



ENPRA Newsletter – Issue 1

Welcome to the first newsletter from the ENPRA project

Launched in May 2009, ENPRA (Engineered NanoParticle Risk Assessment) is a major new European Framework 7 project to develop and implement a novel integrated approach for engineered nanoparticle (ENP) risk assessment.

With an estimated economic impact of \$292 billion by 2010 across industrial, consumer and medical products, nanotechnology is already one of the key industries within Europe and worldwide. Key to its long term growth and sustainability is establishing end-user confidence that the technologies developed are safe. ENPRA aims to support long term growth and sustainability of nanotechnologies by expanding the classic exposure-dose-response paradigm of risk assessment, to develop an effective approach for the assessment and management of potential health risks from exposure to engineered nanoparticles.

Worth €3.7 million, the 3 ½ year project is led by the Institute of Occupational Medicine (IOM) in Edinburgh under the co-ordination of Dr Lang Tran, IOM's Director of Computational Toxicology. It harnesses the knowledge and capabilities of 15 European and 6 US partners including three US Federal Agencies: EPA, NIOSH and NIH-NIEHS, and utilises the latest advances within *in vitro*, *in vivo* and *in silico* approaches to nanotechnology environment, health & safety (EHS) research.

A few words from the coordinator

The aim of ENPRA is to develop an approach for the Risk Assessment of Engineered Nanoparticles (ENP). This approach uses *in vitro*, *in vivo* and *in silico* models to assess the hazard of ENP and then combines the results with an assessment of workplace and consumer exposure of these materials for a rigorous final assessment of the potential health risk.

We are currently (i) distributing ENP samples to all our partners for use in *in vitro* and *in vivo* experiments and (ii) harmonising the protocols for ENP dispersion. The toxicology and characterisation WP are expected to develop fully from early 2010.

Lang Tran, Director of Computational Toxicology, Institute of Occupational Medicine

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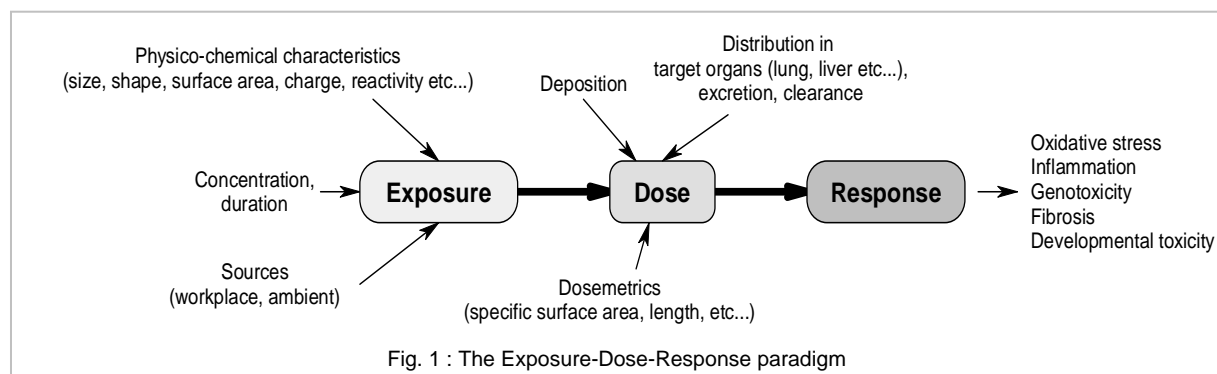
An introduction to ENPRA

Aims

Harnessing the latest advances in toxicology for nanotechnology EH&S issues, the fundamentally novel rationale of ENPRA goes beyond traditional toxicity assessment of ENP and seeks to:

- identify the critical ENP physico-chemical characteristics responsible for the observed toxicity;
- investigate the cellular and molecular mechanisms underlying the observed association;
- develop systems, verifiable with in vivo experiments, which could be used as potential high throughput alternative toxicity tests;
- use a Structure-Activity method to facilitate such identification and use this to predict the hazard of new materials;
- extrapolate the results from in vitro to in vivo and to other relevant occupational or consumer situations;
- incorporate all possible data as weight-of-evidence for a risk assessment of ENP.

