.08 nm and moderate polydispersity of 0.350 ± 0.04. XPS analysis confirmed the formation of pure magnetite. FT-IR analyses confirmed the presence of CS and AA on nanoparticle surface. Fe_3O_4@CS-AA NPs exhibited significant toxicity against human hepatocarcinoma cells (HepG2), starting at 30 $\mu g.mL^{-1}$ concentration. Thus, Fe_3O_4@CS-AA NPs could find important biomedical applications exhibiting considerable cytotoxicity against tumor cells.



Session 5
5.1 Toxicology

A91670DC

In vitro model to evaluate cyto-genotoxicity of amorphous SiO2 nanoparticles at low concentrations on respiratory tract

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Amorphous SiO2 nanoparticles (NPs) compared to crystalline SiO2 are considered having low toxicity. However, due to their increasing commercial use as additives to cement, paint, cosmetics, food and in the medical sector, their potential toxicity to humans need to be clarified. SiO2 NPs demonstrated to induce inflammation, oxidative stress and cytotoxicity in several studies but a few data are available on their genotoxicity. Since inhalation is an important route of exposure to nanomaterials we evaluated on human bronchial epithelial cells (BEAS-2B) cytotoxic and genotoxic/oxidative effects induced after 24h exposure to low concentrations (2, 10 and 40 µg/ml) of SiO2 NPs with small diameter (25 nm) synthesized by precipitation. We also analyzed, by dynamic light scattering (DLS) the size distribution of the agglomerates/aggregates in culture medium at the tested concentrations. Percentage of viable, dead and apoptotic cells were evaluated by cytofluorimetric viacount assay, membrane damage was studied detecting LDH release and genotoxic and oxidative effects were evaluated by fpg-comet assay. We found slight, although statistically significant, decrease of viable cells percentage together with increase of dead and apoptotic cells percentages at 10 and 40 µg/ml. We also found increased LDH release only at 40 µg/ml. Fpg-comet assay showed slight dose-dependent increase of direct DNA damage, evaluated as % tail DNA, and a slight induction of oxidative DNA damage. DLS analysis of SiO2 NPs batch dispersion (1mg/ml in water) showed monodisperse and stable distribution with mean ZAV Diameter value of 204 nm. Otherwise, SiO2 NPs in BEGM showed ZAV Diameters that increased with a dose dependent trend ranging from 407 to 820 nm demonstrating the tendency to agglomerate in BEGM medium and confirming the need to perform also TEM and SEM analyses to well characterize the experimental exposure conditions. The findings demonstrate that, the tested SiO2 NPs induce slight genotoxic/oxidative effects on human bronchial epithelial cells at low no cytotoxic concentrations. Such results represent preliminary data within an Italian National Project on Occupational Exposure of ENMs, which aims also to apply the present in vitro model to evaluate the effects of such SiO2 NPs collected at the workplace where they are produced, to obtain a measure of the real occupational exposure to SiO2 NPs and of their potential toxic effects.

Session 5
5.1 Toxicology

A91624EF

OPTIMIZATION OF THE VITROCELL 24/48 IN VITRO INHALATION EXPOSURE SYSTEM FOR NANOPARTICLES

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Epidemiological and animal studies are both widely used approaches to investigate potential adverse effects and conduct risk assessments on inhaled chemicals and drugs. However, results are not always easy to interpret or reproduce and such experiments are extremely expensive, time consuming and use large numbers of animals. For these reasons, there is an increasing demand for the development of alternative approaches that make use of reliable in vitro inhalation testing strategies. These testing methods will require realistic lung cell models, realistic inhalation exposure systems and proper dosimetry techniques to increase the predictive ability of in vitro cell models and therefore accelerate the shift from in vivo towards in vitro testing.

The exposure of mammalian cells or tissues to substances which can be inhaled is frequently performed under submerged conditions. In doing so, the test substances are dispersed in liquid and dosed into the culture medium. A more realistic direct exposure of mammalian cells or tissue to airborne substances is exposure at the air-liquid interface (ALI) where the cell systems are not covered with culture medium.

The Vitrocell® 24/48 in vitro inhalation exposure system has been specifically designed and engineered to perform a complete dose-response profile in one run. Seven dilutions with 6 inserts each, are used for exposure to the substances and 6 inserts in the same system for clean air control.

Experiments with the 24/48 system were performed to test different humidification systems, trumpet heights, flows and cell models (A549, CALU3) to find the most optimal settings for nanoparticle exposure. The results of these experiments will be presented as well as the results of the exposure of cells to nano-Y2O3.

The Vitrocell 24/48 In Vitro Inhalation Exposure Systems was awarded to VITO by the PETA International Science Consortium.

Session 5
5.1 Toxicology

A91672AB

CHRONIC MICE EXPOSITION TO AEROSOL EMITTED FROM TIO2 NANO-ADDITIVED PAINTS SANDING: EFFECT ON LOCOMOTOR ACTIVITY

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The aim of the present study is to determine by a realistic approach the impact on the central nervous system of particles released from nanocomposite materials, such as nano-additived paints with TiO_2 nanoparticles (NPs). Having identified the presence of TiO_2 NPs at the surface and in the dry paint, abrasion tests confirmed a production of a bi-populated aerosols that also contained TiO_2 NPs after the mechanical abrasion process. Such emitted aerosols were used for in vivo studies to evaluate their potential neurotoxicity in rodents after repeated inhalation that mimics workers' exposure. Emitted aerosol was coupled to the exposure chamber containing groups of 30 to 36 C57Bl6 mice for 1h30/day, 5 days/week, during 8 weeks.

The number concentration averaged of the aerosol emitted, in the measurement range of 0.3 to 20 µm, for the expositions were of 1.70 ±0.37 107 part/L for the paint with TiO_2 NPs. A control group consisted of mice exposed to emitted aerosol from paint without TiO_2 NPs. Then the neurologic effects were investigated using motor performance parameters (coordination and balance), measured on a rotarod. The test apparatus is made of a cylinder separated into six compartments by acrylic discs that rotate at different controlled speed. Before and after chronic exposure, motor activity was registered individually for each mouse exposed, once a week, for 8 weeks, at 20 rotations per minute (rpm) or using an accelerating program from 4 to 40 rpm. Both set of tests were repeated 3 times for each individual. In order to study the effect of the exposition on the locomotor activity, a linear mixed model was fitted in each exposed group. The model explained the trend of the average time spent on the rotarod during the 8 weeks of experiment. Besides, a group of 6 mice was collected at 1, 2, 3, 4 and 8 weeks after exposure in order to study the time dependent effect on the histopathology of the brain.

Both rotarod tests showed that groups exposed to paint containing TiO_2 NPs impaired significantly their motor performances. On the contrary, the group exposed to aerosol from paint without NPs did not show a decrease of their performances, but a progression instead.

These results indicated that exposure to TiO_2 NPs present in emitted aerosol from paint, could possibly impair the locomotor abilities in mice chronically exposed. This will have to be highlighted by the results of ongoing brain histopathological studies.

