LifeNanoExplore

Integrated Approach for Exposure and Health Effects Monitoring of ENMs in workplaces and urban areas

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Nanotech France 2021

NanoExplore is part funded by the European Commission Life with grant agreement LIFE17 ENV/GR/000285

1. Introduction

- NanoExplore focuses on the possible effects derived from exposure to ENMs, a new type of chemicals of concern,
- ENM properties differ significantly from those of bulk chemicals of the same composition due to their much larger specific surface area and surface activity or much larger deposition rate in the respiratory system,
- ENMs may lead to unanticipated effects in human health, like pro-inflammatory effects or development of fibrosis and /or cancer, as well as to significantly alter ecosystems, causing adverse effects on the metabolism of a living being

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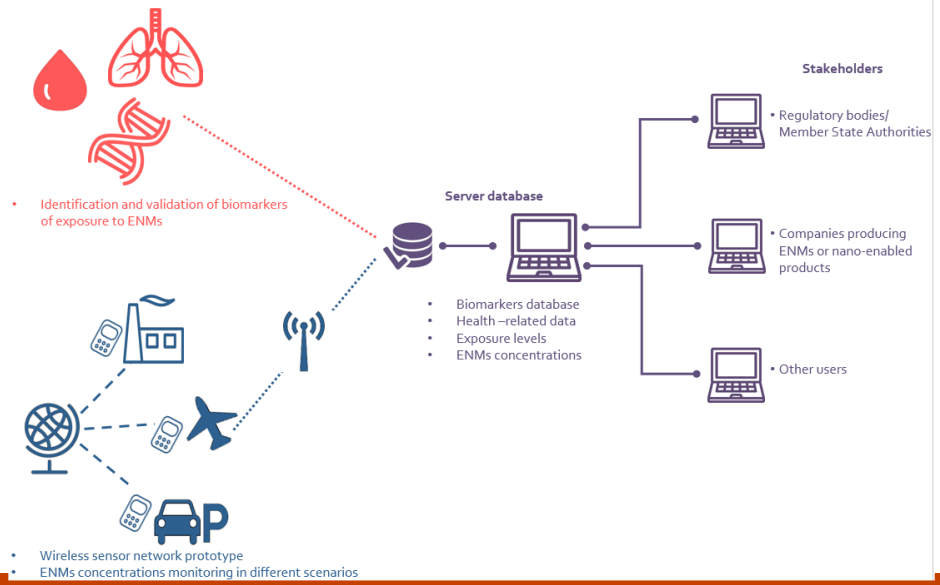
2. Aim

- The aim of the present work is to develop and demonstrate the feasibility of **an integrated approach** to conduct **biomonitoring studies**, characterize **exposure levels** and **elucidate possible health effects** deriving from exposure to engineered nanomaterials (ENM) in indoor workplaces and urban areas.



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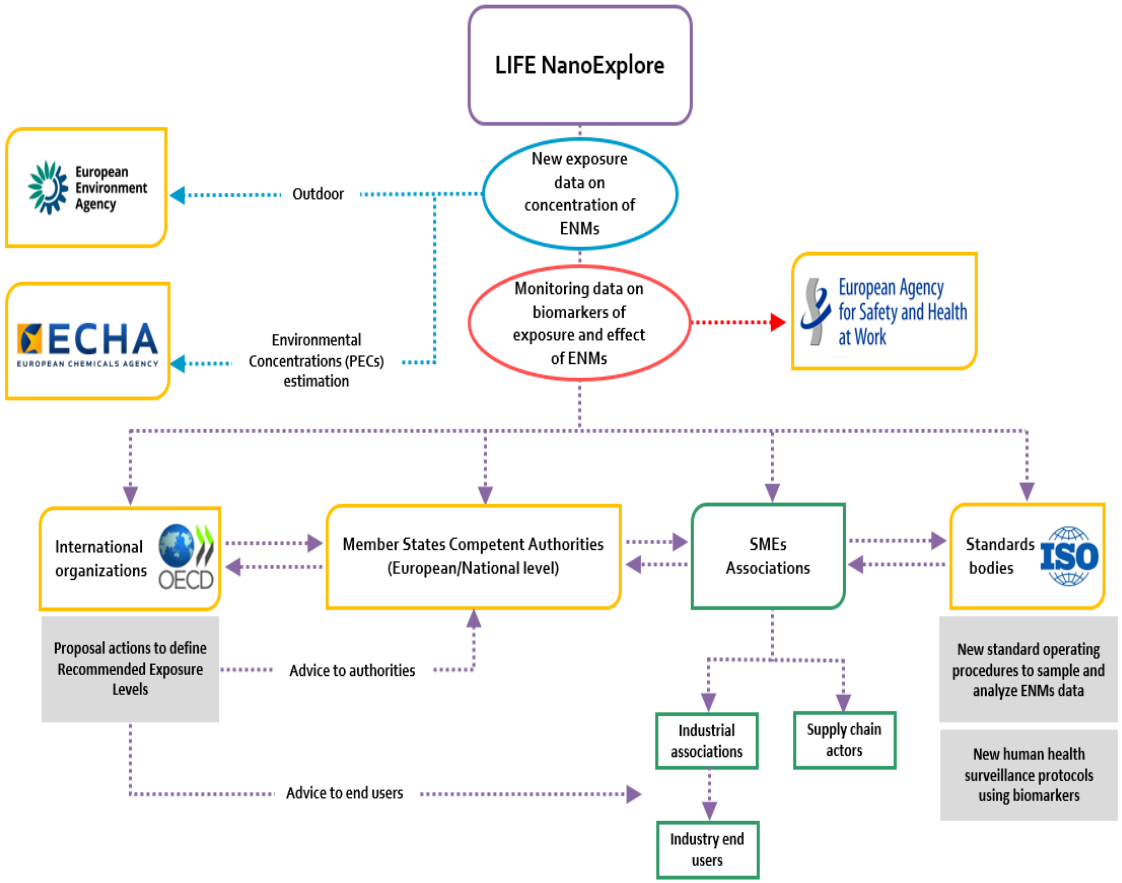
3. Concept and Expected Impact