ENPRA will develop and implement a novel, integrated approach for ENP Risk Assessment. This approach is based on the Exposure-Dose-Response Paradigm for ENP (Figure 1). This paradigm states that exposure to ENP of different physico-chemical characteristics via inhalation, ingestion or dermal. Our exposure is likely to lead to their distribution, beyond the portal-of-entry organ to other body systems. The cumulative dose in a target organ will eventually lead to an adverse response in a dose-response manner approach will adapt the traditional Risk Assessment approach to ENP and will cover: Hazard Identification; Dose-Response Assessment; Exposure Assessment and Risk Assessment, Management.



Objectives

The specific objectives of ENPRA are classified into five main areas:

(i) Hazard Identification: Characterize a panel of commercially available ENP carefully chosen to address the relevant hazards, properties and potential mechanisms;

(ii) Dose-response Assessment: Assess the hazards of these ENP by means of in vitro toxicology tests based on:

- five body systems - pulmonary; hepatic; renal; cardio-vascular; and developmental systems;
- for five endpoints - oxidative stress; inflammation and immune-responses; genotoxicity; fibrogenicity; and developmental toxicity.

(iii) Verify the in vitro findings with validation tests



- (iv) **Exposure and Risk Assessment** - Use data from this project and other sources to:
 - model exposure and the exposure-dose response relationships by means of mathematical modelling such as PBPK and QSAR-like methods, and extend these deterministic models into probabilistic models
 - conduct the risk assessment with uncertainty analysis;
- (v) **Risk Management:** Develop and implement a strategy for dissemination to maximize the anticipated high impact of our findings.

www.enpra.eu goes live!

The ENPRA website is now accessible at www.enpra.eu; it presents a general overview of the project and the up to date reporting on its activity. With news & events listings, and a regular newsletter, the website will keep you informed of the latest progress of ENPRA and connected to related projects and other useful nanotechnology sites.

Interested parties may register at <http://www.enpra.eu/Registration.aspx> to receive ENPRA newsletters, and gain access to all of the public areas of the website, together with some extended areas that will contain project news and reports, as they become available.

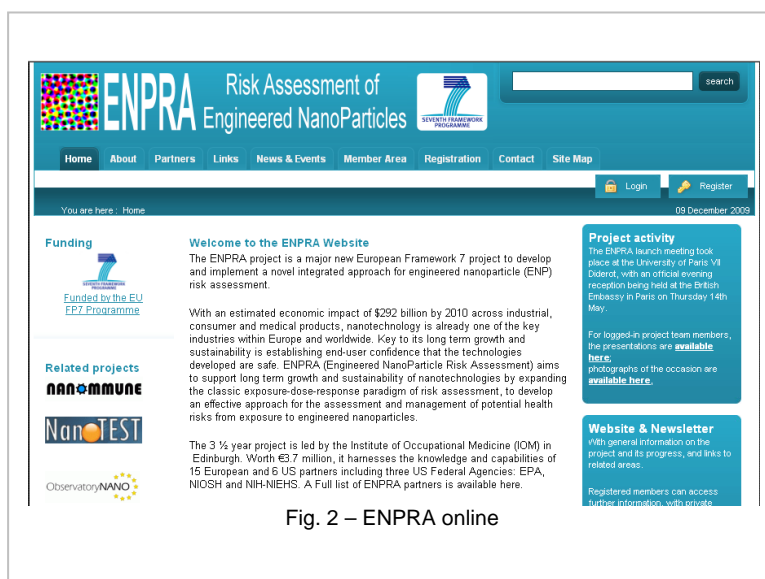


Fig. 2 – ENPRA online

First ENPRA Expert Panel Meeting: harnessing collective expertise to highlight key progress in Nanosafety

On November 26th, partners of the ENPRA project attended the **1st ENPRA Expert Panel Meeting** in Paris. A bi-annual event organized by the Observatory for Micro & Nanotechnologies (OMNT-CEA/CNRS, FR), the meeting gathered together over **20 key experts in nanotechnology environment, health and safety research** from the UK, Italy, Germany, Belgium and the Netherlands, as well as several French experts from OMNT.