* Equally contributed to the study

Session 5
5.1 Toxicology

A91820FP

Lysosomes mediate cationic carbon dot toxicological responses in a model of human macrophages

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Carbon dots (CDs) are widely studied for potential applications in biomedicine due to their very small size, water solubility and intrinsic fluorescence. This requires assessing their efficacy, but also their safety. We developed fluorescent cationic CDs prepared from branched poly (ethyleneimine) for gene therapy applications, and found that these nanoparticles (NPs) are not fully harmless to cells. To assess the mechanisms involved in the cytotoxicity of these NPs, we characterized the cell uptake and the toxicological endpoints evoked by the CDs in THP-1-derived macrophages. Furthermore, we investigated the role of the lysosome in these responses. By confocal laser scanning and transmission electron microscopy, we found that CDs are rapidly internalized by THP-1 cells and addressed to the lysosomes. The NPs induced a dose- and time-dependent loss in cell viability, with an EC_{50} of 16.5 µg/mL at 24 h (MTT assay). This cytotoxicity was associated with a dose-dependent loss in lysosome integrity (neutral red assay, EC_{50} of 14 µg/mL at 24 h), an oxidative stress evidenced by an increase in ROS production and a decrease in reduced glutathione, and an IL-8 release. CDs evoked also a dose-dependent perturbation in mitochondrial membrane potential measured with the JC-10 probe and the activation of the NLRP3 inflammasome highlighted by IL-1β secretion. Inhibition of the lysosomal protease cathepsin B with CA-074 Me significantly reduced CD-induced mitochondrial dysfunction and NLRP3 inflammasome activation, suggesting implication of the lysosome in the toxicological effects of the NPs. Our study provides for the first time a mechanistic pathway for the toxicological effects of cationic CDs in immune cells.

Session 5
5.1 Toxicology

A91821FP

Impact of the physicochemical characteristics of nanoparticles on their toxicity: in vitro screening of a carbon particle library

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Nanoparticles (NPs) may cause adverse effects. The nature and intensity of these effects depend on their physicochemical characteristics, although it is largely unknown to what extent and whether some characteristics prevail over others. To study this issue, we synthesized a library of 34 NPs by pyrolysis of various carbon sources (citric acid, ammonium citrate, glucose, poly (ethylene glycol) (PEG)...), in the presence of diverse passivation agents (ethanolamine, N, N-dimethylethylenediamine, poly (ethyleneimine)…) and catalysts (HCl, H_3PO_4, H_2SO_4…). The charge, size and elemental composition (C, H, N) of these NPs were determined, as well as their toxicity towards THP-1-derived macrophages. Size of the NPs varied between 7.5 and 39.5 nm according to TEM observations, and 7.2 and 283.7 nm according to DLS measurements. In culture medium, some NPs formed aggregates, whereas others were highly dispersed. Ten NPs exhibited a negative charge (-9.7 to -44.1 mV) and 24 a positive one (+11.4 to +41.4 mV), as determined by zeta potential measurements. The 34 NPs triggered various levels of viability loss when incubated with cells at 0 to 200 µg/mL for 24 h. Thus, they were sorted in 3 groups: 1-toxic NPs (EC_{50}=16.1 to 103.0 µg/mL), 2-weakly toxic NPs (EC_{80}=5.8 to 124.0 µg/mL) and 3-harmless NPs (viability loss at 200 µg/mL<20%). Negative NPs were all non-cytotoxic, whereas positive NPs were found in the 3 groups. For positive NPs, no correlation was found between the toxicity and the size, but NPs that were prone to aggregate in serum-containing culture medium were more toxic than fully dispersed ones. Furthermore, there was a positive correlation between NP charge and toxicity. Through the whole library, a direct relationship was found between the NP nitrogen content and toxicity. The nature of the nitrogen-containing passivation agent impacted the NP toxicity, a greater effect being observed with high molecular weight polyamines when compared to oligomers with lower molecular weight. At last, PEG decoration at the surface of NPs decreased the toxicity of cationic NPs. In conclusion, intrinsic size of NPs could not be directly related to toxicity whereas charge was clearly identified as the main factor influencing NP safety, cationic NPs being generally associated with cytotoxicity. Aggregation in culture medium, nitrogen content and nature of the passivation agent also influenced NP safety, making it difficult to predict NP toxicity from the only charge.

Session 5
5.1 Toxicology

A91852ND

Effect of coating in the interaction of CeO2 NPs with model membranes

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Cerium (III) oxide nanoparticles (NPs) exist in a broad range of fields from industrial and pharmaceutical applications to consumer products. It is found in large abundance in nature (more prevalent than gold and silver) and likely released into the aquatic environment, thus present in our daily lives; posing a potential hazard to our health. Therefore, it is important to study their toxicological behaviour. Many particles at the nano-scale require surfactants or stabilisers to properly disperse and conserve in good conditions with time. In addition, un-coated NPs have to be cleaned after synthesis to avoid contamination. However, reactants at low concentration can remain attached to the particle's surface and could potentially play a role in their activity.

The effect of coating on CeO2 NPs was analysed using a high-throughput electrochemical screening platform able to show membrane modifications and disruptions caused by a nanoparticle. Its sensor system utilises a mercury coated platinum working electrode where phospholipids can be deposited. In this way, the interaction of nanoparticles with a model membrane (DOPC lipid) can be studied in a controlled environment.

Two un-coated NPs of 5nm quantum dots and 10nm side cubes were synthesised and characterised using TEM, DLS, XRD, EDX and electron diffraction patterns. To study the effect of the NP coating, the particles were functionalised with citrate and PVP, which are among the most commonly-used stabilisers, and dispersed in water.

The two un-coated CeO2 NPs showed no interaction with the DOPC layer. However, citrate and PVP coated NPs did produce a modification within the DOPC layer. Our findings suggest that the properties of surface functionalised CeO2 NPs have a great influence on their lipid interaction.

A91874SF

TOXICITY OF DIFFERENT CLASSES OF MANUFACTURED NAOMATERIALS IN ALVEOLAR EPITHELIAL CELLS

BRANDÃO Fátima [1,2], **FRAGA Sónia [1,2]**, COSTA Carla [1,2], BESSA Maria João [1,2], HAASE Andrea [3], TEIXEIRA João Paulo [1,2]

The toxicological assessment of the potential toxicity of manufactured nanomaterials (MNMs) is urgently needed due to their increased use for commercial and industrial applications. Thus, this study evaluated the cyto- and genotoxicity of a panel of MNMs, including SiO_2 NPs, graphene oxide, and nano-sized pigments in rat alveolar epithelial cells (RLE-6TN), a primary target during inhalation exposure.

RLE-6TN cells were exposed for 24 h to different concentrations (0-56 µg/cm^2) of the different classes of MNMs: (1) differently capped (naked, phosphonate- and amino-modified), sized (7, 15 and 40 nm), and with different hydrophilicity/hydrophobicity SiO_2 NPs variants, (2) graphene oxide, and (3) nano-sized pigments (Cu-pthalocyanine and Cu- pthalocyanine halogenated) all dispersed in serum-free culture medium by cup horn sonication in order to evaluate their cytotoxic potential. Cytotoxicity was assessed by determining the LDH release and WST-1 metabolization in RLE-6TN cells. To evaluate the genotoxic potential of these MNMs, RLE-6TN cells were exposed to subtoxic concentrations of the different variants tested (0-28 µg/cm^2) and the DNA damage was assessed by the alkaline comet assay.

Hydrophilic SiO_2 NPs induced a concentration-dependent cytotoxicity in RLE-6TN cells, being the cytotoxic effect more evident in cells exposed to the smallest SiO_2 NPs. Moreover, amino and phosphonate surface modification mitigated the cytotoxicity of the unmodified SiO_2 NPs. Exposure to the hydrophobic SiO_2 NPs did not induce significant cytotoxicity on RLE-6TN cells. Graphene oxide NPs caused a concentration-dependent cytotoxicity in RLE-6TN cells. In turn, the nano-sized pigments slightly increased LDH release but failed to affect WST-1 metabolization by RLE-6TN cells. DNA damage was only observed in cells after 24 h of exposure to the two highest tested concentrations of 40 nm SiO_2 NPs.

Our data shows that the cytotoxic profile of SiO_2 NPs is influenced by the size and hydrophilic/hydrophobic nature of MNMs. In turn, amino and phosphonate surface modification attenuates cytotoxicity of SiO_2 NPs on RLE-6TN and might constitute a strategy to increase biocompatibility of SiO_2 NPs. Graphene oxide NPs were the most cytotoxic among the MNMs tested. Nevertheless, further research must be conducted to support these findings.