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4. Objectives

- To develop a **wireless sensor network** of unattended, low-cost, portable and battery-powered devices that cooperatively monitor the concentration of ENMs in indoor workplaces and urban areas.
- To develop a **web-based software application** aimed at the acquisition, management and processing of data on the concentration of ENMs monitored by the wireless sensor network in industrial settings and /or relevant urban areas.
- To define a panel of **biomarkers** of nanomaterial exposure and effects via inhalation and dermal uptake
- To carry out a **risk analysis of possible effects on human health** deriving from exposure to ENMs in selected case studies.
- To refine currently available **recommended exposure levels (RELs)** for metal oxides and low soluble carbon based materials.
- To **validate and demonstrate the feasibility of the NanoExplore approach** for the risk assessment of ENMs in Europe by implementing a pilot study

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5. Development of the measuring device

Main characteristics of the monitoring station design and functionality:

a. Compact and portable with a weatherproof box
b. Flexible design, subsystems included
c. Unattended and remote operation
d. Battery powered for indoor use and solar cell for outdoor use
e. Data storage
f. Ability to provide an appropriate flowrate of the sample to be analysed with TEM grids
g. Tailored designed software to control the instrument settings
h. Low-cost.

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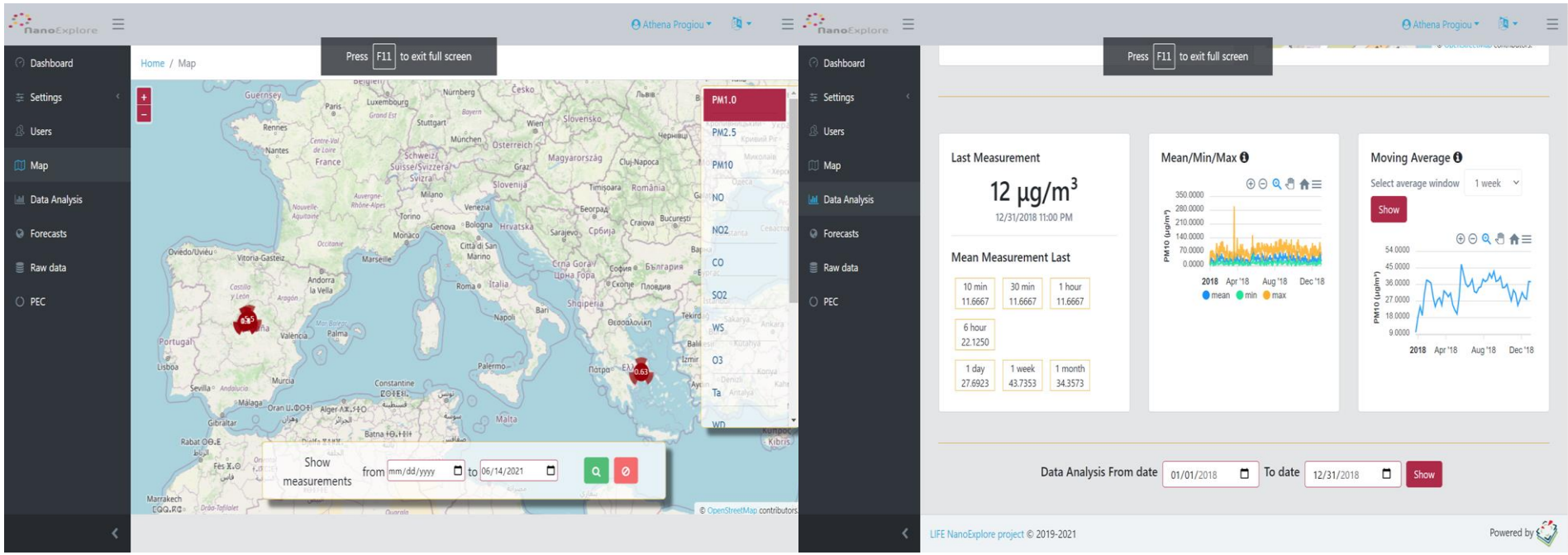
6. Development of the web platform