With the aim of undertaking a **scientific watch on Nanosafety issues**, this meeting offered participants a unique opportunity to comment and discuss with their peers recent key developments in their fields of expertise. From toxicology to legal aspects, a wide range of areas potentially impacted by nanoparticle safety issues were addressed during the day's proceedings.

The day began with an invited talk from Mrs. Maila Puolamaa of the European Commission's REACH Unit, DG Enterprise. Her presentation to the panel outlined the REACH regulations, detailing objectives, how it is being put into practice, key-steps and the registration deadlines, and providing a particular focus on how the EC are approaching management of nanoparticulate substances which fall within its remit.



During the next part of the day, the gathered experts presented and discussed their selection of recent and noteworthy publications in the field of Nanosafety. Among these, the following topics were discussed in detail:

- occupational risks associated with nanoparticle exposure
- *in vitro* and *in vivo* evidence of nanoparticle-induced DNA damage
- the role and relevance of experimental conditions for nanoparticle risk assessment.

A detailed summary of those topics reviewed and the comments resulting from their discussion will be compiled in the 1st Expert Panel Meeting summary report (expected release February 2010). Short extracts of this document will be available online on the ENPRA website.

The 2nd edition of the Expert Panel meetings will be held in **Ispra (Italy) on April 13th**, in conjunction with the ENPRA Stakeholders' Workshop Information. Full details of the meeting will be posted on the ENPRA website in due course.

ENPRA research progress

A co-ordinated plan for *in vivo* validation tests – report from ENPRA WP5

One of ENPRA's key objectives is to assess the hazards of engineered nanoparticles (ENP) by means of *in vitro* toxicology tests and subsequently to validate these findings *in vivo*. This task falls to ENPRA **Workpackage 5 (WP5)**, which is led by **Dr. Ilse Gosens**, toxicological researcher and project manager at the **National Institute for Public Health and Environment (RIVM, NL)**.

WP5 has 2 main objectives:

- to perform a "kinetics study" using commercialized ENP to assess the time course of the ENP distribution across the key target organs and,
- to establish "dose-response relationships" for a panel of ENP and selected bioassays.

Already, preliminary tests have been undertaken for the "**kinetics study**". Partners from the Helmholtz Zentrum München German Research Center for Environmental Health (HMGU, GE) and Joint Research Center (JRC, IT), are currently collaborating to set up a procedure for radiolabelling commercialized titanium dioxide (TiO₂) nanoparticles, which will subsequently be used for inhalation and instillation studies in mice. Assessment of the biological fate of ENP following inhalation or instillation exposure may then be undertaken via time course biodistributions of the labelled-TiO₂.

One important issue related to the validation of *in vitro* findings within a European multicenter-based project such as ENPRA, is the potential variability on experimental procedures from one team to another. To address this issue, and ensure **standardisation of *in vivo* experimental procedures** used by WP5 members, a series of training days for ENPRA partners which focus on harmonising methodology in experimental procedures were scheduled.

The first of these, which focussed on **harmonising methodology used for *in vivo* instillation in mice**, was held at HMGU in Munich on **November 16th, 2009**. Organized by **Drs Manuela Behnke and Nicklas Raun Jacobsen (HMGU)**, the training session was attended by partners from several institutions including Université Catholique de Louvain and Katholieke Universiteit Leuven (BE), University of Edinburgh (UK), RIVM (NL) and the National Research Centre for the Working Environment (NRCWE; DK).



The morning session was dedicated to demonstration of the intra-tracheal instillation procedure by Drs Behnke and Raun Jacobsen, and was followed by a practical training session for all participants. The practical element was followed by a general discussion on the technique which allowed participants to share their experiences and views on the experimental procedure outlined. At the end of the day's proceedings, the group had reached a consensus on all technical aspects of the procedure and produced a relevant and efficient methodology for testing *in vivo* effects of airway exposure to ENP. The completed plan is now being put into practice, and the first dose-response studies after lung exposure to ENP are expected to be conducted over the coming months.

Up-coming events

Second NanolImpactNet conference

The 2nd NanolImpactNet conference "For a healthy environment in a future with nanotechnology" is to be held at the CHUV in **Lausanne (CH) from March 9th to 12th 2010**.