This work was supported by FCT through the ERA-NET SIINN project NanoToxClass (SIINN/0001/2013).

Session 5
5.1 Toxicology

A91875SF

TOXICITY OF CERAMIC NANOPARTICLES IN HUMAN ALVEOLAR EPITHELIAL A549 CELLS AT AIR-LIQUID INTERFACE

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Several ceramic industries have already incorporated within their production processes the manufacture of different types of ceramic nanoparticles (NPs), as well as the application of those nanomaterials on conventional products, which increases the risk of human exposure to these nanoparticles, particularly in occupational settings.

The aim of this study was to investigate the *in vitro* toxicity of ceramic NPs (ZrO_2, CeO_2 and Sb_2O_3•SnO_2 NPs) in human alveolar epithelial cells, a primary target following inhalation exposure. Human A549 cells were grown for 7 days onto Transwell inserts and cells exposed for 2 and 4h to aerosolized ZrO_2 (46 and 91 µg/cm^2), CeO_2 (17 and 34 µg/cm^2) and Sb_2O_3•SnO_2 (6 and 12 µg/cm^2) NPs at the air-liquid interface, using a Vitrocell® exposure system. Cytotoxicity was assessed by the LDH release and WST-1 metabolization assays immediately after exposure or in the recovery time (24h). DNA damage was also assessed by the alkaline comet assay in the recovery time. The % of DNA in the tail and the olive tail moment (OTM) were used as a measure of the amount of DNA damage.

A concentration-dependent increase in LDH release was observed after 2 and 4h of exposure to all the tested aerosolized NPs comparing with cells exposed to clean air (exposure control). This decrease in plasma membrane integrity was more marked in cells exposed for 4h to the ZrO_2 (59.77±2.46% of positive control) and CeO_2 (52.36 ±3.15% of positive control) NPs aerosols than to Sb_2O_3•SnO_2 NPs (19.11±3.43% of positive control). However, 24h after exposure, no differences in LDH release levels were observed among the exposed cells (exposure control and NPs aerosol-exposed cells). A concentration-dependent decrease in cellular metabolic activity of similar magnitude, as assessed by the WST-1 assay, was also observed 24h after exposure to all tested NPs. No significant increase in %tail DNA and OTM was detected comparing with control cells suggesting that DNA damage induced by exposure to the NPs aerosols is absent or minimal in the recovery period. Under our experimental conditions, exposure to the NPs aerosols affected both plasma membrane integrity and cellular metabolic activity, this effect being more marked for ZrO_2 and CeO2 NPs aerosols. Further research should be conducted to get further insight into the mechanisms involved in the toxicity of the selected ceramic NPs.

This work was supported by the FCT through the CERASAFE project (SIINN/0004/2014).

Session 5
5.1 Toxicology

A91876JT

TOXICITY ASSESSMENT OF ENGINEERED AND AIRBORNE PROCESS-GENERATED NANOPARTICLES IN HUMAN ALVEOLAR EPITHELIAL A549 CELLS

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Nanotechnology offers many possibilities in the ceramic sector by providing innovation of the industrial processes and products. However, nanoparticles (NPs) used in the manufacture of ceramic goods or released to the workplace air during production may pose a serious hazard for human health. This study aimed to investigate *in vitro* toxicity of both engineered (ENPs) (ZrO_2, CeO_2, SnO_2 and Sb_2O_3•SnO_2) and process-generated nanoparticles (PGNPs) [released during High Velocity Oxy-Fuel (HVOF) spraying] in human alveolar epithelial cells, a primary target following inhalation exposure.

The airborne particulate matter (PM) < 2.5 µm (PM 2.5) and ultrafine (< 0.2 µm, UFP) fractions were sampled at an industrial facility onto Teflon filters and in suspension using an aerosol concentration enrichment system (VACES). Human A549 cells were exposed for 24h to different NPs concentrations [ENPs: 5-150 µg/cm^2; PGNPs: 0.625-40 µg/cm^2]. LDH release and WST-1 assays were performed to assess cytotoxicity, and the alkaline comet assay conducted to assess genotoxicity.

Lower levels of LDH release were observed after exposure to all tested ENPs compared with controls, though a significant concentration-dependent decrease was observed for ZrO_2 NPs-exposed cells. A significant concentration-dependent increase in A549 cellular metabolic activity was observed for all tested ENPs after 24h exposure. Chemical analysis of the airborne NPs revealed that they are mainly constituted by WC, CrC and Ni. Exposure to these PGNPs significantly affected plasma membrane integrity and cellular metabolic activity of A549 cells. Analysis of cell viability concentration-response curves of A549 exposed cells revealed a half maximal inhibitory concentration (IC_{50}) of 47.69 µg/cm^2 (IC: 21.47-509.10) for the PM 2.5 fraction and of 2.40 µg/cm^2 (IC: 2.09-2.74) for the UFP fraction. Regarding genotoxicity, an increase in DNA damage was detected in A549 cells exposed to any kind of ENPs compared to the control.

Under our experimental conditions, while all tested ENPs were not cytotoxic, a mild genotoxicity was observed. Cells exposed to the airborne PGNPs (PM 2.5 and UFP fractions) exhibited a decrease in cell viability, this effect being more marked in cells exposed to the UFP fraction on a per microgram basis. These findings highlight the potential health risks associated with exposure to this kind of aerosols.

This work was supported by the FCT through the CERASAFE project (SIINN/0004/2014).

Session 5
5.1 Toxicology

A91884JT

EFFECT OF CYTOCHALASIN-B ON TiO2 NANOPARTICLES UPTAKE BY DIFFERENT CELL LINES

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The *in vitro* cytokinesis-block micronucleus cytome assay (CBMN) is widely used for genotoxicity evaluation of nanomaterials (NMs). However, cytochalasin-B (Cyt-B) used in this test may affect the uptake of NMs due to possible interference with endocytosis. Thus, the aim of this study was to investigate the influence of Cyt-B on the uptake of TiO2 nanoparticles (TiO2 NPs) by four different human cell lines: lung cells (A549), glial cells (A172), neurons (SH-SY5Y), and liver cells (HepG2).

A549 cells were exposed for 29 h (doubling cell time) to 4 concentrations of TiO2 NPs (10-200 µg/mL) both in the absence and presence of Cyt-B (6 µg/mL). In turn, A172, SHSY5Y, and HepG2 cells were exposed for 24 h to TiO2 NPs in the absence and presence of Cyt-B (3 and 6 µg/mL), and with a pre-treatment with Cyt-B (6 µg/mL) for 1 h followed by co-exposure to TiO2 NPs and Cyt-B (6 µg/mL). Analysis of TiO2 NP uptake was assessed using flow cytometry.

Results showed that A549, A172 and SH-SY5Y cells were able to internalize TiO2 NPs both in the absence and presence of Cyt-B. For HepG2 cells, TiO2 NPs uptake was also observed when compared to controls, but a significant decrease in uptake was observed for concentrations above 50 µg/mL in the presence of Cyt-B (6 µg/mL; both 24 h co-treatment and 1h pre-treatment followed by co-treatment), when compared with uptake in the absence of Cyt-B.

These data suggest that the mechanism of uptake for TiO2 NPs by A172, SH-SY5Y and A549 cells is likely other than endocytosis. In addition, results suggest that the choice of cell type and the selection of a suitable Cyt-B concentration must be carefully considered prior to genotoxicity evaluation of NMs with CBMN assay.

This work was supported by Xunta de Galicia (reference ED431B 2016/013). F. Brandão is supported by the grant SFRH/BD/101060/2014, funded by FCT (subsidized by national fund of MCTES) and V. Valdiglesias by a Xunta de Galicia postdoctoral fellowship (reference ED481B 2016/190-0).