Acquisition, management and processing of ENM concentration data.



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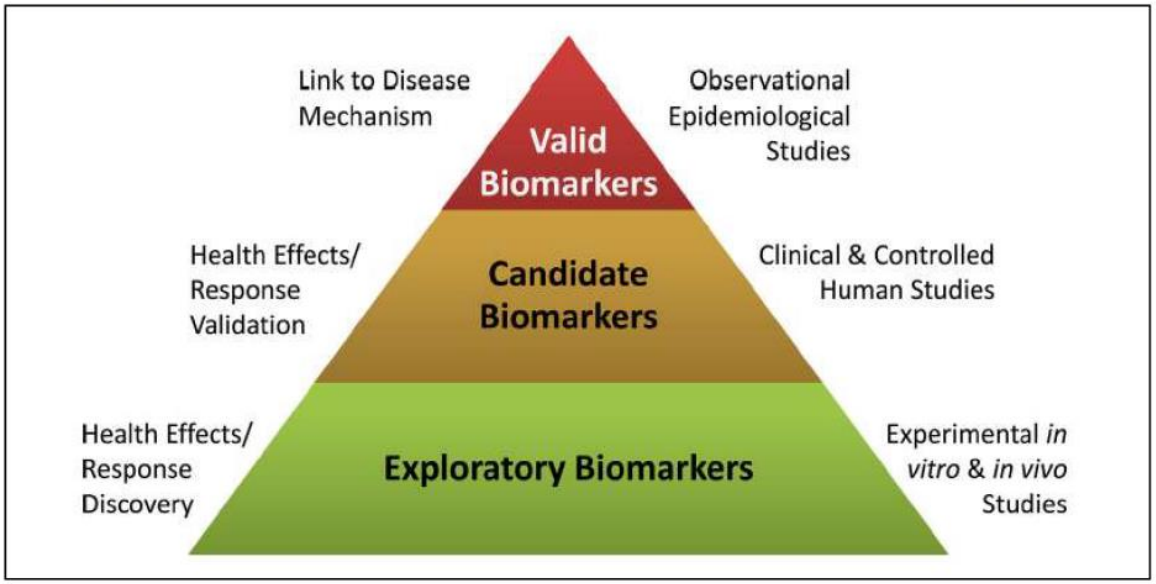
7. Validation of candidate biomarkers [a]

Layout of biomarkers research as condition of the responsible development of nanotechnologies and safety of workers exposed to ENM



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7. Validation of candidate biomarkers [b]

This action includes the following:

- assessment of existing studies and the most critical issues in designing epidemiological studies in nanomaterial workers;
- integration and development of a harmonized protocol of the collaborative study of human biomarkers with respect to nanoparticle exposure;
- determination of reference values for biomarkers selected.

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7. Validation of candidate biomarkers [c]

Candidate biomarkers were specified

- from a pre-selection of BMs applied in air pollution studies related to combustion-derived UFPs,
- on the basis of relevant health endpoints that have been tentatively ascribed to ENMs including cardiovascular, pulmonary, and inflammatory effects
  - ✓ Inflammatory BMs (e.g. Interleukin 6 - IL-6, Glutathione Peroxidase activity - GPX) and peroxydated products in blood (e.g. eicosanoids, such as 8-isoprostane and LTB4);
  - ✓ Oxidative Stress Biomarkers, including oxidation of nucleic acids and of nitrosative stress in blood and urine;
  - ✓ Pro-inflammatory biomarkers in urine (e.g. Leukotriene); pulmonary effect biomarkers, including the analysis of CC16 (Clara cell protein) or FENO (Fractional exhaled nitric oxide) in exhaled breath condensate (EBC) and the determination of the Oxidative Potential in Exhaled Air (OPEA), a non-invasive metric related to lung inflammation.