The first day will consist in a training school for junior scientists on "handling protocols and standardisation of nanomaterials in toxicological research". It will be followed by a 3-day conference on the following themes:

- Session 1: Interaction between nanomaterials and biological barriers
- Session 2: Nanomaterial behaviour with regard to environmental and physical barriers
- Session 3: Quality control in nanomaterial research
- Session 4: Nanotechnology as a tool for impact assessment
- Session 5: From research to policy

An additional special session (Special stakeholder session on food) related to the emerging concern about the potential health effects of nanoparticles and nanomaterials in the food industry will be organised. Stakeholders will be invited to participate to the debates.

For registration, preliminary program and further details please click [here](#).

ENPRA Stakeholders' Information Workshop

The first ENPRA Stakeholders' Information Workshop is to be held on **14th – 15th April 2010 in the premises of the Joint Research Centre (JCR) in Ispra, Italy**. This meeting will gather ENPRA members, ENPRA US partners (from Rochester & Duke universities, EPA, NIOSH...), collaborators from other FP7 projects, as well as venture capitalists, SME, nanotechnology industry, representatives of EU national authorities, the European Commission and OECD representatives. Aimed at informing the stakeholder's of the latest scientific progress in the field of nanoparticles risk assessment both within the ENPRA project and other related FP7 projects, this event will be the opportunity to bring closer the main protagonists of the nanotechnology community. Organized in plenary and break-out sessions, the meeting will present an overview of various aspects of hazard, exposure and risk assessment of engineered nanoparticles.

This one and a half day meeting will be preceded, on April 13th, by the 2nd ENPRA Expert Panel Meeting and followed by several ENPRA restricted sessions, on April 15-16th.

A detailed programme and registration procedures will be available soon.



ENPRA annual Project Meeting

The first annual ENPRA Project Meeting is to be held **on May 30th and June 1st 2010, in Edinburgh Scotland**. The meeting, which is closed to the public, has been timed to fall in conjunction with the Nanotoxicology 2010, which is being held from the 2nd – 4th June at Edinburgh Napier University's Craiglockhart Campus. Further details of the ENPRA meeting will be released to consortium members in due course, and a summary report of the meeting will be made available in summer 2010. In the meantime, ENPRA's project management team would like to encourage all consortium members to register and submit abstracts for presentation at this exciting conference (details below).

Nanotoxicology 2010

The 3rd of the Nanotoxicology conference series, Nanotoxicology 2010 is aimed at professionals and students in nanotechnology environment, health and safety (EHS) research. Taking place from **June 2nd - 4th 2010 in Edinburgh Scotland**, Nanotoxicology 2010 promises to form a key date in the calendar for 2010.

The conference is now open for abstract submissions (oral and poster presentations), and early bird registration. Nanotoxicology 2010 **Early Bird registration** provides a preferential rate for delegates, and will remain available **until the 30th January 2010** after which full registration costs will be implemented.

The final **deadline for registration is the 1st May 2010**. The final **deadline for Abstract Submissions is March 19th 2010**. A limited number of Bursaries are available to student applicants to the conference from the Colt Foundation. Follow these links to learn more about the registration or abstract submission process:

[Registration fees](#)

[Abstract Submissions](#)



Program

The Scientific Programme for Nanotoxicology 2010 is divided into sections which allow focus on specific types of nanomaterials. Each section will include talks spanning disciplines including exposure assessment, characterisation, human toxicology, ecotoxicology and risk assessment. Such a format will promote interaction between different disciplines and would allow issues specific to certain materials to be addressed. Click here to learn more about the conference's themes and key topics

Speakers

Nanotoxicology 2010 will bring together multidisciplinary expertise from across the field, and has already confirmed keynote speakers from institutions working at the cutting-edge of the field, including:

Günter Oberdörster - University of Rochester
Ken Donaldson – University of Edinburgh
Kevin Dreher – US EPA
Stig Irving Olsen – Technical University of Denmark
Martin Philbert – University of Michigan
Andrew Maynard – Project on Emerging Nanotechnologies

Additional keynote and invited speakers are being added as they are confirmed – to see the latest list of speakers please [click here](#).