Session 5
5.1 Toxicology

A92289AS

Cytotoxicity of polymeric films containing silver nanoparticles and nitric oxide donor against tumor cell lines

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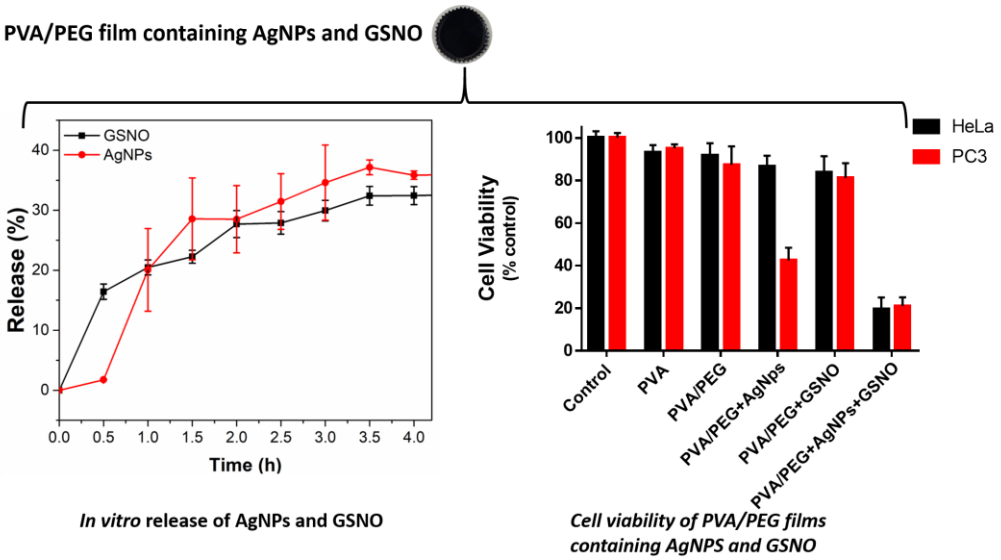
Silver nanoparticles (AgNPs) have been extensively explored in the field of nanotechnology due their promising applications in cancer treatment. Similarly, the free radical nitric oxide (NO) is an endogenous signaling molecule involved in several physiologic and pathophysiologic processes in mammals, including anticancer activity. Indeed, NO is able to sensitize cancer cells to chemotherapeutic drugs. In this work, AgNPs were biogenically synthesized by green tea extract, as a reducing and capping agent. The NO donor, S-nitrosoglutathione (GSNO), was also prepared. AgNPs and/or GSNO were incorporated into solid films of polyvinyl alcohol (PVA)/ polyethylene glycol (PEG), which are non-toxic polymers used in biomedical applications. The obtained films were characterized by several techniques, including X-ray diffraction, Fourier transform infrared spectroscopy, scanning electron microscopy, energy dispersive X-ray spectroscopy. The kinetics of AgNPs and GSNO diffusion from the polymeric films were evaluate. The results demonstrated a sustained release of AgNPs and GSNO from the polymeric films (Figure 1).The effects of the polymeric films in the human cervical carcinoma (HeLa) and prostate cancer (PC3) cell lines viability was assayed by MTT (Figure 1). The results demonstrated that the combination of AgNPs and GSNO into polymeric films significantly decrease the cell viability of both cell lines. In conclusion, polymeric films of PVA/PEG containing AgNPs and GSNO might find important applications against tumorigenic cells, due to the sustained and localized release of AgNPs and GSNO.



In vitro release of AgNPs and GSNO

Cell viability of PVA/PEG films containing AgNPS and GSNO

Session 5
5.1 Toxicology

A92510GK

TOXICITY ASSESSMENT OF CERIA NANOPARTICLES; A POROUS MORPHOLOGY STUDY

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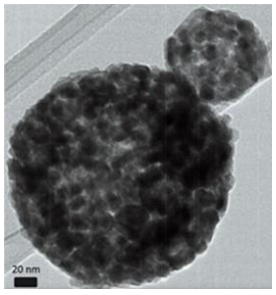
Surface area has recently been proved to be an important biological relevant dose metric for nano-/microparticles toxicological impact (Schmid et al, 2016), studying the aggregates and agglomerates of primary engineered nanoparticles ENP. In the current study, spherical cerium oxide particles have been synthesized by an aerosol spray pyrolysis method attributing to their polycrystalline spherical shape a porous morphology that has demonstrated advanced catalytic soot oxidation activity depending principally on their surface area (Kastrinaki et al, 2015). The respective porous particles have been morphologically and structurally characterized and have been evaluated for their toxicity assessment, relating the porous structure with Reactive Oxygen Species (ROS) generation.

The cerium oxide particles are synthesized by Aerosol spray pyrolysis method (ABS) managing by the different chemical and physical parameters of the process to control their structural and morphological parameters such as crystallite size, pore size, surface area and particle size distribution. Evaluation of total cellular ROS generation was performed with a ROS-Glo™ H2O2 Assay in 25 and 100 μg/cm^2 dose. Acellular ROS generation induced by the cerium oxide particle in the presence of oxidative environment was also evaluated with a spin trap based Electron Spin Resonance technique (ESR).

The only ABS particles that exhibit measurable ROS Fluorescence units are the ABS-B particles which have a relative high surface area. The results show though that surface area of porous particles is not directly related to ROS formation since particles with higher or lower surface area than the ABS-B particles exhibit no ROS values, relating possibly ROS formation with particle surface morphology of pore and crystallite size for cell uptake and ROS formation.

Schmid O., Stoeger T., (2016), J. of Aerosol Science, 99, (2016), 133–143

Kastrinaki et al., (2015), Emission Control Science and Technology, 1 (3), 247-253



Session 5
5.1 Toxicology

A91473MA

ECOTOXICITY EVALUATION: PREPARATION OF POLY-?-CAPROLACTONE AND CHITOSAN NANOPARTICLES AS CARRIERS OF THIAMETOXAM PESTICIDE

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Huanglongbing (HLB) is probably the most serious disease of citrus, nowadays. The severity of disease is mainly the rapid and efficient dissemination of the bacteria associated with HLB by psyllids Diaphorina citri (D. citri) and the absence of genetic resistance in citrus. Chemical control is the main way to control the psyllids, and there are different insecticides registered for this purpose. Thiamethoxam (neonicotinoid insecticide) is one of the active ingredients used in the control of HLB. Pesticide formulations nanocapsules allow a controlled release of active as well as protection against their premature degradation, allowing the use of conventional insecticide in a more sustainable way. Thus, studies of the effectiveness of encapsulated pesticide formulations are extremely important for enabling its use in agriculture. This study reports the encapsulation of the insecticide thiamethoxam in polymeric particles from poly-ε-caprolactone (PCL) and chitosan by double emulsion and solvent evaporation method using different concentrations of chitosan and two Pluronic (poloxamer) copolymers, F 127 and F68. These nanoparticles were characterized in terms of size, polydispersity, and encapsulation efficiency. The microalgae Pseudokirchneriella subcapitata (bioindicator chloroficea) was used to evaluate to ecotoxicity of nanopesticide in comparation of commercial formulation. The nanopesticide obtained resulted in homogeneous and monodisperse particles, with the mean diameter obtained of 166.3 nm, polydispersity indices were lower than 0.4 and positive superficial charge (+25 mv).The encapsulation efficiency, measured by by liquid chromatography, it was 34%. The ecotoxicity results demonstrated that the nanopesticide was less toxic that commercial formulations, in the same concentrations.