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7. Validation of candidate biomarkers [d]

Factors affecting the validity of biomarkers:

- **Significance:** exposure, effect, individual susceptibility
- **Specificity:** in relation to the pollutant or pollutant family
- **Sensitivity**: capacity to distinguish populations with different exposure levels, susceptibilities or degrees of effect
- **Knowledge of its background** in the general population
- **Existence of dose-response curves** between exposure level and marker concentration
- Estimation of the **inter- and intra-individual variability**
- Knowledge of **confounding factors** that can affect marker

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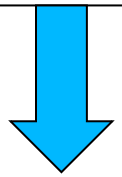
7. Validation of candidate biomarkers [e]

Development of an appropriate epidemiological protocol adapted to workplaces in which nanomaterials are produced/used/disposed.

- Determine the most suitable study design for a pilot collaborative biomarker study
- Calculate the size of study population, that would maximise the statistical power of the study under realistic conditions
- Elaborate the most efficient and feasible strategy of companies recruitment and individuals by considering: a) the number of potentially exposed individuals in different settings/companies, b) the propensity and barriers to participate with respect to the national/regional specificities



Harmonised study protocol for the first international collaborative study of individuals exposed to ENMs

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7. Validation of candidate biomarkers [f]

Study 1: Determination of reference/baseline values for biomarkers measured in urine and exhaled breath condensate (EBC)

- Systematic review : studies were selected on healthy adult subjects and professionally exposed to potentially harmful agents (urine and EBC)
- Descriptive statistics of biomarkers determined in the universal control group and exposed professionals

Study 2. Determination of reference/baseline values for Oxidative Potential measured in Exhaled Air

- OPEA measurements in a large representative sample of healthy individuals, to characterize its inter- and intra-subject variability and determine the baseline values by sex, age and smoking status.
- Reference values of oxidative stress biomarkers in exhaled air, EBC and urine in healthy non exposed adult population are stablished.

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8. Implementation of field campaigns [a]

Pilot biomonitoring study to assess the **feasibility of the hamonised protocol** of the collaborative study and **refine the NanoExplore integrated approach**

- in a well-characterized limited number of **unexposed and exposed workers**,
- including
  - 30 workers from production facilities,
  - 20 workers from office positions,
  - 30 individuals working in civil infrastructures and
  - 20 control participants.

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8. Implementation of field campaigns [b]

Recruitment of the study participants

- Standardized questionnaires
- Permission from the corresponding national Ethical committees.

Eligibility criteria will be verified:

- Written consent for participation in the study, inclusion into cohort and follow-up including sampling of EBC, exhaled air and urine.
- Known occupational exposure to ENMs selected.
- Suspected exposure to carbonaceous agglomerates (soot and/ or ash) coming mainly from the combustion of engine fuel and lube oil.
- Availability of medical reports.
- Availability of information on associated occupational exposure
- Availability of information on potential confounding factors.
- Availability of information on exposure duration and frequency.
- Isolation from production areas in office positions.

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8. Implementation of field campaigns [c]

Exposure assessment: characterization of the exposure in the workstations where exposed workers perform the task of concern.

The main parameters to be reported will be:

- Number of Particles/cm^3
- Mass concentration in mg/cm^3
- Surface Area in $\mu g/ cm^3$
- Particle diameter in nm
- Particle Size Distribution in nm
- Mass of NMs / Filter mass in ng/mg of filter
- Relevant physicochemical information: surface chemistry, agglomeration /aggregation state

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8. Implementation of field campaigns [d]

Biomonitoring studies: Measurement of biomarkers and of their relevance with respect to nanoparticles

- Sampling and analysis of the effect biomarkers in biological fluids, including exhaled air, exhaled breath condensate (EBC), urine, buccal epithelium, in order to detect potential early effects on the pulmonary and cardiovascular system.
- Samples will be analysed in laboratory. In parallel, the characterization of the health status of workers, creation and completing of a log-book of exposure activities will be performed.
- The same biomarkers will be measured twice, considering 6 months between campaign in order to identify any significant difference in any of the biomarkers.
- Data validation and statistical analysis of the relationship between nanoparticles exposure and selected biomarkers

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9. Results

- Integrated system for the assessment, monitoring and surveillance of the exposure and effects deriving from exposure to ENMs in indoor workplaces and urban areas, by setting up a new health impact assessment model based on the combination of
  - a wireless sensor,
  - proven biomarkers
  - a harmonised protocol to conduct the biomonitoring studies and
  - a tailored designed software for data acquisition and management
- A well-defined list of recommended exposure levels (REL) for metal and metal oxide based ENMs and low solubility carbon based materials.
- A complete guidance on the use of human biomonitoring and exposure data in indoor workplaces and the environment for REACH regulation implementation and epidemiological purposes.
- Recommendations for measures and policies to protect workers and population from the health effects of airborne nanopollutants.
- Human biomonitoring and wireless sensor networks might become a particularly important tool for decision-makers.

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Thank you very much for your attention!

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