Session 5
5.2 Environmental interactions of nanomaterials

A91829CA

Impact of emissions of airborne TiO2 ENM on atmospheric NO2 concentrations

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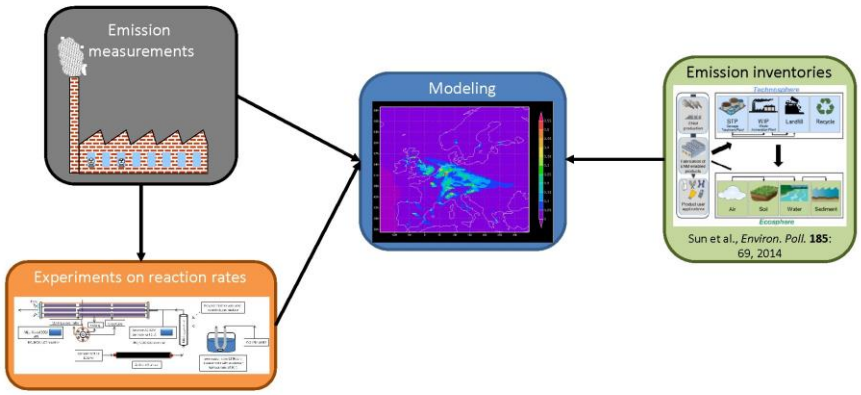
Titanium dioxide is one of the most produced engineered nanomaterials (ENMs) worldwide. Its high photocatalytic activity is key to many applications. Like any other ENM, TiO_2 may be released into the atmosphere during nearly any phase of its lifecycle, where it may interact with atmospheric gases. It is well known and widely exploited that TiO_2 photocatalytically reduces NO_2 in the presence of UV light, however, the effect of accidentally released TiO_2 ENMs on ambient NOx concentrations is widely unknown. We here present a comprehensive study on experimental laboratory investigations on the reaction rates of NO_2 in the presence of TiO_2 ENM (Evonik P25) under UV irradiation. The study is carried out in a dedicated test rig, where defined concentrations of TiO_2 ENMs and NO_2 are exposed to UV light. Both the UV light intensity and exposure time are adjustable. In a parallel study, the emission rates of engineered metal oxide nanomaterials from industrial facilities have been experimentally determined in field measurements and are used as surrogates for the TiO_2 concentrations used in our lab-experiments. Experimental data on both the emission rates, as well as the chemical reaction rates, are used along with emission inventory data as input parameters for long range modeling of TiO_2 and NO_x concentrations across Europe using LOTOS-EUROS (see Figure 1) to better understand the dispersion of engineered nanomaterials and their impact on atmospheric chemistry. The poster will present results of the laboratory experiments and the field measurements and how these data are used in the model. First modeling results will be shown and it will be discussed how modeling can help improve the understanding of the presence and effects of engineered nanomaterials in the atmosphere.



Session 5
5.2 Environmental interactions of nanomaterials

A91885OA

Phytotoxicity of Silver Vanadates Nanowires: Effects on Seed Germination and Root Development

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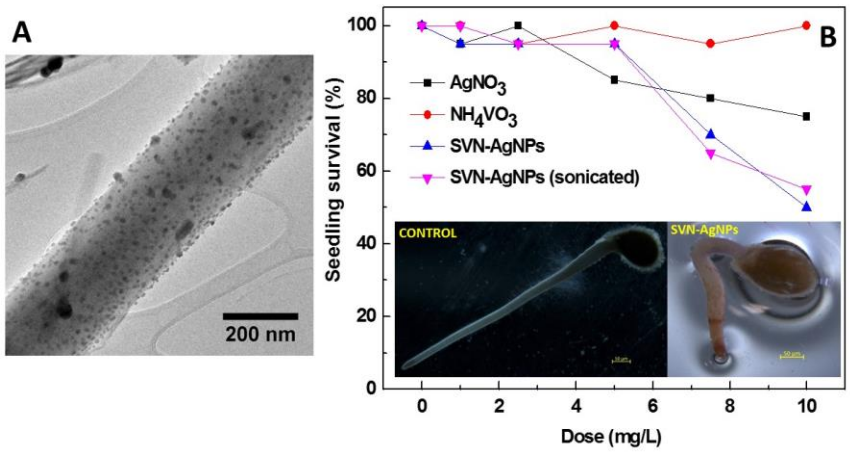
Silver vanadate nanowires decorated with silver nanoparticles (SVN-AgNPs) are promising materials for nanotechnological innovation. Here, we performed the synthesis, characterization, and phytotoxicity assessment of SVN-AgNPs on cherry tomato (L. esculentum) seeds. The nanowires were obtained by a simple and fast precipitation reaction using silver nitrate (AgNO3) and ammonium vanadate (NH4VO3) salts at room temperature. The SVN-AgNPs showed lengths in the order of microns and diameters around 60 nm, and decorated with spherical silver nanoparticles with diameters ranging from 5 to 40 nm (Figure 1A). This nanomaterial was well-characterized by TEM, SEM, DRX, FT-IR, XPS, and BET techniques. Seeds of cherry tomato (n=30) were growth in Agar culture medium with photoperiod (14 daylight) and temperature (28°C) for 3 days. It was not observed phytotoxic effect on seed germination rate until 10 mg/L of SVNs-AgNPs. However, the phytotoxicity effects of nanowires were evident on the root development and seedling survival. Root length decreased in dose-dependent manner after exposure to SVN-AgNPs and AgNO3. For example, 2.5 mg/L of SVN-AgNPs caused 50% reduction in root size. In addition, the nanowires induced a morphological change on the tomato roots, making them curly, disrupting the absorption of water and nutrition processes and consequently delaying the root growth. Furthermore, it was observed a negative impact on seeding survival rate for SVN-AgNPs and AgNO3 after 3 days of exposure. However, it was not observed effects on seedling survival after the exposure to NH4VO3 (Figure 1B). These results are indicating that silver is the main chemical element involved on the phytotoxicity adverse effects. This work is the first contribution towards nanoecotoxicity assessment and ecological implications of silver vanadates nanowires in terrestrial environment.



Session 5
5.2 Environmental interactions of nanomaterials

A91686WF

NANOTOXICOLOGICAL ASPECTS OF BACILLUS CALMETTE-GUÉRIN THERAPY ASSOCIATED TO PLATELET-RICH PLASMA 16-970 nm ON BLADDER CANCER

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For many years on Bacillus Calmette-Guérin (BCG) intravesical immunotherapy is using on non-muscle invasive bladder cancer (NMIBC). Our study describes the effects of a promising therapeutic alternative for this standard treatment. A new combination of BCG with Platelet-rich plasma (PRP) (16 nm [exosomes], 105 nm [microparticles] and 972 nm [microaggregates] with 2%, 26% and 72%, respectively) 1 in an animal model was studied. Interesting, this study describes the possible mechanisms of this therapeutic combination involving Toll-like Receptors (TLRs) 2 and 4 signaling pathways. NMIBC was induced by treating female Fischer 344 rats with N-methyl-N-nitrosourea (MNU). The animal experiments were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 3901-1. After treatment with MNU, the animals were distributed into four experimental groups: Control (without MNU) group, MNU (Cancer) group, MNU+PRP group, MNU+BCG group and MNU+PRP+BCG group. Data from in vitrostudy demonstrated that PRP treatment alone or associated with BCG triggered significant cytotoxicity in bladder carcinoma cells (HTB-9). Sixty female Fischer 344 rats seven weeks old treated with PRP associated to BCG clearly showed better histopathological recovery from the cancer state and decrease of urothelial neoplastic lesions progression in around 70-75% of rats when compared to groups that received the monotherapies administered separated. The rats from Control and Control+PRP groups showed intense and moderate TRIF and IRF3 immunoreactivities, respectively in relation to MNU group, which exhibited weak immunoreactivities. The animals from MNU+BCG and MNU+PRP exhibited moderate immunoreactivities for theses antigens. The combined treatment with PRP and BCG was able to increase TRIF and IRF3 immunoreactivities. Besides this, therapeutic association led to distinct activation of immune system TLRs 2 and 4-mediated, resulting in increased MyD88, TRIF, IRF3, IFN-γimmunoreactivities. In conclusion, our results obtained suggest that interferon signaling pathway activation by PRP treatment in combination with BCG immunotherapy may allow novel therapeutic boards for non-muscle invasive bladder cancer.Acknowledgement: This work was supported by NanoBioss/Sisnano (CNPq-Brazil, Process number 402280/2013-0), INOMAT (CNPq/MCTI), Brazilian Network of Nanotoxicology (CIGENANOTOX), and FAPESP.

Reference: 1. Maurer-Spurej, E. et al. Transf. Apheresis Sci. 55, 35 (2016)

Session 5
5.3 Safe use of nano objects for medicine applications

A91687WF

NANOSTRUCTURED LIPID CARRIER Co-LOADED WITH DOXORUBICIN AND siRNA: ITS TOXICITY AND ANTITUMOR ACTIVITY AGAINST BLADDER CANCER

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The nanostructured lipid carrier (NLC) was prepared from two solid lipids Cupuaçu butter and bis-diglyceryl polyacyladipate-2 at 60:40 and buriti oil (25%) as liquid lipid and stabilized by a surfactant 1.5% of Pluronic F68 and behentrimomiun chloride (cationic surfactant) loaded with Doxorrubicina (DOX) in a high pressure homogenizer at 5.000 a 20.000 rpm. The use of NLC with DOX and the histopathological analyses showed on induced rats with non-muscle invasive bladder cancer (NMIBC) that 20% of the rats exhibited benign lesions (papillary hyperplasia) and 80% malignant lesions. Besides this, considering the malignant lesions, 40% were High-grade Papillary Carcinoma (pTa), 20% Low-grade Papillary Carcinoma (pTa) and 20% lesions of Urothelial Carcinoma with invasive of lamina Propria (pT1). The histopathology analyses of the treatment only with free DOX demonstrated a 25% of animals exhibited papillary hyperplasia, 50% High-grade Papillary Carcinoma (pTa) and 25% Urothelial Carcinoma with invasive Lamina propria. The use of NLC/siRNA (vascular endothelial growth factor (VEGF)) showed 40% of the animals exhibited benign lesions (Papillary hyperplasia) and 60% malignant lesions. However, the malignant lesions 20% were of the Papillary Carcinoma in situ (pTis) and 40% of Low-grade Papillary Carcinoma (pTa) (Table 1). Our results are indicative that NLC/siRNA reduced the severity of NMIBC related to free DOX as also with DOXIL®. Then, the NLC/siRNA/DOX appears as an excellent anticancer nanocarrier with very low toxicity.

Acknowledgement: This work was supported by NanoBioss/Sisnano (CNPq-Brazil, Process number 402280/2013-0), INOMAT (CNPq/MCTI), Brazilian Network of Nanotoxicology (CIGENANOTOX – MCTI/CNPq), and FAPESP.

Histopathology	Squamous metaplasia and urothelial carcinoma with invasion of the lamina propria (pT1)	Urothelial carcinoma with invasion of the lamina propria (pT1)	High grade papillary carcinoma (pTa)	Low-grade papillary carcinoma (pTa)	Carcinoma in situ (pTis)	Papillary hyperplasia	Normal
Injury type	Malignant	Malignant	Malignant	Malignant	Malignant	Benign	———
Control n=5	———	———	———	———	———	———	5 (100%)
MNU Cancer n=5	———	3 (40%)	2 (40%)	1 (20%)	———	———	
DOX n= 4	———	1 (25%)	2 (50%)	———	———	1 (25%)	
NCL n=5	1 (20%)	1 (20%)	2 (40%)	1 (20%)	———	———	
NCL-DOX n=5	———	1 (20%)	2 (40%)	1 (20%)	———	1 (20%)	
NCL-DOX-siRNA n=5	———	———	———	2 (40%)	1 (20%)	2 (40%)	
BCG n=5	3 (60%)	2 (40%)	———	———	———	———	

Session 5
5.3 Safe use of nano objects for medicine applications

A91690WF

CYTOTOXICITY AND ANTIUMOR ACTIVITY OF BIOGENIC SILVER NANOPARTICLES AGAINST NON-MUSCLE INVASIVE BLADDER

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Bladder cancer is the fifth most common form of malignancy in the United States, and for most of the last three decades, the treatment and outcomes for patients with this disease have not changed. Nanomedicine aims to provide the means to target chemotherapies directly and selectively to cancerous cells and enhance their therapeutic efficacy. In this scenario, we employed biogenic Silver Nanoparticles (AgNPs) as an anticancer agent against non-muscle invasive bladder cancer (NMIBC). Bladder cancer was chemically induced with N-methyl-N-nitrosourea (MNU) on C57BL/6Junib female mice and treated by intravesical route with biogenic silver nanoparticles concentrations of 0.5, 0.2, and 0.05 mg/mL. The histopathological analyzes showed the treated with AgNP 0.5 group presented 50% of pTa and 50% of pTis, indicating that this treatment was not effective in regressing the neoplastic lesions. MNU + AgNP 0.2 group showed 50% of tumor regression, and 50% of the animals presented flat hyperplasia. Finally, treatment with 0.05 AgNP led to 100% tumor regression, with 50% of the animals showing normal urothelium and 50% showing flat hyperplasia, considering a benign lesion. Further, to understand the antitumor effect of AgNPs, we evaluated the molecular mechanism of cytotoxicity in human bladder carcinoma 5637 cell. The results showed the dose-time dependent cytotoxicity, and detailed analysis demonstrated induction of cell death via apoptosis. Besides, we found that AgNP inhibition in cell migration and proliferation. Thus, these findings confirm the antitumor properties of AgNPs, and suggest that they may be a cost-effective alternative and promising candidate for the treatment of bladder cancer.

Keywords: Biogenic silver nanoparticle; bladder cancer; apoptosis.

Session 5
5.3 Safe use of nano objects for medicine applications

A91247Md

Toxicity of cationic solid lipid nanoparticles in rats

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Cationic solid lipid nanoparticles (cSLN) represent one alternative to deliver poorly water-soluble drugs and oligonucleotides (DNA, siRNA, miRNA). However, the available information to guarantee the use of cSLN in vivo is still scarce, in vivo toxicity is one of the major challenges for nanotechnology translation from the bench to bedside. Hence, we investigate the toxicity of cSLN formulation in adult male Wistar rats. The animals were examined at 24 and 72 h after intravenous injection (n=6/group) of 1 mL of cSLN (38 mg of total lipids/200g body weight). The cSLN-treated rats were clinically indistinguishable from controls. No changes in hematological parameters were observed between the groups throughout the experimental period, but for neutrophils and lymphocytes count. The cSLNs-24 h group exhibited an increased percentage of neutrophils (417%, $p<0.01$), while the percentage of lymphocytes decreased (176%, $p<0.01$) when compared to both control and vehicle groups. This effect was transient as the values in the cSLNs-72 h group returned to basal levels. Histopathological evaluation of cSLN-treated group demonstrates inflammatory cell infiltration within alveolar and hepatic tissue 24 h post-treatment. No tissue alteration was observed in the spleen and kidneys. Ly6G, a marker of neutrophils, confirm that the inflammatory infiltrates observed composed by neutrophils. Besides the neutrophils presence, cSLN did not influence the biomarkers of liver function albumin, total bilirubin, alanine transaminase, and aspartate transaminase. Regarding the biomarkers of kidney function, we did not observe alterations in creatinine levels; but found a transitory decrease of 38% in urea levels at 24 h in the cSLN-treated animals, compared with the control group ($p<0.01$). The levels of urea had returned to the control rate in the cSLNs-72 h group, which may indicate that the alteration was short-lived. cSLN did not affect microvascular blood bed nor caused dye extravasation in plasma. Likewise, the amount of dye extracted from brain hemispheres of the cSLN-treated animals did not differ from that in the brain of control and vehicle groups confirming the integrity of blood-brain barrier. Few minor and transient alterations were found, but overall, cSLN showed to be highly biocompatible under the experimental conditions of this study. The mechanistic understanding of biocompatibility and toxicity of cSLN is needed for providing a safe clinical translation.

Session 5
5.3 Safe use of nano objects for medicine applications

A91615ND

Nanotoxicity and Dermal Application of Nanostructured Lipid Carrier Loaded with Hesperidin from Orange Residue

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Nanototoxicity and Dermal Application of Nanostructured Lipid Carrier Loaded with Hesperidin from Orange Residue

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Flavonoids from citrus fruits, because of its features; they have been considered as new bullets in cancer therapy. Flavonoids can present antioxidant, anti-inflammatory and anticancer properties and associated to a lower risk of cancer. The nanostructured lipid carriers (NLC) are drug delivery systems composed by a mixture of solid and liquid lipid and it can increase the physical stability and promote the sustained release of the drug. So, the main objective of this research was to combine the potential of the flavonoid as a natural anti-oxidant compound with the nanostructured lipid carriers to form a system able to deliver efficiently the flavonoid to the skin cells. These NLC were prepared through high pressure homogenization technique and were evaluated in function of several standards properties. The samples exhibited good stability through time and temperature: size was around 215 nm and zeta potential -35 mV during a period of 90 days. The encapsulation and the loading efficiency was respectively 96% and 2.25% up to 90 days of storage. The cell viability tests showed that the free as well as the encapsulated flavonoid did not presented toxicity in vitro to the melanoma cells tested: A375, CHL01 and SKMEL147 through MTT, neutral red and crystal violet assays. In its antioxidant capacity, hesperidin at 45 µmol L-1 was able to reduce significantly the radical of DPPH assay to 92, 58 ± 0, 82%. On the other hand, the produced nanoparticles were applied in a skin lotion formulation, which showed a good stability and showing a new application for the produced nanoparticles as an anti-aging and moisturizing cosmetic product. All data suggested that, at the level studied, a non-significant toxicity on cells were observed.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91623ND

Toxicological and Clinical Evaluation of Bladder Cancer in Dogs by a Nanostructured Pharmaceutics (OncoTherad).

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Toxicological and Clinical Evaluation of Bladder Cancer in Dogs by a Nanostructured Pharmaceutics (OncoTherad).

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Canine as models in which the disease occurs naturally mimic humans as closely as possible and may be useful in evaluating new therapies, including with OncoTherad therapy. The aim was to establish the safety of nanopharmaceutic such as OncoTherad. Then, the effects of intravesically immunotherapy with OncoTherad on the progression of bladder cancer and its possible toxicological effect was evaluated in 6 dogs. After the diagnosis of urothelial carcinoma and the consent of dog owners, treatment with OncoTherad was initiated (approved by the Ethics Committee on the Use of Animals (CEUA) - UNICAMP (protocol number: 4481-1 / 2017)). The dogs received 25 mg/2 mL of OncoTherad by intravesical (probing) to the urinary bladder of each dog. These animals received a weekly dose of OncoTherad for six consecutive weeks. The therapeutic effects of OncoTherad were evaluated by ultrasonography during the course of treatment. All the dogs exhibited the presence of tumor mass with irregular contours, mixed echogenicity, hyperechoic ecotexture and exhibiting hematuria: Before instillation and after 6 instillations of OncoTherad, the tumor mass volume reduced in average of 62.5 ± 12.6% in relation to the initial ultrasound. At the end of 24 instillations, the tumor mass reduced 84.5 ± 3.8% of its volume. The biochemical analysis of all the canines was monitored. Hemoglobin, Leukocytes, Platelets, Liver Function (ALT) and Renal Function (urea and creatinine) indicated that complete treatment with OncoTherad (24 applications) was not toxic for the 6 canines, reached normal values with the proposed treatment, with no signs of systemic toxicity at the proposed therapeutic dose. Thus, these results indicated that intravesically immunotherapy with OncoTherad was effective in reducing and preventing the progression of urothelial neoplastic lesions in spontaneous canine urinary bladder cancer.

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Session 5
5.3 Safe use of nano objects for medicine applications

A91684MH

Study of histopathologic effects of nanocrystobalite food additive on cardiac and renal teratogenic parameters in rats

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Objectives: nanocrystobalite (Nano Dioxide Silicon) are a group of nanoparticles that are used as antimicrobial food additives in the food industry, in feed and in poultry and in food packaging. Considering the possibility of the introduction of this nanomaterial into human food and also its transmission through the placenta of the mother to the infant, evaluation of its risk is important due to its effects and toxicity. The aim of this study was to evaluate the histopathologic effects of nanocrystobalite on vital organs of the rat embryo, including the heart, due to its vital role in animal and kidney health due to the important role of the kidneys in treating blood from waste materials and disposing of metabolites.

Materials & Methods: In this research, 80 rats were divided into 4 groups of 20 and 900, 600, 300 (control) mg / kg / day of crossover nanoparticles of 20-30 nm for 21 days with an oral dose of 1-2 ml / 100 g for each bush was given to the rats. On the twentieth day of pregnancy, the mother's rats were euthanasie with ether and chloroform to examine the kidneys and the heart, and fetal organs were referred to the pathology department for examination.

Results & Conclusion: According to the results, it can be concluded that Sio2 can have destructive effects in various doses on the kidney and heart of the rat embryo, which can lead to lesions such as urinary necrosis, hyperemia and bleeding in the glomeruli of the kidneys, and hyperemia and hemorrhage in the heart. Given that in this study the type of complication was similar between the groups, it can be concluded that nanocrystobalite did not produce dose-dependent effects. This experiment was carried out in the animal phase, and in the animal phase, it had destructive effects on the internal organs of the embryos. Therefore, the entry of this nanoparticle into the human body, especially during the critical period of pregnancy, will not be safe.

Session 5
5.3 Safe use of nano objects for medicine applications

A91712WF

CELL VIABILITY OF THE ONCOTHERAD IMMUNOTHERAPY ON URINARY BLADDER CARCINOMA CELLS: NEW THERAPEUTIC PERSPECTIVE FOR BLADDER CANCER

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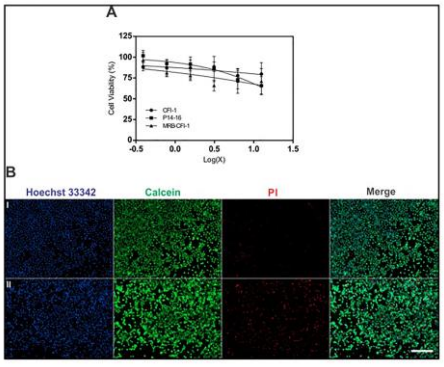
The treatment of non-muscle invasive bladder cancer (NMIBC) remains a challenge in the pharmaceutical field due the recurrence and progression of the disease, as well as the pronounced side effects still associated to the available therapeutic modalities. OncoTherad (MRB-CFI-1) is a nanostructured inorganic phosphate complex (CFI-1) associated to glycosidic protein (P14-16), which exhibits immunomodulatory and antitumor properties, developed by our research group1. Thus, this study describes cell viability of the OncoTherad (MRB-CFI-1) and its components (CFI-1 and P14-16) on urinary bladder grade II carcinoma cells (5637 cell line), after 24 hours of incubation. The cell viability of OncoTherad (MRB-CFI-1)and its components, CFI-1 and protein P14-16, was 76.01% ± 12.39, 68.63% ± 9.47 and 75.71% ± 11.52, respectively, using the maximum concentration of 12.5 mg, as demonstrated in the MTT reduction assay (Figure 1A). Also, the impact of OncoTherad (MRB-CFI-1)treatment on cell membrane integrity was verified, where calcein negative cells were observed, indicating loss of cell viability, and propidium iodide (PI) positive cells, indicating cell death (Figure 1B). The results with 12.5 mg of the OncoTherad (MRB-CFI-1) showed 75.25% ± 6.19 calcein positive and 25.50% ± 2.52 positive PI for cell death. Therefore, all techniques reported comparable dose–response relationship and the OncoTherad (MRB-CFI-1) immunotherapy showed low toxicity, as expected from immunomodulatory drugs. Taken together, the data obtained demonstrated that OncoTherad (MRB-CFI-1) immunotherapy could be considered a safe and effective therapeutic option for patients with bladder cancer.

[1] Fávaro, W.J., Durán N. Brazilian Patent PIBR 10 2017 012768 0 (2017).



Session 5
5.3 Safe use of nano objects for medicine applications

A91715AW

PROFILING OF CHANGES IN GENES RELATED TO TOXICITY IN CACO-2 CELLS IN RESPONSE TO EXPOSURE TO CITRATE GOLD NANOPARTICLES

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Some studies have suggested that citrate gold nanoparticles (AuNPs) are not toxic and are therefore safe for applications in nanomedicine. Many of these in vitro studies base these findings on the fact that the viability of the cells is not affected by treatment with AuNPs. In a previous study (Sibuyi et al. 2017) we demonstrated the application of peptide functionalised citrate AuNPs for the selective induction of apoptosis in CaCo-2 cells. In our study, CaCo-2 cells also displayed a high tolerance to citrate AuNPs that were not functionalised with the therapeutic peptides. However, very little is known about how the uptake of citrate AuNPs may affect gene expression patterns within cells. Adverse effects of citrate AuNPs on cells may hamper the use of AuNP in nanomedicine. Consequently, this study aimed to investigate the effects of citrate AuNPs on gene expression in CaCo-2 cells. Monodisperse spherical citrate AuNPs (14nm size) was synthesised. The uptake in CaCo-2 cells was monitored using ICP-OES, and the viability of the cells was assessed using the WST-1 assay. CaCo-2 cells were treated for 24hrs with 12.5nM of citrate AuNPs, and the expression levels of a panel of 84 genes that are related to stress and toxicity were evaluated using the RT2 Profiler PCR array. Gene expression was quantified using the LightCycler 480 Instrument. Although the WST-1 assay shows that citrate AuNPs are not toxic to the CaCo-2 cells, gene expression profiling revealed that internalisation of gold nanoparticles does affect the expression of several genes.

Reference

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Session 5
5.3 Safe use of nano objects for medicine applications

A91825MD

NANOPARTICLE-NEURON INTERACTIONS: MOLECULAR BASIS OF NEURONAL ACTIVITY AND CALCIUM HOMEOSTASIS MODULATION

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Engineered silica nanoparticles (NPs) have attracted increasing interest in several applications, particularly in the field of nanomedicine, thanks to the high biocompatibility of this material. The understanding of the mechanisms elicited by their interaction with the biological target is a prerequisite for their optimal and controlled use, especially when dealing with cells that are particularly vulnerable to environmental stimuli, like neurons. We have combined different electrophysiological approaches with calcium imaging, in order to analyze the impact of SiO2 NPs (50 ± 3 nm in diameter) on electrical activity in GT1-7 neuroendocrine cells. This provides a detailed analysis of the impact of a nanoparticle on neuronal excitability. We found that nontoxic dose of NPs (20 μg mL−1) induces a cationic inward current that depolarizes the membrane potential, with a modulation of the firing of action potentials. Recordings of electrical activity with multielectrode arrays provide further evidence that the NPs evoke a temporary increase in firing frequency, without affecting the functional behavior on a time scale of hours. Ca2+ imaging data on cell populations and electrophysiological recordings suggest that TRPV4, Cx and Panx-like channels are the major components of the inward currents elicited by SiO2 NPs. In particular, we recorded currents not only in whole-cell configuration, but also in outside out membrane patches. That allows to expose the extracellular side of the excised membrane patch to NPs. Hence, a direct membrane-delimited pathway couples SiO2 NPs to channel activation. Furthermore, pre-incubation with the antioxidant N-acetyl-L-cysteine (NAC) strongly reduces [Ca2+] increase and the membrane lipid peroxidation that we observed after 30 min of NPs incubation. Our findings suggest that SiO2 NPs directly activate a complex set of calcium permeable channels, possibly by catalyzing free radicals production. In conclusion, our results set the basis for understanding the dose-dependent SiO2 NP neurotoxiciy that we previously observed in our neuronal cell model at higher doses. This provides useful insights for predicting and counteracting adverse reactions of nanomaterial for medicine.

Session 5
5.3 Safe use of nano objects for medicine applications

A91556KA

NANO-PARTICLE EXPOSURE MEASUREMENT DURING COMMUTE

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Nano-size particles are the most dominant in numbers in the atmosphere. However, the nano-particle control in terms of individual efforts is very limited. Especially, during the commuting, people can easily be exposed to the nano-particles that are generated by internal combustion engines, new particle formation process, and other sources.

To understand the nano-particle exposure during commute, we developed a compact back-pack type particle measurement system [Fig. 1]. The system consists of Scanning mobility Particle Sizer (Hy-SMPS), Hy-OPC, GPS, Temperature, and Humidity sensors. And the system measurement results can be controlled and monitored using a mobile phone in real time. Hy-SMPS with water based Condensation Particle Counter (CPC) is house made and the operating range is from 8 – 250 nm. Since Hy-SMPS is operating with water based CPC it is non-noxious compare to the conventional n-Butanol based CPC. The scanning time of Hy-SMPS is 45 second. Hy-OPC is also house-made and it has PM1, PM2.5, and PM10 measurement capability. The back-pack particle measurement system can be operated about 5 hours. The whole system weight is about 6 kg with 1.6 kg battery.

The nano-particle exposure measurement results will be presented at the conference in detail.

Session 7
7. Urban particles and emerging pollutants

A92285BH

INDOOR AND OUTDOOR PM2.5 IN AN URBAN APARTMENT WITH AIR CLEANING AND VENTILATION IN SEOUL

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We are prone to be exposed to indoor fine particles than outdoor ones because we stay indoors during about 80-90% of a day. Exposure to indoor particles can be reduced by operations of ventilation systems or indoor air cleaners. Indoor and outdoor PM2.5 concentrations were monitored in an apartment in Seoul with an operation of an air cleaner and a range hood during and after cookings. Power consumptions of air cleaner and range hood were monitored to determine which operation modes of the systems have been applied. Without any operations of air cleaners or ventilation systems, indoor to outdoor ratio (I/O) of PM2.5 was about 0.7 and the trend of indoor PM2.5 is almost consistent with that of outdoor PM2.5. Indoor PM2.5 was mostly dominated by outdoor sources except for cooking. I/O ratio could be controlled to 0.1-0.14 by operation of air cleaners continuously and a range hood with window opening during and after cooking for 30-40 minutes. The averaged power consumption of two air cleaners were 10.8 and 17.0 W, which are enough to make indoor PM2.5 concentrations be lower than the WHO annual guideline of 10 $\mu g/m^3$ in residential homes except for cooking time. Clean air delivery rates (CADRs) of the air cleaners were 7.9 and 8.1 m^3/min in real environments, respectively, which are about 0.80-0.83 of those in chamber tests. The use of range hood with window opening after cooking could have an effect on a rapid PM2.5 decrease, which corresponds to CADR ~ 8.9 m^3/min. The performance of the range hood was similar or a little gigher those of air cleaners.

Therefore, air cleaners were effective to remove indoor PM2.5 of outdoor sources as usual and range hoods (with window opening) were more effective to remove a high concentration of PM2.5 during cooking.

Session 7
7. Urban particles and emerging pollutants